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Devices, systems and methods for diagnosing and treating sinusitus and other disorders of the ears, nose and/or throat

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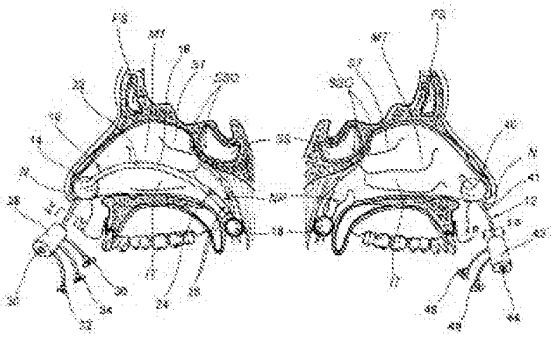
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Sinusitis, enlarged nasal turbinates, tumors, infections, hearing disorders, allergic conditions, facial fractures and other disorders of the ear, nose and throat are diagnosed and/or treated using minimally invasive approaches and, in many cases, flexible catheters as opposed to instruments having rigid shafts. Various diagnostic procedures and devices are used to perform imaging studies, mucus flow studies, air/gas flow studies, anatomic dimension studies, endoscopic studies and transillumination studies. Access and occluder devices may be used to establish fluid tight seals in the anterior or posterior nasal cavities/nasopharynx and to facilitate insertion of working devices (e.g., scopes, guidewires, catheters, tissue cutting or remodeling devices, electrosurgical devices, energy emitting devices, devices for injecting diagnostic or therapeutic agents, devices for implanting devices such as stents, substance eluting devices, substance delivery implants, etc.

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FIELD OF THE INVENTION

[0001] The present invention relates generally to medical devices and methods and more particularly to minimally invasive, catheter based devices, systems and methods for treating sinusitis and other ear, nose & throat disorders.

BACKGROUND

[0002] The human nose is responsible for warming, humidifying and filtering inspired air and for conserving heat and moisture from expired air. The nose is also an important cosmetic feature of the face. The nose is formed mainly of cartilage, bone, mucous membranes and skin. The right and left nostrils lead into right and left nasal cavities on either side of the intranasal septum. The right and left nasal cavities extend back to the soft palate, where they merge to form the posterior choanae. The posterior choanae opens into the nasopharynx. The roof of the nose is formed, in part, by a bone known as the cribriform plate. The cribriform plate contains numerous tiny perforations through which sensory nerve fibers extend to the olfactory bulbs. The sensation of smell occurs when inhaled odors contact a small area of mucosa in the superior region of the nose, stimulating the nerve fibers that lead to the olfactory bulbs.

[0003] The paranasal sinuses are cavities formed within the bones of the face. The

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paranasal sinuses include frontal sinuses, ethmoid sinuses, sphenoidal sinuses and maxillary sinuses. The paranasal sinuses are lined with mucous-producing epithelial tissue. Normally, mucous produced by the linings of the paranasal sinuses slowly drains out of each sinus through an opening known as an ostium, and into the nasopharnyx. Disorders that interfere with drainage of mucous (e.g., occlusion of the sinus ostia) can result in a reduced ability of the paranasal sinuses to function normally. This results in mucosal congestion within the paranasal sinuses. Such mucosal congestion of the sinuses can cause damage to the epithelium that lines the sinus with subsequent decreased oxygen tension and microbial growth (e.g., a sinus infection).

[0004] The nasal turbinates are three (or sometimes four) bony processes that extend inwardly from the lateral walls of the nose and are covered with mucosal tissue. These turbinates serve to increase the interior surface area of the nose and to impart warmth and moisture to air that is inhaled through the nose. The mucosal tissue that covers the turbinates is capable of becoming engorged with blood and swelling or becoming substantially devoid of blood and shrinking, in response to changes in physiologic or environmental conditions. The curved edge of each turbinate defines a passageway known as a meatus. For example, the inferior meatus is a passageway that passes beneath the inferior turbinate. Ducts, known as the nasolacrimal ducts, drain tears from the eyes into the nose through openings located within the inferior meatus. The middle meatus is a passageway that extends inferior to the middle turbinate. The middle meatus contains the semilunar hiatus, with openings or ostia leading into the maxillary, frontal, and anterior ethmoid sinuses. The superior meatus is located between the superior and medial turbinates. Nasal Polyps:

[0005] Nasal polyps are benign masses that grow from the lining of the nose or paranasal sinuses. Nasal polyps often result from chronic allergic rhinitis or other chronic inflammation of the nasal mucosa. Nasal polyps are also common in children who suffer from cystic fibrosis. In cases where nasal polyps develop to a point where they obstruct normal drainage from the paranasal sinuses, they can cause sinusitis. Sinusitis:

[0006] The term "sinusitis" refers generally to any inflammation or infection of the paranasal sinuses. Sinusitis can be caused by bacteria, viruses, fungi (molds), allergies or combinations thereof. It has been estimated that chronic sinusitis (e.g., lasting more than 3 months or so) results in 18 million to 22 million physician office visits per year in the United States.

[0007] Patients who suffer from sinusitis typically experience at least some of the following symptoms:

headaches or facial pain
nasal congestion or post-nasal drainage
difficulty breathing through one or both nostrils
bad breath
pain in the upper teeth
Proposed Mechanism of Sinus Pain & Diagnosis

[0013] The sinuses consist of a series of cavities connected by passageways, ultimately opening into the nasal cavity. As described previously, these passageways and cavities are formed by bone, but covered in mucosa. If the mucosa of one of these passageways becomes inflamed for any reason, the cavities which drain through that

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passageway can become blocked. This trapping of mucous can be periodic (resulting in episodes of pain) or chronic. Chronically blocked passageways are targets of infection. Ultimately, it is the dimensions of the bony passageways and thickness of the overlying mucosa and its chronicity that dictate the duration and severity of sinus symptoms. Thus, the primary target for sinus therapy is the passageway, with the primary goal to regain drainage. Often CT will not reveal these dimensional issues, especially when the patient is not currently experiencing severe symptoms. Therefore there exists a need to dynamically evaluate the sinus passageways under normal conditions, in response to challenging stimuli. As suggested herein, if it would be possible to assess sinus disease and its dynamic component, one might better target therapy for sinusitis and possibly be able to treat patients in a more focused and minimally invasive manner. Such focus on the passageway and the use of flexible instrumentation suggests an entirely new approach to sinus intervention: one utilizing flexible catheters and guidance tools, with passageway and cavity modifying devices capable of being delivered with minimal damage to the surrounding tissues. Deviated Septum:

[0014] The intranasal septum is a cartilaginous anatomical structure that divides one side of the nose from the other. Normally, the septum is relatively straight. A deviated septum is a condition where the cartilage that forms the septum is abnormally curved or bent. A deviated nasal septum may develop as the nose grows or, in some cases, may result from trauma to the nose. A deviated septum can interfere with proper breathing or may obstruct normal drainage of nasal discharge, especially in patient's whose nasal turbinates are swollen or enlarged due to allergy, overuse of decongestant medications, etc. Such interference with drainage of the sinuses can predispose the patient to sinus infections.

[0015] A deviated nasal septum that interferes with proper function of the nose can be surgically corrected by a procedure known as septoplasty. In a typical septoplasty procedure, an endoscope is inserted into the nose and the surgeon makes an incision inside the nose, lifts up the lining of the septum, and removes and straightens the underlying bone and cartilage that is abnormally deviated. Such surgical septoplasty procedures can effectively straighten a deviated septum but, because the nasal cartilage has some memory, the septum may tend to resume its original deviated shape. Reduction/Removal of Nasal Turbinates

[0016] Various surgical techniques, including endoscopic surgery, have been used for reduction and/or removal of the inferior turbinate in patient's whose inferior turbinate is chronically enlarged such that it is obstructing normal breathing and/or normal drainage from the paranasal sinuses. Typically, chronic enlargement of the inferior turbinates is the result of allergies or chronic inflammation. Enlargement of the inferior turbinate can be especially problematic in patient's who also suffer from a deviated septum that crowds or impinges upon the soft tissue of the turbinate. Thus, a septoplasty to straighten the deviated septum is sometimes performed concurrently with a reduction of the inferior turbinates. Sinus Tumors

[0017] Most polyps are benign, but one form of a nasal polyp, known as an inverting papilloma, can develop into a malignancy. Unlike most benign polyps, which typically occur on both sides of the nose, an inverting papilloma is usually found on just one side. Thus, in cases where a unilateral polyp is observed, it is usually biopsied to determine if it is malignant. If an inverting papilloma is detected before it becomes malignant and is removed completely, it will typically not recur. However, using the

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technology that has heretofore been available, it has sometimes been difficult to determine if the papilloma has been entirely removed unless and until regrowth of the polyp is observed on long term post-surgical follow-up.

[0018] Various benign sinus tumors have also been known to occur, but are relatively rare. The most common form of malignant sinus tumor is squamous cell carcinoma. Even with surgery and radiation treatment, squamous cell carcinoma of the paranasal sinus is associated with a relatively poor prognosis. Other types of malignant tumors that invade the paranasal sinuses include adenocarcinoma and, more rarely, lymphoma and even more rarely, melanoma. Facial Fractures

[0019] The most common cause of fractures of the facial bones is auto accidents, but facial fractures are also frequently caused by sports injuries, industrial accidents, falls, assaults and gunshot wounds. Some facial fractures involve bones that are accessible from inside the nasal cavities or paranasal sinuses. Notably, the nose is the most commonly injured facial structure due to its prominent position on the face. Thus, fractures of the nasal bone (with or without resultant deviated septum) are not uncommon. Other facial fractures such as fractures of the orbital floor and/or the ethmoid or frontal sinuses are also accessible from inside the nose or sinuses. A common type of orbital floor fracture is a "blowout" fracture that typically results from blunt trauma to the eye where the force is transmitted downwardly causing the relatively thin bone that forms the floor of the orbit to fracture downwardly. This can cause the periorbital tissues to herniate into the maxillary sinus and sometimes can also create a "trap door" of bone that extends downwardly into the maxillary sinus. Endoscopic Sinus Surgery and Other Current Procedures

[0020] Functional Endoscopic Sinus Surgery

[0021] The most common corrective surgery for chronic sinusitis is functional endoscopic sinus surgery (FESS). In FESS, an endoscope is inserted into the nose and, under visualization through the endoscope, the surgeon may remove diseased or hypertrophic tissue or bone and may enlarge the ostia of the sinuses to restore normal drainage of the sinuses. FESS procedures can be effective in the treatment of sinusitis and for the removal of tumors, polyps and other aberrant growths from the nose. Other endoscopic intranasal procedures have been used to remove pituitary tumors, to treat Graves disease (i.e., a complication of hyperthyroidism which results in protrusion of the eyes) and surgical repair of rare conditions wherein cerebrospinal fluid leaks into the nose (i.e., cerebrospinal fluid rhinorrhea).

[0022] Surgery to reduce the size of the inferior turbinates can be accomplished with endoscopic visualization (with magnification where desired) and is typically performed with the patient under general anesthesia. An incision is typically made in the mucosa that lines the turbinate to expose the underlying bone. Some quantity of the underlying bone may then be removed. If selective removal of some of the mucosa or soft tissue is also desired, such soft tissue can be debulked or removed through by traditional surgical cutting or by the use of other tissue ablation or debulking apparatus such as microdebriders or lasers. Less frequently, chronically enlarged inferior turbinates have been treated by cryotherapy. It is typically desirable to remove only as much tissue as necessary to restore normal breathing and drainage, as removal of too much tissue from the turbinates can impair the ability of the turbinates to perform their physiological functions of warming and humidifying inspired air and conserving warmth and moisture from expired air. Complications associated with inferior turbinate surgery include

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bleeding, crusting, dryness, and scarring.

[0023] In some patients, the middle turbinate is enlarged due to the presence of an invading air cell (concha bullosa), or the middle turbinate may be malformed (paradoxically bent). Severe ethmoid sinusitis or nasal polyps can also result in enlargement or malformation of the middle turbinates. Since a substantial amount of drainage from the sinuses passes through the middle meatus (i.e., the passage that runs alongside middle turbinate) any enlargement or malformation of the middle turbinate can contribute to sinus problems and require surgical correction. Thus, in some FESS procedures carried out to treat sinusitis, the middle meatus is cleared (e.g., the polyps or hypertorophic tissue are removed) thereby improving sinus drainage. However, the middle turbinate can include some of the olfactory nerve endings that contribute to the patient's sense of smell. For this reason, any reduction of the middle turbinate is typically performed in a very conservative manner with care being taken to preserve as much tissue as possible. In patients who suffer from concha bullosa, this may involve removing the bone on one side of an invading air sac. In the cases where the middle turbinate is malformed, just the offending portion(s) of the turbinate may be removed.

[0024] Extended Endoscopic Frontal Sinus Surgery

[0025] Because of its narrow anatomical configuration, inflammation of the frontal sinuses can be particularly persistent, even after surgery and/or medical therapy has resolved the inflammation in the other paranasal sinuses. In cases of persistent inflammation of the frontal sinuses, a surgery known as a trans-septal frontal sinusotomy, or modified Lothrop procedure, is sometimes performed. In this procedure, the surgeon removes a portion of the nasal septum and the bony partition between the sinuses to form one large common drainage channel for draining the frontal sinuses into the nose. This complicated procedure, as well as some other ear, nose and throat surgical procedures, can carry a risk of penetrating the cranial vault and causing leakage of cerebrospinal fluid (CSF). Also, some sinus surgeries as well as other ear, nose and throat procedures are performed close to the optic nerves, the eyes, and the brain and can cause damage to those structures. To minimize the potential for such untoward complications or damage, image-guided surgery systems have been used to perform some complex head and neck procedures. In image guided surgery, integrated anatomical information is supplied through CT-scan images or other anatomical mapping data taken before the operation. Data from a preoperative CT scan or other anatomical mapping procedure is downloaded into a computer and special sensors known as localizers are attached to the surgical instruments. Thus, using the computer, the surgeon can ascertain, in three dimensions, the precise position of each localizer-equipped surgical instrument at any given point in time. This information, coupled with the visual observations made through the standard endoscope, can help the surgeon to carefully position the surgical instruments to avoid creating CSF leaks and to avoid causing damage to nerves or other critical structures.

[0026] Shortcomings of FESS

[0027] Although FESS continues to be the gold standard therapy for severe sinuses, it has several shortfalls. Often patients complain of the post-operative pain and bleeding associated with the procedure, and a significant subset of patients remain symptomatic even after multiple surgeries. Since FESS is considered an option only for the most severe cases (those showing abnormalities under CT scan), a large population of

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patients exist that can neither tolerate the prescribed medications nor be considered candidates for surgery. Further, because the methodologies to assess sinus disease are primarily static measurements (CT, MRI), patients whose symptoms are episodic are often simply offered drug therapy when in fact underlying mechanical factors may play a significant role. To date, there is no mechanical therapy offered for these patients, and even though they may fail pharmaceutical therapies, no other course of action is indicated. This leaves a large population of patients in need of relief, unwilling or afraid to take steroids, but not sick enough to qualify for surgery.

[0028] One of the reasons why FESS and sinus surgery is so bloody and painful relates to the fact that straight instrumentation with rigid shafts are used. Due to the fact that the sinuses are so close to the brain and other important structures, physicians have developed techniques using straight tools and image guidance to reduce the likelihood of penetrating into unwanted areas. In an effort to target deep areas of the anatomy, this reliance on straight instrumentation has resulted in the need to resect and remove or otherwise manipulate any anatomical structures that may lie in the path of the instruments, regardless of whether those anatomical structures are part of the pathology. With the advances in catheter based technology and imaging developed for the cardiovascular system, there exists a significant opportunity to reduce the morbidity of sinus interventional through the use of flexible instrumentation and guidance.

[0029] If flexible tools could be developed such that sinus intervention may be able to be carried out with even less bleeding and post-operative pain, these procedures may be applicable to a larger group of patients. Further, as described here, flexible instrumentation may allow the application of new diagnostic and therapeutic modalities that have never before been possible.

[0030] Laser or Radiofrequency Turbinate Reduction (Soft Tissue Only)

[0031] In cases where it is not necessary to revise the bone that underlies the turbinate, the surgeon may elect to perform a laser or radiofrequency procedure designed to create a coagulative lesion in (or on) the turbinate, which in turn causes the soft tissue of the turbinate to shrink. Also, in some cases, a plasma generator wand may be used create high energy plasma adjacent to the turbinate to cause a reduction in the size of the turbinate.

[0032] One example of a radio frequency procedure that may be used to shrink enlarged inferior turbinates is radiofrequency volumetric tissue reduction (RFVTR) using the Somnoplasty(R) system (Somnus Medical Technologies, Sunnyvale, Calif.). The Somnoplasty(R) system includes a radio frequency generator attached to a probe. The probe is inserted through the mucosa into the underlying soft tissue of the turbinate, usually under direct visualization. Radiofrequency energy is then delivered to heat the submucosal tissue around the probe, thereby creating a submucosal coagulative lesion while allowing the mucosa to remain in tact. As the coagulative lesion heals, the submucosal tissue shrinks thereby reducing the overall size of the turbinate. Radiofrequency volumetric tissue reduction (RFVTR) can be performed as an office procedure with local anesthesia.

[0033] Many of the above-described procedures and techniques may be adaptable to minimaly invasive approaches and/or the use of flexible instrumentation. There exists a need in the art for the development of such minimally invasive procedures and techniques as well as instrumentaion (e.g., flexible instruments or catheters) useable to

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perform such procedures and techniques.

SUMMARY OF THE INVENTION

[0034] In general, the present invention provides methods, devices and systems for diagnosing and/or treating sinusitis or other conditions of the ear, nose or throat.

[0035] In accordance with the present invention, there are provided methods wherein one or more flexible catheters or other flexible elongate devices as described herein are inserted in to the nose, nasopharynx, paranasal sinus, middle ear or associated anatomical passageways to perform an interventional or surgical procedure. Examples of procedures that may be performed using these flexible catheters or other flexible elongate devices include but are not limited to: delivering contrast medium; delivering a therapeutically effective amount of a therapeutic substance; implanting a stent, tissue remodeling device, substance delivery implant or other therapeutic apparatus; cutting, ablating, debulking, cauterizing, heating, freezing, lasing, dilating or otherwise modifying tissue such as nasal polyps, abberant or enlarged tissue, abnormal tissue, etc.; grafting or implanting cells or tissue; reducing, setting, screwing, applying adhesive to, affixing, decompressing or otherwise treating a fracture; delivering a gene or gene therapy preparation; cutting, ablating, debulking, cauterizing, heating, freezing, lasing, forming an osteotomy or trephination in or otherwise modifying bony or cartilaginous tissue within paranasal sinus or elsewhere within the nose; remodeling or changing the shape, size or configuration of a sinus ostium or other anatomical structure that affects drainage from one or more paranasal sinuses; removing puss or aberrant matter from the paranasal sinus or elsewhere within the nose; scraping or otherwise removing cells that line the interior of a paranasal sinus; removing all or a portion of a tumor; removing a polyp; delivering histamine, an allergen or another substance that causes secretion of mucous by tissues within a paranasal sinus to permit assessment of drainage from the sinus; implanting a cochlear implant or indwelling hearing aid or amplification device, etc.

[0036] Further in accordance with the invention, there are provided methods for diagnosing and assessing sinus conditions, including methods for delivering contrast media into cavities, assessing mucosal flow, assessing passageway resistance and cilliary function, exposing certain regions to antigen challenge, etc

[0037] Still further in accordance with the invention, there are provided novel devices for performing some or all of the procedures described herein.

[0038] Further aspects, details and embodiments of the present invention will be understood by those of skill in the art upon reading the following detailed description of the invention and the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0039] FIG. 1A (Prior Art) is a frontal view of a human head showing the locations of the paranasal sinuses.

[0040] FIG. 1B (Prior Art) is a side view of a human head showing the locations of the paranasal sinuses.

[0041] FIG. 2A is a partial sectional view of head of a human patient showing the right

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nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with an anterior/posterior occluder & access device of the present invention inserted therein.

[0042] FIG. 2B is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses, with an anterior occluder & access device of the present invention inserted therein.

[0043] FIG. 2C is a cross sectional view through line C-C of FIG. 2A.

[0044] FIG. 2D is a cross sectional view through line D-D of FIG. 2B.

[0045] FIG. 2E is a perspective view of a posterior occluder/suction/access device of the present invention that is insertable through the oral cavity.

[0046] FIG. 2F is a cross-sectional view through Line 2F-2F of FIG. 2E.

[0047] FIG. 2G is a partial sectional view of head of a human patient showing the right nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with an anterior occluder & access device of the present invention inserted in the right nasal cavity and a posterior occluder/suction/access device of FIG. 2E inserted through the oral cavity.

[0048] FIG. 2H is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses, with an anterior occluder & access device of the present invention inserted in the left nasal cavity and the same posterior occluder/suction/access device that appears in FIG. 2G extending through the oral cavity.

[0049] FIG. 2I is a perspective view of a posterior occluder/suction device of the present invention that is insertable transnasally.

[0050] FIG. 2J is a cross-sectional view through Line 2J-2J of FIG. 21.

[0051] FIG. 2K is a partial sectional view of head of a human patient showing the right nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with the posterior occluder/suction device shown in FIG. 21 inserted through the right nasal cavity.

[0052] FIG. 2L is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses and showing the posterior occluder portion of the device of FIG. 2K residing in and occluding the nasopharynx at a location posterior to the septum and superior to the glottis.

[0053] FIG. 2M is a partial sectional view of head of a human patient showing the right nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with an extended posterior occluder/suction device inserted through the right nasal cavity.

[0054] FIG. 2N is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses and

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showing the posterior occluder and distal tubular extension portions of the device of FIG. 2M residing in the nasopharynx posterior to the septum and superior to the glottis.

[0055] FIG. 2O is a partial sectional view of head of a human patient showing the right nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with a posterior occluder/slidable suction device inserted through the right nasal cavity.

[0056] FIG. 2P is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses and showing the posterior occluder and distal portion of the slidable suction cannula of the device of FIG. 2O residing in the nasopharynx posterior to the septum and superior to the glottis.

[0057] FIG. 2Q is a partial sectional view of head of a human patient showing the right nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with another posterior occluder/tapered suction device inserted through the right nasal cavity.

[0058] FIG. 2R is a partial sectional view of head of a human patient showing the left nasal cavity, the left side of the nasopharynx and the associated paranasal sinuses and showing the posterior occluder and distal portion of the tapered suction cannula of the device of FIG. 2Q residing in the nasopharynx posterior to the septum and superior to the glottis.

[0059] FIG. 3A is a partial perspective view of one embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0060] FIG. 3B is a partial perspective view of another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0061] FIG. 3C is a partial perspective view of another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0062] FIG. 3C' is a cross sectional view through line 3C'-3C' of FIG. 3C.

[0063] FIG. 3D is a partial perspective view of yet another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0064] FIG. 3E', 3E" and 3E"' are partial perspective views of still another embodiment of an occluder/suction device of the present invention showing various steps in a process by which the occluder/suction device is positioned within an anatomical passageway.

[0065] FIG. 3F is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0066] FIGS. 3F', 3F" and 3F"' show alternative constructions of the distal portion of the suction cannula of the occluder/suction device shown in FIG. 3F.

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[0067] FIG. 3G is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0068] FIG. 3H is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0069] FIG. 3I is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0070] FIG. 3J is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0071] FIG. 3K is a partial perspective view of still another embodiment of an occluder/suction device of the present invention positioned within an anatomical passageway.

[0072] FIGS. 3L' and 3L" show partial longitudinal sectional views of another occluder/suction device of the present invention.

[0073] FIGS. 3M' and 3M" show partial perspective views of another occluder/suction device of the present invention positioned within an anatomical passageway.

[0074] FIG. 4 is a longitudinal sectional view of the oropharynx and anterior neck of a human patient having a nasopharyngeal occluder/endotracheal tube device of the present invention inserted through the right nasal cavity and into the trachea.

[0075] FIG. 5A is a partial perspective view of a side cutting or ablation device being used in accordance with the present invention.

[0076] FIG. 5B is a partial perspective view of a device having laterally deployable needles, electrodes or other treatment delivering projections, being used in accordance with the present invention.

[0077] FIG. 5C is a partial perspective view of a drill (e.g., a tissue drill, bone drill, or trephine device) being used in accordance with the present invention.

[0078] FIG. 5D is a partial perspective view of a catheter having a laterally deployed needle or tube for delivering a substance or apparatus to a target location and an optional on-board imaging or guidance apparatus, being used in accordance with the present invention.

[0079] FIG. 5E is a partial perspective view of a balloon catheter being used in accordance with the present invention.

[0080] FIG. 5F is a partial perspective view of a balloon catheter having blades or electrodes thereon, being used in accordance with the present invention.

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[0081] FIG. 5G' is a partial perspective view of a balloon catheter having a stent positioned thereon being inserted into an occluded region within the nose, nasopharynx or paranasal sinus in accordance with the present invention.

[0082] FIG. 5G" shows the balloon catheter and stent of FIG. 3G', with the balloon inflated and the stent expanded so as to open or dilate the occluded region within the nose, nasopharynx or paranasal sinus.

[0083] FIG. 5G"' shows the balloon catheter and stent of FIG. 3G' with the stent implanted, the balloon deflated and the catheter being withdrawn and removed.

[0084] FIG. 5H is a partial perspective view of a tissue shrinking electrode device being used in accordance with the present invention.

[0085] FIG. 5I is a partial perspective view of a cryogenic or plasma state treatment device being used in accordance with the present invention.

[0086] FIG. 5J is a partial perspective view of an expandable tissue expanding device positioned within a passageway in the nose, nasopharynx or paranasal sinus in accordance with the present invention.

[0087] FIG. 5K is a partial sectional view of one embodiment of a forward cutting/suction catheter of the present invention.

[0088] FIG. 5K' shows the device of FIG. 5K being used to remove a nasal polyp or other obstructive mass from an anatomical passage within the nose or paranasal sinus.

[0089] FIG. 5L is a partial sectional view of a forward cutting/suction catheter/endoscope device of the present invention.

[0090] FIG. 5M is a partial sectional view of a side cutting/suction catheter device of the present invention.

[0091] FIG. 5N is a partial sectional view of a side cutting/suction catheter device of the present invention having an optional guidewire lumen and optional endoscopic component(s).

[0092] FIG. 5O is a partial perspective view of the distal end of a guide catheter/endoscope of the present invention.

[0093] FIG. 5P is a partial perspective view of a balloon catheter/pressure-expandable intranasal stent/endoscope device of the present invention.

[0094] FIG. 5Q is a partial perspective view of a delivery catheter/self expanding intranasal stent/endoscope device of the present invention.

[0095] FIG. 5Q' is a cross-sectional view through line 5Q'-5Q' of FIG. 5Q.

[0096] FIG. 5R' shows an example of an optional modified shape of the balloon and stent of FIG. 5P.

[0097] FIG. 5R" shows another example of an optional modified shape of the balloon

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and stent of FIG. 5P.

[0098] FIG. 5S is a partial perspective view of a snare catheter of the present invention with optional endoscopic component(s).

[0099] FIG. 5T is a partial perspective view of a forceps device of the present invention having optional endoscopic component(s).

[0100] FIG. 5U is a partial perspective view of a system of the present invention comprising a guide catheter, endoscope and guidewire.

[0101] FIG. 5U' is a cross-sectional view through line 5T'-5T' of FIG. 5T.

[0102] FIG. 5V is a partial perspective view of a microdebrider catheter of the present invention.

[0103] FIG. 5W is a partial perspective view of a bone remodeling device of the present invention.

[0104] FIGS. 5W' and 5W'' show steps in a method for using the bone remodeling device of FIG. 5W.

[0105] FIGS. 5X'-5X'''' are partial perspective views of alternative designs for bone remodeling devices of the present invention.

[0106] FIGS. 5Y-5Y'''' are perspective views of examples of substance delivering implant devices useable in the present invention.

[0107] FIG. 6A is a perspective view of one embodiment of a sphenoid sinus guide catheter of the present invention.

[0108] FIG. 6B is a perspective view of a frontal sinus guide catheter of the present invention.

[0109] FIG. 6C is a perspective view of one embodiment of a maxillary sinus guide catheter of the present invention.

[0110] FIG. 6D is a perspective view of one embodiment of an ethmoid sinus guide catheter of the present invention.

[0111] FIG. 6E is a perspective view of one embodiment of a plugging guide catheter of the present invention useable for temporarily plugging the opening into a nasolacrimal duct or Eustachian tube.

[0112] FIG. 7A is a sectional view of a paranasal sinus with a catheter introducing an expandable electrode cage into the sinus in accordance with the present invention.

[0113] FIG. 7B is a sectional view of a paranasal sinus that is filled with a diagnostic or therapeutic substance and wherein a plug tipped catheter is being used to plug the ostium of the sinus to retain the substance within the sinus, in accordance with the present invention.

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[0114] FIG. 7C is a sectional view of a paranasal sinus with a catheter introducing a diagnostic or therapeutic substance into contact with the tissue lining the sinus, in accordance with the present invention.

[0115] FIG. 7D is a sectional view of a paranasal sinus with a catheter having emitters and/or sensors for 3 dimensional mapping or navigation, in accordance with the present invention.

[0116] FIG. 7E is a sectional view of a paranasal sinus with a catheter delivering a coil apparatus into the sinus to embolize the sinus and/or to deliver a diagnostic or therapeutic substance into the sinus in accordance with the present invention.

[0117] FIG. 7F is a sectional view of a paranasal sinus with a guide catheter, guide wire and over-the-wire flexible endoscope inserted into the sinus, in accordance with the present invention.

[0118] FIG. 7G shows the guide catheter and endoscope of FIG. 5F with a working device (e.g., a biopsy instrument) inserted through a working channel of the endoscope to perform a procedure within the sinus under endoscopic visualization, in accordance with the present invention.

[0119] FIGS. 8A-8E show steps in a sinus treatment procedure conducted in accordance with the present invention.

[0120] FIGS. 9A-9C show steps in a cochlear implant procedure conducted in accordance with the present invention.

DETAILED DESCRIPTION

[0121] The following detailed description and the accompanying drawings are intended to describe some, but not necessarily all, examples or embodiments of the invention only and does not limit the scope of the invention in any way.

[0122] A number of the drawings in this patent application show anatomical structures of the ear, nose and throat. In general, these anatomical structures are labeled with the following reference letters:

Nasal Cavity NC

Nasopharynx NP

Superior Turbinate ST

Middle Turbinate MT

Inferior Turbinate IT

Frontal Sinus FS

Ethmoid Sinus ES

Sphenoid Sinus SS

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Sphenoid Sinus Ostium SSO

Maxillary Sinus MS

[0123] The human nose has right and left nostrils or nares which lead into separate right and left nasal cavities. The right and left nasal cavities are separated by the intranasal septum, which is formed substantially of cartilage and bone. Posterior to the intranasal septum, the nasal cavities converge into a single nasopharyngeal cavity. The right and left Eustachian tubes (i.e., auditory tubes) extend from the middle ear on each side of the head to openings located on the lateral aspects of the nasopharynx. The nasopharynx extends inferiorly over the uvula and into the pharynx. As shown in FIGS. 1A and 1B, paranasal sinuses are formed in the facial bones on either side of the face. The paranasal sinuses open, through individual openings or ostia, into the nasal cavities. The paranasal sinuses include frontal sinuses FS, ethmoid sinuses ES, sphenoidal sinuses SS and maxillary sinuses MS.

[0124] The present invention provides a comprehensive system of devices and associated methods for diagnosing and treating disorders of the ears, nose and throat in a less invasive fashion than current day approaches. Specifically, examples of which are described below, the invention provides devices that wholly or partially effect a fluid-tight seal of the operative field (e.g., the nasopharynx and/or one or more of the sinus cavities or regional ducts). This fluid-tight sealing of the operative field allows the cavities, ducts and passageways to be imaged using fluid/gas based agents in combination with various imaging modalities without the nsk of aspiration or uncontrolled leakage of fluid from the operative field. Further, this fluid-tight sealing of the operative field permits the retention and collection of any blood or flushing fluids released during the procedure. Another aspect of the invention is a set of methods and devices useable to assess the static and dynamic nature of the paranasal sinuses and to provide for the guidance of specific therapies to particular sinuses or particular target regions (e.g., stenotic sinus ostia, infected tissues within sinuses, tumors, other target structures). Another aspect of the invention is the use of devices and methods which are designed for minimally invasive entry into the sinus passageways or regional ducts under image and/or endoscopic guidance to provide local therapy such as dilation, ablation, resection, injection, implantation, etc. to the region of concern. These devices and methods may be disposable or temporary in their application, or they may be implantable with on-going functionality (such as implantable drug delivery systems, cochlear implants, etc.). In a number of embodiments, the present invention utilizes flexible catheters and various working devices that are mounted on or delivered through elongate flexible members or catheters, to diagnose and treat a wide range or ear, nose and throat disorders including; nasal polyps, sinusitis, enlarged turbinates, deviated septum, tumors, infections, deformities, etc. The following pages describe a number of specific devices and methods that are useable in accordance with this invention. It is to be understood that any component, element, limitation, attribute or step described in relation to any particular device or method described herebelow, may be incorporated in or used with any other device or method of the present invention unless to do so would render the resultant device or method unusable for its intended purpose.

[0125] A. Occluders & Access Port Devices

[0126] Many of the procedures of the present invention require the insertion and

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positioning of one or more flexible catheters or other flexible elongate working devices (examples of which are shown in FIGS. 5A-5Y"" and described herebelow) within the nose, nasopharynx, middle ear or paranasal sinuses. To facilitate the insertion and proper positioning of such catheters and/or other elongate working devices and to prevent undesirable drainage of blood or debris from the operative site, the present invention includes a number of different occluder and/or access port devices, examples of which are shown in FIGS. 2A-2R, that are inserted through the nose and/or oral cavity and function to a) prevent unwanted drainage or escape of fluid (e.g., gas or liquid) and b) facilitate the insertion and positioning of guides and working devices, examples of such working devices being shown in FIGS. 5A-5Y"" and 6A-6E.

[0127] FIGS. 2A-2B show partial sectional views of opposite sides of the head of a human patient having an anterior/posterior occluder & access device 10 inserted through the right nasal cavity and anterior occluder & access device 12 positioned in the anterior region of the left nasal cavity. Specifically, FIG. 2A shows the nasal cavity, the right side of the nasopharynx and the associated paranasal sinuses, with an anterior/posterior occluder & access device 10 of the present invention inserted therein. The anterior/posterior occluder & access device 10 comprises an anterior occluder 14 which occludes the right nasal cavity on the right side of the nasal septum, a posterior occluder 18 that occludes the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis) and a tube 16 that extends between the anterior occluder 14 and posterior occluder 18. Devices for posterior occlusion and anterior occlusion may be used alone or in combination. They may be coaxially deployed or alternatively they may be deployed in a singular fashion, one in each orifice. It should be noted that any combination of these sealing modalities may be employed to achieve one or more of the stated objectives. A cross-section through the tube 16 is shown in FIG. 2C. Other cross-sectional configurations could also be possible, including those that comprise more lumens to permit the passage of multiple devices or fluids (e.g., liquid or gases). In some embodiments, it may be desirable for the device 10 (or any of the other occluder/access devices described herein) to have separate lumens for infusion and aspiration, thereby allowing for concurrent infusion of an irrigation fluid or other fluid and suctioning of the irrigation fluid or other fluid from the operative field. Such continuous turnover of fluid within a sealed operative field may be useful for clearing blood or debris from the operative field to facilitate unobstructed viewing of the anatomical structures using an endoscope or for various other reasons. A port body 28 as attached to the proximal end of the tube 16. A device insertion aperture 30 extends through the port body 28 into working lumen 50 of tube 16. One or more outlet openings 22, 24 are at location(s) in the tube such that a device (e.g., a catheter, fluid injector or other elongate device examples of which are shown in FIGS. 5A-5Y"" and described herebelow) or fluid(s) may be inserted into the device insertion opening 30, advanced through the working lumen 50 and out of a selected one of the outlet openings 22, 24 to a position within the nose, nasopharynx or paranasal sinus. In the particular embodiment shown in FIG. 2A the anterior and posterior occluders 14, 18 comprise balloons, but various other types of occluders could be used in place of balloons, examples of which are shown in FIGS. 3A-3K and described herebelow. Balloon inflation/deflation lumens 52, 56 extends from proximal Luer connectors 32, 36, through the tube 16 and to the anterior occluder 14 and posterior occluder 18, respectively. Thus, a syringe or other fluid expelling and/or withdrawing device may be connected to connector 32 and used to selectively inflate and/or deflate the anterior occluder 14. Another syringe or other fluid expelling and/or withdrawing device may be connected to connector 36 and used to selectively inflate and/or deflate the posterior occluder 18. As may be appreciated from the showing of FIG. 2B, the posterior

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occluder (when fully inflated) may be sized and shaped to occlude the entire posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis), thereby preventing blood or other fluid or debris from draining into the patient's pharynx from either the right or left nasal cavity. When fully inflated, the anterior occluder 14 of the device 10 occludes only the right nasal cavity and serves to prevent blood, other fluid or debris from draining around the tube 16 and out of the right nostril during the operative procedure. A one way valve, such as a flapper valve, duckbill valve, hemostatic valve or other one way valve of the type well known in the art of biomedical device design, may be positioned within the port body 28 to permit a catheter or other elongate device (examples of which are shown in FIGS. 5A-5T and described herebelow) to be advanced in the distal direction though insertion port 30, through the port body 28 and through the working lumen 50 but to prevent blood, other fluid or debris from draining through the working lumen 50 out of the device insertion port 30. In this manner, the device 10 forms a substantially fluid tight anterior seal in the anterior aspect of the right nasal cavity and a substantially fluid tight posterior seal in the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). Since a substantially fluid tight seal is formed, one or more valves (not shown) may be provided to relieve positive or negative pressure created between the anterior or posterior occluders 14, 18 as a result of the injection of matter (e.g., contrast medium, irrigation solution, medicament, etc.) into the operative field and/or suctioning or removal of matter (e.g., blood, other fluid or debris) from the operative field. Additionally, a suction lumen 54 may extend from suction Luer connector 34, through suction lumen 54 and to suction openings 26 may be formed in the tube 16. A suction pump may be connected to the suction connector 34 to aspirate blood, other fluid and/or debris out of the right nasal operative region defined between anterior occluder 14 and posterior occluder 18. It should be appreciated that, while the occlusion/access devices shown in the drawings and described herein are designed to isolate a relatively large operative field (e.g., one or both nasal cavities, sinus, nasal cavities-nasopharynx, etc.), once a specific problem has been diagnosed and/or once a specific target region has been identified, the occluders 14, 18 may be repositioned and/or other occluder devices may be inserted to isolate and form a fluid tight seal of just a portion of the original operative field (e.g., just one sinus, one nasal cavity, one Eustachian tube, etc.) thereby allowing the procedure to go forward with only the necessary region(s) of the nose, nasopharynx, paranasal sinuses or other structures sealed off and/or instrumented, to minimize trauma and improve patient comfort.

[0128] It should be appreciated that in any embodiment of an anterior/posterior occluder & access device, such as the device 10 shown in FIGS. 2A and 2B, the distance between the anterior occluder 14 and posterior occluder 18 may be adjustable so as to accommodate variations in anatomy and/or specific target regions or isolated operative fields of interest. The anterior and posterior occluders 14, 18 may be separate devices where the anterior occluder may slide or pass through one lumen of the posterior occluder, which may contain several lumens (e.g., inflation, working channel, irrigation, etc.), and may or may not be integrated with the posterior occluder. The posterior occluder may also contain several lumens (e.g., inflation, working channel, irrigation, etc.). Additionally, all lumens for both the anterior and posterior occluders may contain valves so as to prevent leakage or flow of gas, fluid, blood, etc.

[0129] It is to be further appreciated that in embodiments that have anterior and posterior outlet openings 22, 24 (as shown in the example of FIGS. 2A-2B) tools, instrumentation and fluids may be delivered via either of the posterior or anterior access ports 22, 24. In some cases, access via a posterior outlet 24 is desirable to gain

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a better perspective on the target anatomical lumen or lumen (i.e. openings to the ethmoid cells).

[0130] As shown in FIGS. 2B and 2D, in some procedures wherein the anterior/posterior occluder & access device 10 is inserted through one nasal cavity, it may be desirable to position a separate anterior occluder & access device 12 within the opposite nasal cavity to prevent drainage of blood, other fluid or debris from the other nostril and to facilitate insertion of catheters or other elongate devices (examples of which are shown in FIGS. 5A-5T and described herebelow) into the left nasal cavity and the paranasal sinuses or other anatomical structures accessible from the other nasal cavity. As shown, in FIG. 2B, the anterior occluder & access device 12 may comprise a tube 41 having an anterior occluder 40 and a port body 42 attached thereto. A device insertion aperture 44 extends through the port body 42 and through a working lumen 58 of tube 41 to an outlet aperture in the distal end of tube 41. A one way valve (such as the valve described hereabove in connection with the anterior/posterior occluder & access device 10) may optionally be provided within port body 42 to prevent draining of blood, other fluid or debris out of insertion aperture 44. In the particular embodiment shown in FIGS. 2B and 2D, the anterior occluder 40 is a balloon, but such occluder 40 may be of various other constructions, examples of which are shown in FIGS. 3A-3M" and described herebelow. To facilitate inflation and deflation of this balloon type anterior occluder 40, a balloon inflation/deflation lumen 60 extends from Luer connector 48, through tube 41 to the balloon-type anterior occluder 40. A syringe or other fluid expelling and/or withdrawing device may be connected to connector 48 and used to selectively inflate and/or deflate the anterior occluder 40. Optionally, a side tube and Luer connector 46 may be connected to the working lumen 58 of tube 41 to allow blood, other fluid and debris to be suctioned from the left nasal cavity through the working lumen 58 of tube 41. In some embodiments, dedicated suction and/or irrigation lumen(s) with separate suction and/or irrigation ports may be formed in tube 41 in a manner similar to that described hereabove with respect to the anterior/posterior occluder & access device 10.

[0131] FIGS. 2E-2H show an alternative system for occlusion and access, wherein anterior occluder & access device(s) 12 is/are positioned in one or both nostrils or nasal cavities and an orally insertable posterior occluder device 300 is inserted through the patient's oral cavity and positioned so as to occlude the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). The embodiment of the orally insertable posterior occluder device 300 shown in FIGS. 2E-2G comprises a curved tube 302 having an occluder 304 positioned at or near the distal end thereof. The device 300 is configured such that it may be inserted through the patient's oral cavity to a position where the occluder 304 is located within, and disposed, so as to substantially occlude the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). The posterior occluder 304 may also be positioned next to the Eustachian tube to block the Eustachian tube, thereby preventing fluid from tracking into the Eustachian tube during the procedure (if access to the Eustachian tube or middle ear or inner ear is not desired). Further, it may be necessary to place specific targeted balloons or occluders in ducts or channels which are not intended to be intervened upon (lacrimal ducts, Eustachian tubes, etc.). In such cases, these extra ductal occluders serve to prevent aberrant fluid/gas loss and/or to maintain the integrity of the lumen, while other nearby structures are being modified. In the particular example shown in FIGS. 2E-2G, the occluder 304 comprises a balloon. However, such occluder 304 may be constructed in various alternative ways, examples of which are shown in FIGS. 3A-3K and described

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herebelow. As may be appreciated from the cross-sectional showing of FIG. 2F, in this example a balloon inflation/deflation lumen 318 may extend from Luer connector 314, through tube 302 to the balloon-type occluder 304. A syringe or other inflation/deflation apparatus may be attached to the Luer connector 314 and used to inflate and deflate the balloon 304. A stopcock or other valve (not shown) may also be provided on balloon inflation tube 318 to maintain inflation of the balloon when desired. In routine use, the occluder 304 is initially deflated and the device 300 is inserted through the oral cavity and advanced to its desired position with the deflated occluder positioned within the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). Thereafter, the occluder 304 may be expanded (e.g., inflated) such that it occludes or blocks the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis), thereby substantially preventing blood, other fluid or debris from draining into the patient's esophagus or trachea during the procedure. In some cases, as shown in FIGS. 2E-2H, the tube 302 may have one or more lumen(s) 310 that extend(s) through the occluder 304 and open (s) through an opening 310 distal to the balloon. Working devices, such as catheters or other elongate devices examples of which are shown in FIGS. 5A-5Y"" and described herebelow may be advanced through such a lumen 310 and into the patient's nasopharynx, nasal cavities, paranasal sinuses, middle ears, etc. Alternatively, suction may be applied to such a lumen 310 to suction blood, other fluid or debris from the area superior to the occluder 304. In some cases, the lumen 310 shown may be divided into a working lumen and a suction lumen. The suction lumen may terminate in separate suction port(s) (not shown) at the distal end of the tube and a connector (not shown) at the proximal end, such that suction may be applied through a lumen that is separate from the lumen through which the working device(s) is/are passed. A port body 306 may be positioned on the proximal end of the tube 302. A device insertion port 308 may extend through the port body 306 into a lumen 310 of the tube 302. A one way valve, such as a flapper valve, duckbill valve, hemostatic valve or other one way valve of the type well known in the art of biomedical device design, may be positioned within the port body 306 to permit a catheter or other elongate device to be advanced in the distal direction though insertion port 308, through the port body 306 and through a lumen 310 but to prevent blood, other fluid or debris from draining through the lumen 310 and out of the device insertion port 308. In some cases, the orally insertable posterior occluder device 300 may be used without any anterior occluder device(s) positioned in the nostril(s) or nasal cavity(ies). In other cases, it will be desirable to use this orally insertable posterior occluder device 300 in combination with one or two anterior occluder & access devices 12 as shown in the example of FIGS. 2G and 2H. The use of these devices 300, 12 in combination serves to establish a substantially fluid tight operative field between the posterior occluder 304 and the anterior occluder(s) 40 while allowing various catheters and other operative instruments to be inserted into the operative field through optional access ports 44 and/or 308.

[0132] FIGS. 2I-2L show a trans-nasally insertable posterior occluder device 301 that does not include any anterior occluder. This device 301 comprises a curved tube 303 having an occluder 305 positioned at or near the distal end of the tube 303. As shown in FIGS. 2K-2L, this device 301 is inserted through either the right or left nasal cavity and advanced to a position where the occluder 305 substantially occludes the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). In the particular example shown, this occluder 305 comprises a balloon. However, such occluder 305 may be constructed in various alternative ways, examples of which are shown in FIGS. 3A-3K and described herebelow. As may be appreciated from the cross-sectional showing of FIG. 2J, in this example a balloon inflation/deflation

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lumen 317 may extend from Luer connector 311, through tube 303 to the balloon-type occluder 305. A syringe or other inflation/deflation apparatus may be attached to the Luer connector 311 and used to inflate and deflate the balloon-type occluder 305. A stopcock or other valve (not shown) may also be provided on balloon inflation lumen 317 to maintain inflation of the balloon when desired. In routine use, the occluder 305 is initially deflated and the device 301 is inserted through the right or left nasal cavity and advanced to its desired position where the deflated occluder 305 is positioned within the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). Thereafter, the occluder 305may be expanded (e.g., inflated) such that it occludes or blocks the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis), thereby substantially preventing blood, other fluid or debris from draining into the patient's esophagus or trachea during the procedure. Optionally, distal suction ports 309 and/or proximal suction ports 307 may open into lumen 315 of the tube 303 and such lumen 315 may be attached to a suction connector 313. In this manner, suction may be applied to remove blood, other fluid or debris from the nasopharynx superior to the occluder 305 and/or from the nasal cavity through which the device 3301 is inserted. As may be appreciated from the showings of FIGS. 2K and 2L, in this example, the trans-nasal posterior occluder device 301 is inserted through the right nasal cavity. A working device WD such as a catheter or other elongate operative apparatus (examples of which are shown in FIGS. 5A-5Y"" and described herebelow) may be advanced into the right nasal cavity adjacent to the tube 303 or through the left nasal cavity which remains open, as no anterior occlusion is provided by this trans-nasal posterior occluder device 301. This arrangement may be particularly suitable for procedures where the physician desires to directly visualize, through the nostril(s), the anatomical structures within the nose, such as the inferior, middle or superior turbinates IT, MT, ST, as shown in FIGS. 2K-2L.

[0133] FIGS. 2M-2N show a modified version of the trans-nasal posterior occluder 301a which includes all of the elements described above with respect to the trans-nasal posterior occluder device 301 shown in FIGS. 2I-2L as well as a distal extension 303a of the tube 303 that extends distal to the occluder 305 and an additional proximal connector 319. A separate lumen (not shown) extends from connector 319 through tube 303 and through distal tube extension 303a, which terminates in a distal end opening 321. Suction may thus be applied to connector 319 to suction matter through distal opening 321, through the distal tube extension 303a and through tube 303. This distal tube extension 303a and additional lumen may be optionally added to any other the other posterior occluder devices described herein in cases where doing so would not render the device unsuitable for its intended application.

[0134] FIGS. 2O-2P show an alternative posterior occluder system 400 that comprises an intranasal catheter 402 that is inserted into a nasal cavity and an occluder catheter 404 that is inserted through the intranasal catheter 402, as shown. A posterior occluder 406 is located at or near the distal end of the occluder catheter 404. In the particular embodiment shown in FIGS. 2O-2P, the occluder 406 is sized and configured to occlude the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). In the particular example shown, this occluder 406 comprises a balloon. However, such occluder 406 may be constructed in various alternative ways, examples of which are shown in FIGS. 3A-3K and described herebelow. In this example a balloon inflation/deflation lumen may extend from Luer connector 408, through occluder catheter 404 and to the balloon-type proximal occluder 406. A syringe or other inflation/deflation apparatus may be attached to the

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Luer connector 408 and used to inflate and deflate the balloon-type posterior occluder 406. A stopcock or other valve (not shown) may also be provided on the balloon inflation/deflation lumen to maintain inflation of the balloon-type posterior occluder 406, when desired. Optionally, distal tubular extension 412 may extend distally of the posterior occluder 406 and a separate lumen may extend from an optional second connector 410, through distal tubular extension 412 and through an opening 414 such that matter may also be aspirated from the area distal to the posterior occluder 406. A port body 418 is formed on the proximal end of the intranasal tube 402. An insertion port 420 extends through port body 418 into the lumen 422 of the intra nasal tube. A side suction port 416 may also be connected to the lumen 422 of the intranasal tube 402. In routine operation, the intranasal tube 402 is inserted through the nostril into one nasal cavity and advanced to a position where its distal end is within or near the posterior choanae or nasopharynx. With the posterior occluder 406 in a collapsed (e.g., deflated) configuration, the occluder catheter 404 is advanced through the lumen 422 of the intranasal catheter 402 to a position where the posterior occluder is located in the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis). Thereafter, the posterior occluder 406 may be expanded (e.g., inflated) such that it occludes or blocks the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis), thereby substantially preventing blood, other fluid or debris from draining into the patient's esophagus or trachea during the procedure. Thereafter, suction may be applied to suction port 416 to suction blood, other fluid or debris from the area proximal to the posterior occluder 406. During such suctioning, the intranasal tube 402 may be moved back and/or forth as indicated by arrows on FIG. 2O, while the occluder catheter 404 remains stationary. Such ability to move the intranasal catheter 402 during the suctioning process may facilitate complete removal of blood, other fluid and/or debris from the operative field.

[0135] FIGS. 2Q and 2R show a modified posterior occluder system 430 which includes the same elements and components as the posterior occluder system 400 described above, but wherein the distal end 434 of the intranasal tube 402a is tapered and wherein a plurality of side apertures 432 are formed in the intranasal tube 402a such that blood, other fluid or debris may be aspirated into the lumen 422a of the intranasal tube 402a through such side apertures 432.

[0136] B. Variations in Occluder Design and Suction Apparatus:

[0137] Although the above-described examples of occluder/access devices 10, 12, 300, 400 show occluders that are in nature of inflatable balloons, it will be appreciated that these occluders are not limited to balloons and may be of various other designs and types. Further, it is to be understood that various arrangements of access and/or suction tubing/port(s) may be used to facilitate complete removal of blood, fluid or other debris from the areas adjacent to the occluder(s) and/or elsewhere in the operative field or optimal positioning of working devices within the operative field. In fact, certain occluder and/or suction-access tubing/port designs may be more desirable for certain procedures than others depending on a number of factors including the positioning of the patient's head during surgery, whether the patient will be under a general anesthetic, whether an endotracheal tube will be inserted, etc. In some cases, where a posterior occluder is positioned within the posterior choanae, nasopharynx or pharynx posterior to the nasal septum the completeness with which blood, other fluid or debris may be suctioned out of the area adjacent to that posterior occluder may depend on the shape and/or design of the occluder itself as well as the shape and location of the

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suction lumen(s) and port(s) through which the blood, fluid or debris is to be suctioned. Beyond optimized fluid control, the posterior occluder and/or associated access tubing may also serve as an essential guiding element for devices, and alternative shapes and trajectories may be particularly useful to access specific structures. FIGS. 3A-3K show examples of varied occluder types and variations in the arrangements of suction lumen (s) and port(s) through which the blood, fluid or debris may be suctioned from areas adjacent to the occluder or elsewhere within the operative field. The examples shown in FIGS. 3A and 3K may be incorporated into the occluder & access devices shown in FIGS. 2A-2R, when appropriate.

[0138] FIG. 3A shows an occluder 446 mounted on a tube 442, wherein a generally "U" shaped curve is formed in the distal end of the tube such that a distal portion of the tube 442 passes beneath the upper surface 449 of the occluder 446 and curves upwardly such that the distal end of the tube 442 terminates in an opening 444 that is flush with the upper surface 449 of occluder 446. In this manner, any fluid that has accumulated adjacent to the upper surface 449 of occluder 446 may be suctioned into opening 444 and through tube 442. In embodiments where the occluder comprises a balloon, a balloon inflation lumen may extend through the tube and open through an opening 447 into the interior of the balloon, to permit inflation/deflation of the balloon. Optionally, a working device 448, such as a flexible catheter or elongate apparatus examples of which are shown in FIGS. 5A-5T and described herebelow, may also be advanced through the suction lumen of tube 442 and out of opening 444 as indicated on FIG. 3A.

[0139] FIG. 3B shows another alternative wherein an occluder 450 has a depression or well 454 formed in its upper surface. A tube 452 is attached to the occluder by attachment members 456 and the distal end of the tube 452 protrudes into well 454 such that any blood, fluid or debris that collects within the well 454 may be suctioned through the tube 452. In embodiments where the occluder 450 comprises a balloon, the tube 452 may incorporate a balloon inflation/deflation lumen which may extend through an inflation/deflation side tube 458 into the interior of the balloon to facilitate inflation and deflation of the balloon.

[0140] FIGS. 3C and 3C' show another alternative wherein an occluder 460 had a depression or well 462 formed in its upper surface and a tube 464 is attached to the occluder 460, as shown. A lumen of the tube 464 is in communication with the area adjacent the floor of the well to facilitate suctioning of blood, fluid or debris that collects within the well. In embodiments where the occluder 460 comprises a balloon, the tube 464 may incorporate a suction lumen 468 and a balloon inflation/deflation lumen 470. A small curved (e.g., generally "U" shaped) suction tube 466 may be connected in a sealed connection to the distal end of suction lumen 468 and the interior of the well 462 such that blood, other fluid or debris may be suctioned from the well 462, through suction tube 466 and through suction lumen 468.

[0141] FIG. 3D shows a concave occluder 471 that comprises a self expanding concave structure 472 such as a basket formed of a superelastic or resilient mesh material (e.g., nickel titanium alloy wire mesh). The expanding concave structure 472 is covered by a fluid impermeable flexible covering 474 such as a skin formed of flexible polymer (e.g., expanded polytetrafluoroethylene, polyurethane, polyethylene teraphthalate, etc.). When fully expanded the concave occluder 471 occludes the body lumen in which it is positioned (e.g., the nasal cavity, posterior choanae, nasopharynx, pharynx, etc.) and forms a concave well 479. A tube 480 extends into the well 479 of

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the concave occluder 471 and may be used to suction blood, fluid or debris from the well 479. The occluder 471 may be advanced from and withdrawn into a delivery catheter 478. Struts 472 may connect the concave occluder 471 to a delivery member (not shown) within the delivery catheter 478, such delivery member being advanceable to push the occluder 471 out of the delivery catheter 478 and retractable to withdraw the occluder 471 into the delivery catheter 478. When inside the delivery catheter, the occluder 471 may be in a collapsed configuration but when expelled out of the delivery catheter the occluder will resiliently spring or self-expand to its expanded concave configuration, as shown in FIG. 3D. The suction catheter 480 may advance from and/or retract into the delivery catheter 478 concurrently with, or separately from, the occluder 471.

[0142] FIGS. 3E'-3E'" show yet another occluder/suction arrangement wherein the occluder 484 comprises an everting tubular member that is advanceable from a delivery/suction catheter 486. The everting tubular member comprises a frame 488 that is covered with a covering 500. Initially the everting tubular member is in a substantially cylindrical configuration within the lumen of the delivery/suction catheter 486. The frame may be a resilient or superelastic material that is biased to the everted shape shown in FIG. 3E'". Such frame 488 may be formed of mesh material (e.g., nickel titanium alloy wire mesh). The covering 500 may be formed of flexible polymer (e.g., expanded polytetrafluoroethylene, polyurethane, polyethylene teraphthalate, etc.) In operation, the delivery/suction catheter 486 is advanced to the position where it is desired to place the occluder 484. Then, the everting tube is advanced from the distal end opening of the delivery/suction tube 486, as shown in FIGS. 3E' and 3E". As it advances out of the catheter 486, the everting tube member assumes its everted configuration, forming a concave occluder 484 as shown in FIG. 3E'". The occluder 484, when fully everted, occludes the body lumen in which it is positioned (e.g., the nasal cavity, posterior choanae, nasopharynx, pharynx, etc.) and creates a concave well 504. The delivery/suction catheter 486 may be advanced into the concave well 504 such that any blood, fluid or debris that collects within concave well 504 may be suctioned through suction ports 502 and through the distal end of the delivery/suction catheter 486.

[0143] FIG. 3F-3F'" show another embodiment wherein an occluder 510 is positioned on the end of a tube 512. The occluder 510 has an arched upper surface such that a generally "V" shaped annular collection space 518 is created in the region of the coaptation between the occluder 510 and the adjacent wall of the body lumen in which it is positioned (e.g., a nasal cavity, posterior choanae, nasopharynx, pharynx, etc.). A suction tube 516 extends from tube 512 into the annular collection space 518 and blood, other fluid or debris that collects in the annular collection space 518 may be suctioned through suction tube 516 and through a lumen of tube 512, thereby providing for maintenance of a substantially dry environment adjacent to the upper surface of the occluder 510. The occluder 510 may comprise a balloon or any other suitable occlusion member as described herein or known in the art. As shown in FIGS. 3F'-3F'" the suction tube 516 may comprise a simple tube having an open distal end or, alternatively, the device may incorporate a suction tube 516a that has a plurality of side apertures 520 formed near its distal end and/or a suction tube 516 that has a guard member 522, such as a screen, formed over its suction ports or openings to deter solid matter (e.g., blood clots or other debris) from clogging the suction ports or openings.

[0144] FIG. 3G shows an occluder 530 attached to a tube 532 that has a curved (e.g., generally "U" shaped) distal end that does not protrude into the interior of the occluder.

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Suction apertures 536 are formed in the distal portion of the tube 532 to permit blood, fluid or debris that collects adjacent to the upper surface of the occluder 530 to be suctioned through the tube 532. In embodiments where the occluder is a balloon a balloon/inflation lumen may extend through tube 532 and a small balloon inflation tube 538 may extend into the interior of the balloon to permit the balloon to be inflated and deflated. Optionally, in some embodiments, a separate tube 540 may extend through tube 532 and trough occluder 530 to provide access to the area distal to the occluder 530 for purposes of suctioning, introduction of instruments, or other purposes.

[0145] FIG. 3H shows another embodiment wherein the occluder 546 is connected to a tube or elongate member 550 and a suction tube 548 having an expanded (e.g., trumpet shaped) distal end is useable to suction blood, fluid or debris from the area adjacent to the upper surface of the occluder. As can be seen from FIG. 3H, where the upper surface of the occluder is arched and annular collection space may be created around the perimeter of the occluder 546 where the occluder 546 coapts with the wall of the anatomical structure in which it is positioned (e.g., a nasal cavity, posterior choanae, nasopharynx, pharynx, etc.) and the expanded end 552 of the suction tube 548 may be sized and shaped to receive the arched upper surface of the occluder 546 and to suction any blood, fluid or debris from that annular collection space. In embodiments where the occluder is a balloon a balloon/inflation lumen may extend through tube 548 and a small balloon inflation tube may extend into the interior of the balloon to permit the balloon to be inflated and deflated. Optionally, in some embodiments, a separate tube 550 may extend through tube 548 and through occluder 546 to provide access to the area distal to the occluder 546 for purposes of suctioning, introduction of instruments or fluid injectors, or other purposes.

[0146] FIG. 3I shows an embodiment wherein the occluder 570 comprises a mass of absorbent material such as a tampon (e.g., cotton, gauze, hydrogel or other material or composite of materials that will absorb fluid and occlude the desired body lumen). In the particular example shown, the occluder is advanced out of an aperture 578 formed in a tube 572 that has a curved (e.g., generally "U" shaped) tip. Suction apertures 576 are formed in the distal portion of the tube 572 to permit blood, fluid or debris that collects adjacent to the upper surface of the occluder 570 to be suctioned through the tube 572. After the procedure is complete or the occlusion is no longer required, the tube 572 and fluid-soaked occluder 570 may be withdrawn from the body without retraction of the occluder 570 into the tube 572. Optionally, a distal end opening 574 may be formed in tube 572 and such distal end opening may be connected to the same lumen as openings 576 or a separate lumen to the optional distal end opening 574 to be used for suctioning, irrigation or introduction of a working device 580 such those shown in FIGS. 5A-5Y"" and described herebelow.

[0147] FIG. 3J shows an occluder embodiment similar to that of the device shown in FIGS. 2O and 2P and described hereabove. In this embodiment, an occluder 600 is attached to a tube or elongate member 604 and a suction tube 602 is movable back and forth over the tube or elongate member 604 to suction blood, fluid or debris from the area adjacent to the upper surface of the occluder 600 or elsewhere in the body lumen in which the occluder 600 is positioned. In embodiments where the occluder 600 is a balloon, a balloon/inflation lumen may extend through tube or elongate member 604 and into the balloon to permit the balloon to be inflated and deflated. Optionally, in some embodiments, a separate tube 606 may extend trough tube or elongate member 604 and through occluder 600 to provide access to the area distal to the occluder 600 for purposes of suctioning, introduction of instruments, or other purposes.

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[0148] FIG. 3K shows an occluder embodiment similar to that incorporated into the device shown in FIGS. 2Q and 2R and described hereabove. In this embodiment, an occluder 610 is attached to a tube or elongate member 614 and a tapered suction tube 612 having one or more suction apertures 616 formed therein is movable back and forth over the tube or elongate member 614 to suction blood, fluid or debris from the area adjacent to the upper surface of the occluder 610 or elsewhere in the body lumen in which the occluder 600 is positioned. Of course, irrigation solution or other fluids may also be delivered through such apertures 616 or through a separate irrigation/infusion lumen that opens through separate irrigation/infusion aperture(s) (not shown). In embodiments where the occluder 610 is a balloon, a balloon/inflation lumen may extend through tube or elongate member 614 and into the balloon to permit the balloon to be inflated and deflated. Optionally, in some embodiments, a separate tube 618 may extend trough tube or elongate member 614 and through occluder 610 to provide access to the area distal to the occluder 610 for purposes of suctioning, introduction of instruments, or other purposes.

[0149] FIGS. 3L'-3L" show yet another occluder/tubing device 1000 comprising an outer tube 1002 and an inner tube 1004 disposed coaxially within the outer tube 1002. An outwardly bendable region 1006 is formed in the wall of the outer tube 1002 near its distal end. The distal end of the outer tube 1002 is affixed to the inner tube 1004. A passageway 1010 extends between the outer tube 1002 and inner tube 1004 and openings 1008 are formed in the wall of the outer tube 1002. In routine operation, this device 1000 is initially disposed in the configuration shown in FIG. 3L' and is inserted into the desired passageway. Thereafter, the inner tube 1004 is pulled in the proximal direction while the outer tube 1002 is held stationary, thereby causing the outwardly bendable region 1006 to protrude outwardly as shown in FIG. 3L" and resulting in occlusion of the body lumen in which the distal portion of the device 1000 is positioned. Suction may be applied to passageway 1010 to remove blood, fluid or other debris from the area adjacent to the upper surface of 1007 of the outwardly protruding bendable region 1006. In this regard, the openings 1008 may be formed close to and/or even in the upper surface 1007 of the outwardly protruding bendable region 1006.

[0150] FIGS. 3M' and 3M" show another occluder/tubing device 1020 comprising an outer tube 1022 an inner tube 1024. The inner tube 1024 is advanceable out of the distal end of the outer tube 1022 and a distal portion of the inner tube 1024 expands as it emerges from the inner tube, thereby forming an occluder that occludes the body lumen or passageway in which it is positioned, as shown in FIG. 3M". Blood, other fluid or debris may be suctioned from the area adjacent to the upper surface of the occluder through the open distal end of the outer tube 1022 and/or through optional side apertures 1026.

[0151] FIG. 4 shows a nasopharyngeal occluder/endotracheal tube device 620 of the present invention inserted through the right nasal cavity and into the trachea. This device 620 comprises a curved tube 622 having a posterior occluder 626 positioned at or near the distal end of the tube 622 and, optionally an anterior occluder (shown in dotted lines on FIG. 4) formed near the proximal end of the tube 622. An endotracheal tube 624 extends through curved tube 622, through the posterior occluder and into the patient's trachea. Optionally, a cuff 628 may be formed on endotracheal tube 624 to provide a second substantially fluid tight seal within the patient's trachea, inferior to the glottis. A hub 630 is formed on the proximal end of tube 622. A ventilator tube 634 extends from the hub and is connected to endotracheal tube 624 and is attachable to a

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ventilator, anesthesia machine, t-tube, Ambu-bag, etc. In embodiments where the posterior occluder 626 is a balloon, a posterior occluder inflation/deflation connector 632 extends from hub 630 and is connected to an inflation/deflation lumen that extends through tube 622 for inflation/deflation of the posterior occluder 626. A cuff inflation/deflation connector 634 may also extend from hub 630 and through the endotracheal tube 624 for inflation/deflation of the endotracheal tube cuff 628. Optionally, suction and/or device insertion ports may also be formed in hub 630, as described above in connection with other occluder/access devices. In routine operation, this device 620 is inserted to a position where the posterior occluder 626 occludes the posterior choanae, nasopharynx or pharynx posterior to the nasal septum (but typically superior to the glottis) and the endotracheal tube 624 extends into the patient's trachea with the optional cuff positioned in the trachea inferior to the glottis.

[0152] C. Working Devices for Delivering Substances or for Cutting, Ablating, Remodeling or Expanding Bone or Soft Tissue

[0153] The present invention provides a variety of apparatus that may be inserted into the nasal cavity, paranasal sinus, nasopharynx or middle ear to perform diagnostic or therapeutic procedures. These devices may be delivered through or incorporated into flexible catheters or flexible rod-like shafts. Such flexible construction allows these devices to be delivered and positioned to perform the desired diagnostic or therapeutic procedures with minimal trauma to other tissues, as can result from the insertion of rigid scopes and rigid instruments in accordance with the methodology of the prior art. It is within the scope of this approach that these devices may be partially flexible or have rigid portions and flexible portions to facilitate their control and guidance to the appropriate region. Further, they may be used in conjunction or combination with other standard rigid apparatus (scopes, etc.) during some part of the procedure, if desired.

[0154] Also, in some but not necessarily all procedures, these working devices (and/or the catheters used to deliver them) may be inserted through lumens of the occluder & access devices 10, 12, 300, 301, 400, 430, etc. as shown in FIGS. 2A-2R and described above. As stated earlier, it may also be desirable to focus the access and occlusion to an even smaller territory, through stand-alone guide catheters or subselective guide catheters with or without balloons or other occluders.

[0155] Optionally, any of the working devices anmd guide catheters described herein may be configured to receive or be advanced over a guidewire unless to do so would render the device inoperable for its intended purpose. Some of the specific examples described herein include guidewires, but it is to be appreciated that the use of guidewires and the incorporation of guidewire lumens is not limited to only the specific examples in which guidewires or guidewire lumens are shown. The guidewires used in this invention may be constructed and coated as is common in the art of cardiology. This may include the use of coils, tapered or non-tapered core wires, radiopaque tips and/or entire lengths, shaping ribbons, variations of stiffness, PTFE, silicone, hydrophilic coatings, polymer coatings, etc. For the scope of this inventions, these wires may possess dimensions of length between 5 and 75 cm and outer diameter between 0.005" and 0.050".

[0156] Also, some of the working devices shown in FIGS. 5A-5Y"" and described herein incorporate assemblies, components or mechanisms (e.g., rotating cutters, radiofrequency electrodes, electrocautery devics, recepacles for capturing matter, cryosurgical apparatus, balloons, stents, radioactive or substance-eluting coatings,

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snares, electro-anatomical mapping and guidance, optical fibers, lenses and other endoscope apparatus, seals, hemostatic valves, etc. The designs and constructions of such components and assemblies are will known in the art. Non-limiting examples of some such designs and constructions are set forth in U.S. Pat. No. 5,722,984 (Fischell et al.), U.S. Pat. No. 5,775,327 (Randolph et al.), U.S. Pat. No. 5,685,838 (Peters, et al.), U.S. Pat. No. 6,013,019 (Fischell et al.), U.S. Pat. No. 5,356,418 (Shturman), U.S. Pat. No. 5,634,908 (Loomas), U.S. Pat. No. 5,255,679 (Imran), U.S. Pat. No. 6,048,299 (Hoffman), U.S. Pat. No. 6,585,794 (Wright et al.), U.S. Pat. No. 6,503,185 (Waksman), U.S. Pat. No. 6,669,689 (Lehmann et al.), U.S. Pat. No. 6,638,233 (Corvi et al.), U.S. Pat. No. 5,026,384 (Farr et al.), U.S. Pat. No. 4,669,469 (Gifford et al.), U.S. Pat. No. 6,685,648 (Flaherty et al.), U.S. Pat. No. 5,250,059 (Andreas et al.), U.S. Pat. No. 4,708,834 (Tsuno), U.S. Pat. No. 5,171,233 (Amplatz), U.S. Pat. No. 6,468,297 (Williams et al.) and U.S. Pat. No. 4,748,869 (Wardle).

[0157] As shown in the examples of FIGS. 5A-5Y"" these working devices include guide catheters, substance delivery catheters, scopes, injectors, cutters, bone breaking apparatus, balloons and other dilators, laser/thermal delivery devices, braces, implants, stents, snares, biopsy tools, forceps, etc.

[0158] FIG. 5A shows a side suction and/or cutting catheter 70 comprising a flexible catheter body 72 having a side opening 74. The catheter 72 is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. and positioned so that the opening 74 is adjacent to matter (e.g., a polyp, lesion, piece of debris, tissue, blood clot, etc.) that is to be removed. Suction may be applied through a lumen of the catheter 72 to suction the matter through the opening 74 and into the catheter 72. In some cases, a cutter such as a rotating cutter, linear slicer, pincher, laser beam, electrosurgical cutter, etc. may be incorporated into the catheter 72 to assist in severing or ablating tissue or other matter that has been positioned in the side opening 74. This catheter may incorporate a deflectable tip or a curved distal end which may force the opening of the catheter against the tissue of interest. Further, this device 70 may have an optional stabilizing balloon (similar to that shown in FIG. 5M and described herebelow) incorporated on one side of the catheter 72to press it against the tissue of interest and may also contain one or more on-board imaging modalities such as ultrasound, fiber or digital optics, OCT, RF or electro-magnetic sensors or emitters, etc.

[0159] FIG. 5B shows an injector catheter 76 that comprises a flexible catheter shaft 78 having one or more injector(s) 80 that are advanceable into tissue or other matter that is located in or on the wall of the body lumen in which the catheter 78 is positioned. The catheter 78 is advanced, with the injector(s) retracted into the catheter body, through a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. and positioned adjacent the area to which a diagnostic or therapeutic substance is to be injected. Thereafter, the injector(s) are advanced into the adjacent tissue or matter and the desired substance is injected. Energy, such as laser, RF, thermal or other energy may be delivered through these injectors 80 or energy emitting implants (such as gamma or beta radioactive seeds) may also be delivered through these injectors 80, either alone or in combination with a fluid carrier or other substance such as a diagnostic or therapeutic substance (as defined herein). It will be noted that this device 76 as well as other working devices and methods of the present invention (including the various implantable devices described herein) are useable to deliver diagnostic or therapeutic substances. The term "diagnostic or therapeutic substance" as used herein is to be broadly construed to include any feasible drugs, prodrugs, proteins, gene

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therapy preparations, cells, diagnostic agents, contrast or imaging agents, biologicals, etc. For example, in some applications where it is desired to treat or prevent a microbial infection, the substance delivered may comprise pharmaceutically acceptable salt or dosage form of an antimicrobial agent (e.g., antibiotic, antiviral, antiparacytic, antifungal, etc.).

[0160] Some nonlimiting examples of antimicrobial agents that may be used in this invention include acyclovir, amantadine, aminoglycosides (e.g., amikacin, gentamicin and tobramycin), amoxicillin, amoxicillin/Clavulanate, amphotericin B, ampicillin, ampicillin/sulbactam, atovaquone, azithromycin, cefazolin, cefepime, cefotaxime, cefotetan, cefpodoxime, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cefuroxime axetil, cephalexin, chloramphenicol, clotrimazole, ciprofloxacin, clarithromycin, clindamycin, dapsone, dicloxacillin, doxycycline, erythromycin, fluconazole, foscarnet, ganciclovir, atifloxacin, imipenem/cilastatin, isoniazid, itraconazole, ketoconazole, metronidazole, nafcillin, nafcillin, nystatin, penicillin, penicillin G, pentamidine, piperacillin/tazobactam, rifampin, quinupristin-dalfopristin, ticarcillin/clavulanate, trimethoprim/sulfamethoxazole, valacyclovir, vancomycin, mafenide, silver sulfadiazine, mupirocin, nystatin, triamcinolone/nystatin, clotrimazole/betamethasone, clotrimazole, ketoconazole, butoconazole, miconazole, tioconazole, detergent-like chemicals that disrupt or disable microbes (e.g., nonoxynol-9, octoxynol-9, benzalkonium chloride, menfegol, and N-docasanol); chemicals that block microbial attachment to target cells and/or inhibits entry of infectious pathogens (e.g., sulphated and sulponated polymers such as PC-515 (carrageenan), Pro-2000, and Dextrin 2 Sulphate); antiretroviral agents (e.g., PMPA gel) that prevent retroviruses from replicating in the cells; genetically engineered or naturally occurring antibodies that combat pathogens such as anti-viral antibodies genetically engineered from plants known as "plantibodies;" agents which change the condition of the tissue to make it hostile to the pathogen (such as substances which alter mucosal pH (e.g., Buffer Gel and Acidform) or non-pathogenic or "friendly" bacteria or other microbes that cause the production of hydrogen peroxide or other substances that kill or inhibit the growth of pathogenic microbes (e.g., lactobacillus). As may be applied to any of the substances listed previously or below, these substances may be combined with any one or more drug-releasing devices or molecular constructs such as polymers, collagen, gels, implantable osmotic pump devices, etc. to permit their release over an extended period of time once deposited. Further, these substances may also be combined with any of the implantable structural devices described below (stents, expanders, etc.) to reduce infection, encrustation, or encapsulation of the implant itself, or to allow the drug to be deposited in the optimal location mucosally, sub-mucosally or into the bone. Examples of implantable substance delivery devices useable in this invention include those shown in FIGS. 5Y'-5Y''''' and described herebelow.

[0161] Additionally or alternatively, in some applications where it is desired to treat or prevent inflamation the substances delivered in this invention may include various steroids. For example, corticosteroids that have previously administered by intranasal administration may be used, such as beclomethasone (Vancenase(R) or Beconase (R)), flunisolide (Nasalide(R)), fluticasone (Flonase(R)), triamcinolone (Nasacort(R)) and mometasone (Nasonex(R)). Also, other steroids that may be useable in the present invention include but are not limited to aclometasone, desonide, hydrocortisone, betamethasone, clocortolone, desoximetasone, fluocinolone, flurandrenolide, mometasone, prednicarbate; amcinonide, desoximetasone, diflorasone, fluocinolone, fluocinonide, halcinonide, clobetasol, augmented betamethasone, diflorasone, halobetasol, prednasone, dexamethasone and

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methylprednisolone,

[0162] Additionally or alternatively, in some applications, such as those where it is desired to treat or prevent an allergic or immune response, the substances delivered in this invention may include a) various cytokine inhibitors such as humanized anti-cytokine antibodies, anti-cytokine receptor antibodies, recombinant (new cell resulting from genetic recombination) antagonists, or soluble receptors; b) various leucotriene modifiers such as zafirlukast, montelukast and zileuton; c) immunoglobulin E (IgE) inhibitors such as Omalizumab (an anti-IgE monoclonal antibody formerly called rhu Mab-E25) and secretory leukocyte protease inhibitor).

[0163] Additionally or alternatively, in some applications, such as those where it is desired to shrink mucosal tissue, cause decongestion or effect hemostasis, the substances delivered in this invention may include various vasoconstrictors for decongestant and or hemostatic purposes including but not limited to pseudoephedrine, xylometazoline, oxymetazoline, phenylephrine, epinephrine, etc.

[0164] Additionally or alternatively, in some applications, such as those where it is desired to facilitate the flow of mucous, the substances delivered in this invention may include various mucolytics or other agents that modify the viscosity or consistency of mucous or mucoid secretions, including but not limited to acetylcysteine (Mucomyst (TM), Mucosil(TM)) and guaifenesin.

[0165] Additionally or alternatively, in some applications such as those where it is desired to prevent or deter histamine release, the substances delivered in this invention may include various mast cell stabilizers or drugs which prevent the release of histamine such as cromolyn (e.g., Nasal Chrom(R)) and nedocromil.

[0166] Additionally or alternatively, in some applications such as those where it is desired to prevent or inhibit the effect of histamine, the substances delivered in this invention may include various antihistamines such as azelastine (e.g., Astylin(R)), diphenhydramine, loratidine, etc.

[0167] Additionally or alternatively, in some embodiments such as those where it is desired to dissolve, degrade, cut, break or remodel bone or cartilage, the substances delivered in this invention may include substances that weaken or modify bone and/or cartilage to facilitate other procedures of this invention wherein bone or cartilage is remodeled, reshaped, broken or removed. One example of such an agent would be a calcium chelator such as EDTA that could be injected or delivered in a substance delivery implant next to a region of bone that is to be remodeled or modified. Another example would be a preparation consisting or or containing bone degrading cells such as osteoclasts. Other examples would include various enzymes of material that may soften or break down components of bone or cartilage such as collagenase (CGN), trypsin, trypsin/EDTA, hyaluronidase, and tosylilysylchloromethane (TLCM).

[0168] Additionally or alternatively, in some applications, the substances delivered in this invention may include other classes of substances that are used to treat rhinitis, nasal polyps, nasal inflammation, and other disorders of the ear, nose and throat including but not limited to anticolinergic agents that tend to dry up nasal secretions such as ipratropium (Atrovent Nasal(R)), as well as other agents not listed here.

[0169] Additionally or alternatively, in some applications such as those where it is

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desired to draw fluid from polyps or edematous tissue, the substances delivered in this invention may include locally or topically acting diuretics such as furosemide and/or hyperosmolar agents such as sodium chloride gel or other salt preparations that draw water from tissue or substances that directly or indirectly change the osmolar content of the mucous to cause more water to exit the tissue to shrink the polyps directly at their site.

[0170] Additionally or alternatively, in some applications such as those wherein it is desired to treat a tumor or cancerous lesion, the substances delivered in this invention may include antitumor agents (e.g., cancer chemotherapeutic agents, biological response modifiers, vascularization inhibitors, hormone receptor blockers, cryotherapeutic agents or other agents that destroy or inhibit neoplasia or tumorigenesis) such as; alkylating agents or other agents which directly kill cancer cells by attacking their DNA (e.g., cyclophosphamide, isophosphamide), nitrosoureas or other agents which kill cancer cells by inhibiting changes necessary for cellular DNA repair (e.g., carmustine (BCNU) and lomustine (CCNU)), antimetabolites and other agents that block cancer cell growth by interfering with certain cell functions, usually DNA synthesis (e.g., 6 mercaptopurine and 5-fluorouracil (5FU), antitumor antibiotics and other compounds that act by binding or intercalating DNA and preventing RNA synthesis (e.g., doxorubicin, daunorubicin, epirubicin, idarubicin, mitomycin-C and bleomycin) plant (vinca) alkaloids and other anti-tumor agents derived from plants (e.g., vincristine and vinblastine), steroid hormones, hormone inhibitors, hormone receptor antagonists and other agents which affect the growth of hormone-responsive cancers (e.g., tamoxifen, herceptin, aromatase ingibitors such as aminoglutethamide and formestane, trriazole inhibitors such as letrozole and anastrazole, steroidal inhibitors such as exemestane), antiangiogenic proteins, small molecules, gene therapies and/or other agents that inhibit angiogenesis or vascularization of tumors (e.g., meth-1, meth-2, thalidomide), bevacizumab (Avastin), squalamine, endostatin, angiostatin, Angiozyme, AE-941 (Neovastat), CC-5013 (Revimid), medi-522 (Vitaxin), 2-methoxyestradiol (2ME2, Panzem), carboxyamidotriazole (CAI), combretastatin A4 prodrug (CA4P), SU6668, SU11248, BMS-275291, COL-3, EMD 121974, IMC-1C11, IM862, TNP-470, celecoxib (Celebrex), rofecoxib (Vioxx), interferon alpha, interleukin-12 (IL-12) or any of the compounds identified in Science Vol. 289, Pages 1197-1201 (Aug. 17, 2000) which is expressly incorporated herein by reference, biological response modifiers (e.g., interferon, bacillus calmette-guerin (BCG), monoclonal antibodies, interluken 2, granulocyte colony stimulating factor (GCSF), etc.), PGDF receptor antagonists, herceptin, asparaginase, busulphan, carboplatin, cisplatin, carmustine, cchlorambucil, cytarabine, dacarbazine, etoposide, flucarbazine, flurouracil, gemcitabine, hydroxyurea, ifosphamide, irinotecan, lomustine, melphalan, mercaptopurine, methotrexate, thioguanine, thiotepa, tomudex, topotecan, treosulfan, vinblastine, vincristine, mitoazitrone, oxaliplatin, procarbazine, streptocin, taxol, taxotere, analogs/congeners and derivatives of such compounds as well as other antitumor agents not listed here.

[0171] Additionally or alternatively, in some applications such as those where it is desired to grow new cells or to modify existing cells, the substances delivered in this invention may include cells (mucosal cells, fibroblasts, stem cells or genetically engineered cells) as well as genes and gene delivery vehicles like plasmids, adenoviral vectors or naked DNA, mRNA, etc. injected with genes that code for anti-inflammatory substances, etc., and, as mentioned above, osteoclasts that modify or soften bone when so desired.

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[0172] Additionally or alternatively to being combined with a device and/or a substance releasing modality, it may be ideal to position the device in a specific location upstream in the mucous flow path (i.e. frontal sinus or ethmoid cells). This could allow the deposition of fewer drug releasing devices, and permit the "bathing" of all the downstream tissues with the desired drug. This utilization of mucous as a carrier for the drug may be ideal, especially since the concentrations for the drug may be highest in regions where the mucous is retained; whereas non-diseased regions with good mucouse flow will be less affected by the drug. This could be particularly useful in chronic sinusitis, or tumors where bringing the concentration of drug higher at those specific sites may have greater therapeutic benefit. In all such cases, local delivery will permit these drugs to have much less systemic impact. Further, it may be ideal to configure the composition of the drug or delivery system such that it maintains a loose affinity to the mucous permitting it to distribute evenly in the flow. Also, in some applications, rather than a drug, a solute such as a salt or other mucous soluble material may be positioned at a location whereby mucous will contact the substance and a quantity of the substance will become dissolved in the mucous thereby changing some property (e.g., pH, osmolarity, etc) of the mucous. In some cases, this technique may be used to render the mucous hyperosmolar so that the flowing mucous will draw water from polyps, edematous mucosal tissue, etc. thereby providing a desiccating therapeutic effect.

[0173] Additionally or alternatively to substances directed towards local delivery to affect changes within the sinus cavity, the nasal cavities provide unique access to the olfactory system and thus the brain. Any of the devices and methods described herein may also be used to deliver substances to the brain or alter the functioning of the olfactory system. Such examples include, the delivery of energy or the deposition of devices and/or substances and/or substance delivering implant(s) to occlude or alter olfactory perception, to suppress appetite or otherwise treat obesity, epilepsy (e.g., barbiturates such as phenobarbital or mephoobarbital; iminostilbenes such as carbamazepine and oxcarbazepine; succinimides such as ethylsuximide; valproic acid; benzodiazepines such as clonazepam, clorazepate, diazepam and lorazepam, gabapentin, lamotrigine, acetazolamide, felbamate, levetiraceam, tiagabine, topiramate, zonisamide, etc.), personality or mental disorders (e.g., antidepressants, antianxiety agents, antipsychotics, etc.), chronic pain, Parkinson's disease (e.g., dopamine receptor agonists such as bromocriptine, pergolide, ropinitrol and pramipexole; dopamine precursors such as levodopa; COMT inhibitors such as tolcapone and entacapone; selegiline; muscarinic receptor antagonists such as trihexyphenidyl, benztropine and diphenhydramine) and Alzheimer's, Huntington's Disease or other dementias, disorders of cognition or chronic degenerative diseases (e.g. tacrine, donepezil, rivastigmine, galantamine, fluoxetine, carbamazepine, clozapine, clonazepam and proteins or genetic therapies that inhibit the formation of beta-amyloid plaques), etc.

[0174] FIG. 5C shows a device 82 that comprises a rotating shaft 84 having a drill, auger or burr 86 that is useable to drill, bore, grind or cut through tissue, bone, cartilage or other matter. This device 82 may deployed as shown or, alternatively, the device 82 may be inserted through a small mucosal incision to preserve the overlying mucosal lining while removing or boring into the bone or cartilage below the mucosal lining.

[0175] FIG. 5D shows a guided injector catheter device 88 for delivering a diagnostic or therapeutic substance as defined above. This device 88 comprises a flexible catheter 90 having an imaging apparatus 96 thereon and an injector 92 that is advanceable from

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and retractable into the catheter 90. The imaging apparatus 96 is useable to image the target location 94 at which the substance is to be deposited and to enable orientation of the catheter 88 such that, when the injector 92 is advanced from the catheter 88, the injector 92 will travel to the desired target location 94. Examples of such catheter 88 are described in U.S. Pat. No. 6,195,225 (Makower), U.S. Pat. No. 6,544,230 (Flaherty et al.), U.S. Pat. No. 6,375,615 (Flaherty et al.), U.S. Pat. No. 6,302,875 (Makower et al), U.S. Pat. No. 6,190,353 (Makower et al.) and U.S. Pat. No. 6,685,648 (Flaherty et al.), the entireties of which are expressly incorporated herein by reference.

[0176] FIG. 5E shows a balloon catheter device 98 comprising a flexible catheter 100 having a balloon 102 thereon. The catheter device 98 is advanced, with balloon 102 deflated, into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. and positioned with the deflated balloon 102 situated within an ostium, passageway or adjacent to tissue or matter that is to be dilated, expanded or compressed (e.g., to apply pressure for hemostasis, etc.). Thereafter, the balloon 102 may be inflated to dilate, expand or compress the ostium, passageway, tissue or matter. Thereafter the balloon 102 may be deflated and the device 98 may be removed. This balloon 102 may also be coated, impregnated or otherwise provided with a medicament or substance that will elute from the balloon into the adjacent tissue (e.g., bathing the adjacent tissue with drug or radiating the tissue with thermal or other energy to shrink the tissues in contact with the balloon 102). Alternatively, in some embodiments, the balloon may have a plurality of apertures or openings through which a substance may be delivered, sometimes under pressure, to cause the substance to bathe or diffuse into the tissues adjacent to the balloon. Alternatively, in some embodiments, radioactive seeds, threads, ribbons, gas or liquid, etc. may be advanced into the catheter shaft 100 or balloon 102 or a completely separate catheter body for some period of time to expose the adjacent tissue and to achieve a desired diagnostic or therapeutic effect (e.g. tissue shrinkage, etc.).

[0177] FIG. 5F shows a balloon/cutter catheter device 104 comprising a flexible catheter 106 having a balloon 108 with one or more cutter blades 110 formed thereon. The device 104 is advanced, with balloon 108 deflated, into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. and positioned with the deflated balloon 108 situated within an ostium, passageway or adjacent to tissue or matter that is to be dilated, expanded or compressed and in which it is desired to make one or more cuts or scores (e.g. to control the fracturing of tissue during expansion and minimize tissue trauma etc.). Thereafter, the balloon 108 may be inflated balloon to dilate, expand or compress the ostium, passageway, tissue or matter and causing the cutter blade(s) 110 to make cut(s) in the adjacent tissue or matter. Thereafter the balloon 108 may be deflated and the device 104 may be removed. The blade may be energized with mono or bi-polar RF energy or simply be thermally heated to part the tissues in a hemostatic fashion, as well as cause contraction of collagen fibers or other connective tissue proteins, remodeling or softening of cartilage, etc.

[0178] FIGS. 5G'-5G"' show a device 160 and method for delivery of a pressure expandable stent 166. This device 160 comprises a flexible catheter 162 having a balloon 164 thereon. Initially, as shown in FIG. 5G', the balloon 164 is deflated and the stent 166 is radially compressed to a collapsed configuration, around the deflated balloon 164. The catheter 162 with the balloon 164 deflated and the collapsed stent 166 mounted thereon is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. that is to be stented. Thereafter, the balloon 164 is inflated causing the stent 166 to expand to a size that frictionally engages the

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surrounding tissue so as to hold the stent 166 in place, as shown in FIG. 5G". In some instances the procedure will be performed for the purpose of enlarging a passageway (e.g., an ostium, meatus, etc.) and the stent 166 will be expanded to a diameter that is sufficiently large to cause the desired enlargement of the passageway and the stent will then perform a scaffolding function, maintaining the passageway in such enlarged condition. After the stent 166 has been fully expanded and implanted, the balloon 164 may be deflated and the catheter 162 removed as shown in FIG. 5G'". In some applications, the stent may contain a diagnostic or therapeutic substance as defined herein and such substance may elute from the stent 166 into the surrounding tissue to bring about a desired diagnostic or therapeutic effect. In some cases, the stent 166 may be permanently implanted. In other cases the stent 166 may be temporarily implanted. In cases where the stent 166 is temporarily implanted, it may be removed in a second procedure conducted to retrieve the stent 166 or the stent 166 may be made of bioabsorbable or biodegradable material such that it degrades or is absorbed within a desired period of time after implantation. In some cases, such as when the stent is to be placed within the ostium of a paranasal sinus, the stent and/or the balloon may be specifically shaped to facilitate and/or cause the stent 166 to seat in a desired position and to prevent unwanted slippage of the stent 166. For example, the stent 166 and/or balloon 164 may have an annular groove formed about the middle thereof or may be hourglass or venture shaped, to facilitate seating of the stent 166 within an ostium or orifice without longitudinal slippage of the stent 166. In some cases it may be desirable to leave a tether or suture attached to the stent 166 to allow for simple removal of the stent 166 in the physician's office or other suitable location. In some cases the procedure may be intended to actually break bone (e.g., where the stent is intended to dilate or enlarge a sinus ostium). Thus, the balloon 164 may be made of polymeric material including, but not limited to flexible polyvinyl chloride (PVC), polyethylene terephthalate (PET), cross-linked polyethylene, polyester, polyamide, polyolefin, polyurethane and silicone. Various balloon properties (strength, flexibility, thickness, etc.) may be modified by, but not limited to, blending, layering, mixing, co-extruding, irradiating, and other means of engineering balloon material(s). This allows for the use of compliant balloons that can conform to the surrounding structure or non-compliant balloons that can deform or break the surrounding structures (e.g., bone).

[0179] FIG. 5H shows an electrosurgical device 208 comprising a flexible shaft 210 (e.g., a catheter or solid shaft) having arched strut members 214 attached thereto. Electrodes 216 are located on the strut members 214. In some cases, the strut members may be of fixed configuration and in other cases the strut members 214 may be collapsible and expandable. In operation, the device 208 is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. Thereafter, current is applied to the electrodes 216 causing tissue adjacent to the struts 214 to be cauterized or heated. The electrodes 216 may be bipolar, monopolar or facilitated by any other suitable form of energy such as a gas or plasma arc. Additionally, sensing elements may also be attached to the catheter and/or strut members to monitor various parameters of the catheter and/or surrounding tissue (e.g., temperature, etc.). In instances where monopolar electrodes are used, a separate antenna electrode (not shown) will be applied to the patient's body in accordance with processes and techniques that are well known in the art.

[0180] FIG. 5I shows a device 218 that delivers a flow 222 of material (e.g., cryogenic material, diagnostic or therapeutic agent, etc.) or energy (laser light, infrared light, etc.) to the tissues adjacent to the passage or body cavity in which the device 218 is positioned. This device comprises a flexible catheter 220 with an outlet aperture or lens

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at or near its distal end, through which the flow of material or energy is delivered. This device may be used to cryogenically freeze polyps or other tissues or to deliver laser energy to turbinates or other tissues for the purpose of ablating the tissue or to heat the tissue to a temperature that results in shrinking of the tissue.

[0181] FIG. 5J shows an implantable pressure exerting device 224 that is implantable within a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. to exert pressure on bone, cartilage, soft tissue, etc. Examples of situations where it is desirable to apply such pressure to an anatomical structure include those wherein it is desired to splint or maintain approximation of a broken bone or those wherein it is desired to cause remodeling or gradual repositioning or reshaping of bone, cartilage, soft tissue or other structures. This implanatble device 224 comprises a pressure exerting member 228 and two or more plate members 226. The device 224 is initially constrained in a collapsed configuration wherein the pressure exerting member 228 is compressed or collapsed and the device 224 is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. where it is desired to apply pressure to an anatomical structure. When the device 224 is in the desired position, the pressure exerting member 228 is expanded or elongated to exert outward pressure on the plate members 226 and onto the anatomical structures against which the plate members 226 are positioned. In some embodiments, the pressure exerting member may comprise a spring. In other embodiments, the pressure exerting member may comprise a ratchet, hydraulic cylinder or other mechanical apparatus that may be adjusted to create a desired amount of pressure on the plate members 226. In some applications, the pressure exerting member 228 may be adjustable in situ (i.e., with the device implanted in the body) so as to allow the operator to periodically change the amount of pressure being applied to the anatomical structures of interest (e.g., the operator may change to position of a ratchet or add fluid to a hydraulic cylinder) thereby bringing about gradual remodeling or movement of an anatomical structure in a manner similar to that achieved during dental orthodontia. Thus, this pressure exerting device 224 has broad applicability in a variety of procedures including those intended to enlarge a sinus ostium or to straighten an intranasal septum.

[0182] FIGS. 5K-5K' and 5L show a forward rotary cutting catheter device 700 that comprises a flexible outer tube 702 and a flexible inner tube 704 disposed coaxially and rotatably mounted within the outer tube 702. One or more bearings 708 (e.g., a helical bearing or a series of individual cylindrical bearings) may be disposed between the outer tube 702 and inner tube 704, as shown. Alternatively, one or both apposing tube surfaces may be made of, lined with, or be coated by etc. a lubricious material such as silicone or PTFE to facilitate movement. A rotating cutter 706 is positioned on the distal end of the inner tube 704. In operation, as shown in FIG. 5K', the device 700 is advanced through a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. to a position where the distal end of the device 700 is positioned just behind some obstructive matter, such as a polyp P. The inner tube 704 and its cutter 706 are rotated as the device is advanced into the obstructive matter P and/or suction is applied through the lumen of the inner tube 704 and/or through the lumen of the outer tube 702 to draw the obstructive matter P into contact with the rotating cutter 706. It is to be appreciated that, although this embodiment shows a rotating cutter 706, various other types of cutters such as lasers, radiofrequency cutters and other mechanical cutters, etc. may be used instead. As the obstructive matter P is severed by the rotating cutter 706 the obstructive matter P or pieces thereof may be suctioned through the lumen of the inner tube 704 and/or through the lumen of the outer tube 702. In some applications, as shown in FIG. 5L, a scope or guidewire 710 may extend

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through the lumen of the inner tube to facilitate advancement and positioning of the device 700 prior to the removal of the obstructive matter P.

[0183] FIGS. 5M and 5N show a side rotary cutting device 714 comprising a flexible outer tube 718and a flexible inner tube 722 that is disposed coaxially and rotatably mounted within the outer tube 718. One or more bearings 730 (e.g., a helical bearing or a series of individual cylindrical bearings) may be disposed between the outer tube 718 and inner tube 722, as shown. Alternatively, one or both apposing tube surfaces may be made of, lined with, or be coated by etc. a lubricious material such as silicone or PTFE to facilitate movement. A rotating cutter 724 is positioned on the distal end of the inner tube 722. A side opening 720 is formed in the outer tube 718 and the cutter 724 is positioned proximal to the side opening 720. A pull member 728 extends through the inner tube 722 and is attached to a retractor head 726. In operation, the device 714 is advanced and/or torqued to a position where the side opening 720 is near a polyp, tissue or other obstructive matter to be removed. The inner tube 722 and its cutter 724 are rotated. In some applications, suction may be applied through the inner tube 722 and/or through the lumen of the outer tube 718 to draw the obstructive matter into the side opening 720. The pull member 728 is pulled in the proximal direction, causing the retractor head 726 to retract or pull the obstructive matter into contact with the rotating cutter 724. As the obstructive matter is severed by the rotating cutter, the severed obstructive matter or pieces thereof may be suctioned through the lumen of the inner tube 722 and/or through the lumen of the outer tube 718. The pull member 728 may then be advanced in the distal direction to return the retractor head 726 to its original position as shown in FIGS. 5M and 5N. An optional balloon 719 or other laterally extendable member may be located on the side of the catheter 718 opposite the side opening 720 to push the side opening 720 against a lumen wall or into the direction of a polyp or other tissue to be removed. Alternatively, the catheter may incorporate a deflectable tip or a curved distal end that may force the side opening of the catheter against a lumen wall or into the direction of a polyp or other tissue to be removed. With specific reference to FIG. 5N, there is shown a side rotary cutting device 714a that includes all of the elements of the device 714 shown in FIG. 5M, but includes a side lumen 731. A scope may be permanently positioned within this side lumen 731 or a scope may be temporarily inserted into (or through) the side lumen 731 to enable the operator to view the area near the side opening 720 and to facilitate the advancement and positioning of the device 714A. Also, the side lumen 731 may function as a guidewire lumen to allow the device 714A to be advanced over a guidewire.

[0184] It is to be understood that any of the devices described within this document may be further modified to include any one of the following devices within its structure: electromagnetic positioning sensor/detector (Biosense/JNJ, Surgical Navigation Technologies/Medtronic, Calypso Medical), RF sensor/transmitter, magnetic direction localizer (Stereotaxis, Inc.), thermal sensor, radiopaque composition, radioactive detection emitter/sensor, ultrasonic scanner/transmitter/receiver, Doppler scanner, electrical stimulator, fiber optic, digital optic, local diagnostic chip containing elements responsive to the presence or absence of certain substances and therefore having the ability to diagnose the presence of fungus, microbes, viruses, blood, abnormal mucous content, cancer cells, drugs of abuse, genetic abnormalities, metabolic bi-products, etc.

[0185] It is to be further understood that any and all of the devices described in this patent application may incorporate, or may be used in conjunction with, endoscopes. Such endoscopes will typically include light transmitting optical fibers for casting light in the area to be viewed by the scope and image transmitting optical fibers for carrying an

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image received by the scope to an eyepiece or monitor device located outside the patient's body. In some embodiments a scope, such as a disposable and/or flexible scope, may be affixed to the working device. Examples of such endoscopes that are suitable for incorporation into the working devices of this invention include that described in U.S. Pat. Nos. 4,708,434; 4,919,112; 5,127,393; 5,519,532; 5,171,233, 5,549,542, 6,551,239 and 6,572,538 as well as published U.S. Patent Application No. 2001/0029317A1, the entireties of which are expressly incorporated herein by reference.

[0186] It is to be further understood that any catheters or elongate flexible devices of this invention may include design elements that impact performance features which include, but are not limited to, durability, flexibility, stiffness, length, profile, lubricity, trackability, steerability, torqueability, deflectability, guidance, and radiopacity. Design elements can include, but are not limited to, use of various polymers and metals, use of varying durometer materials to establish a desired flexibility gradient along the device, blending/mixing/layering/co-extruding etc. various materials, using bearings or lubricious coatings or lubricious materials (e.g., silicone, PTFE, parylene, polyethene, etc.) where two or more surfaces will move relative to each other (e.g., guidewire or instrument lumen, deflecting tendon in lumen, etc.), use of braiding or springs to increase torque control over the device, using materials (e.g. barium, tantalum, etc.) to increase polymer radiopacity, and use of elements to predictably deflect various sections of the catheter (e.g., tension straps or wires, shape memory alloys such as nitinol, etc.).

[0187] It is to be further understood that any of the catheters, scopes, elongate working devices or other devices disclosed in this patent application may be rendered steerable or volitionally bendable, unless to do so would make such device inoperative for its intended purpose. Steerable catheters and scopes are well known in the art and may utilize mechanical steering assemblies (e.g., pull wires, hinges, etc.) or shape memory materials (e.g., nickel titanium alloys, shape memory polymers, etc.) to induce the device to undergo the desired bending or curvature after it has been inserted into the body. Examples of apparatus and construction that may be used to render these devices steerable or volitionally bendable include but are not limited to those described in U.S. Pat. No. 5,507,725 (Savage et al.), U.S. Pat. No. 5,656,030 (Hunjan et al.), U.S. Pat. No. 6,183,464 (Webster), U.S. Pat. No. 5,251,092 (Qin et al.), U.S. Pat. No. 6,500,130 (Kinsella et al.), U.S. Pat. No. 6,571,131 (Nguyen), U.S. Pat. No. 5,415,633 (Lazarus et al.), U.S. Pat. No. 4,998,916 (Hammerslag et al.), U.S. Pat. No. 4,898,577 (Badger et al.), U.S. Pat. No. 4,815,478 (Buchbinder et al.) and publised U.S. Patent Applications No. 2003/0181827A1 (Hojeibane et al.) and 2003/0130598A1 (Manning et al.), the entirities of which are expressly incorporated herein by reference.

[0188] FIG. 5O shows a flexible catheter 733 having a working lumen 734 that extends though the catheter 732 and terminates in a distal end opening. Optionally, a second lumen 736 may also extend though the catheter 732 and terminate in a distal end opening, as shown. An endoscope 738 may be permanently positioned within this lumen 736 or such endoscope 738 may be temporarily inserted into (or through) the lumen 736 to enable the operator to view the area distal to the catheter 732. Additionally or alternatively, a side scope or lumen 740 may be located on the catheter 732 and an endoscope may be permanently embodied by or positioned in or temporarily inserted into (or through) such side scope or lumen 740 to enable the operator to view the area distal to the catheter 732 and, in at least some cases, the distal end of the catheter 732 itself. In any devices which incorporate such optional side

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scope or lumen 740, the side scope or lumen 740 may be of any suitable length and may terminate distally at any suitable location and such side scope or lumen 740 is not limited to the specific positioning and the specific distal end location shown in the drawings. Also, in embodiments that incorporate a side scope or lumen 740 such side lumen may be employed as a guidewire or working lumen to permit the catheter to be advanced over a guidewire or for other working devices to be inserted therethrough.

[0189] FIG. 5P shows a balloon catheter and pressure expandable stent system 744 which includes all of the elements of the balloon expandable stent system shown in FIGS. 5G'-5G"' and, in addition, may incorporate an endoscope or side lumen. Specifically, referring to FIG. 5P, there is shown a balloon catheter and pressure expandable stent system 744 that comprises a flexible catheter 746 having a balloon 750 and pressure expandable stent 748 thereon. A side lumen 756 may be located on the catheter 746 and an endoscope may be permanently positioned in or temporarily inserted into (or through) such side lumen 756 to enable the operator to view the balloon 750 and stent 748 and to advance the catheter 749 to its desired position. Also, in embodiments that incorporate a side lumen 756 such side lumen may be employed as a guidewire lumen to permit the catheter 746 to be advanced over a guidewire. Optionally, a lumen may extend through the catheter 746 and through an opening 752 in the distal end of the catheter 749 and a straight, curved, bendable, deflectable or steerable scope and/or stent 754 may be passed through or received in that lumen to facilitate over the wire and/or scope assisted and/or guided and/or manipulated advancement of the catheter 749 to an intended location. In routine use, the balloon 750 is initially deflated and the stent 748 is radially compressed to a collapsed configuration, around the deflated balloon 750. The catheter 746 with the balloon 750 deflated and the collapsed stent 748 mounted thereon is advanced, under endoscopic guidance or over a guidewire, to a position within a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. that is to be stented. Thereafter, the balloon 750 is inflated causing the stent 748 to expand to a size that frictionally engages the surrounding tissue so as to hold the stent 748 in place. In some instances the procedure will be performed for the purpose of enlarging a passageway (e.g., an ostium, meatus, etc.) and the stent 748 will be expanded to a diameter that is sufficiently large to cause the desired enlargement of the passageway and the stent 748 will then perform a scaffolding function, maintaining the passageway in such enlarged condition. After the stent 748 has been fully expanded and implanted, the balloon 750 may be deflated and the catheter 748 removed. In some applications, the stent 748 may contain a diagnostic or therapeutic substance as defined herein and such substance may elute from the stent 748 into the surrounding tissue to bring about a desired diagnostic or therapeutic effect. In some cases, the stent 748 may be permanently implanted. In other cases the stent 748 may be temporarily implanted. In cases where the stent 748 is temporarily implanted, it may be removed in a second procedure conducted to retrieve the stent 748 or the stent 748 may be made of bioabsorbable or biodegradable material such that it degrades or is absorbed within a desired period of time after implantation. As shown in the examples of FIGS. 5R' and 5R", in some cases, such as when a stent is to be placed within the ostium of a paranasal sinus, the stent and/or the balloon may be specifically shaped to facilitate and/or cause the stent to seat in a desired position and to prevent unwanted slippage of the stent. For example, FIG. 5R' shows a device 1040 comprising a catheter 1042 having a balloon 1044 and stent 1046 mounted thereon as described above. However, in this embodiment, the balloon 1044 and stent 1046 are of a configuration where one end of the balloon 1044 and stent 1046 is larger in diameter than the other end. As described above in connection with other embodiments such as those shown in FIGS.

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5P and 5Q, a side scope or side lumen 1048 may optionally be formed on the catheter 1042 and/or a scope or guidewire 1050 may optionally be passed through a lumen of the catheter 1042 and out of its distal end. FIG. 5R" shows another device 1052 comprising a catheter 1054 having a balloon 1056 and stent 1058 mounted thereon as described above. However, in this embodiment, the balloon 1056 and stent 1058 are of a configuration where both ends of the balloon 1056 and stent 1058 are larger in diameter than the middle of the balloon 1056 and stent 1058. As a result, the stent 1058 has an annular groove or indentation formed circumferentially or about the mid-portion thereof or may be hourglass or venture shaped, to facilitate seating of the stent 1058 within an ostium or orifice without longitudinal slippage of the stent 1058. Again, as described above in connection with other embodiments such as those shown in FIGS. 5P and 5Q, a side scope or side lumen 1060 may optionally be formed on the catheter 1052 and/or a scope or guidewire 1062 may optionally be passed through a lumen of the catheter 1054 and out of its distal end. In cases where the procedure is intended to actually break bone (e.g., where the stent 1046, 1058 is intended to dilate or enlarge a sinus ostium) the specially shaped balloon 1044, 1056 may be made of strong polymeric material as described hereabove to enable it to exert bone-breaking pressure on the adjacent or surrounding bone as it is inflated.

[0190] FIGS. 5Q and 5Q' show a self expanding stent and delivery system 760 comprising a flexible outer sheath 762, a flexible inner tube 764 and a stent 768. This stent differs from the stent 748 of FIG. 5P only in that it is resilient and self-expanding rather than pressure expandable. The stent 768 is biased to an expanded configuration. Initially, it is compressed to a radially collapsed configuration on the outer surface of the inner tube 764 and the outer sheath 762 is advanced over the stent 768 to constrain the stent 768 in its collapsed configuration, as can be seen in the cross-sectional showing of FIG. 5Q'. A scope and/or guidewire 770 may be inserted through the lumen of the inner tube 764. Additionally or alternatively, a side lumen 772 may be located on the outer sheath 762 and an endoscope may be permanently positioned in or temporarily inserted into (or through) such side lumen 772 to enable the operator to view the distal portion of the system 760 and the area ahead of the distal end of the sheath 762 as the system is advanced. Also, in embodiments that incorporate a side lumen 772 such side lumen 772 may be employed as a guidewire lumen to permit the system 760 to be advanced over a guidewire. In routine operation the system 760, with its sheath 762 in a distally advanced position such that it surrounds and constrains the collapsed stent 768, is advanced, under endoscopic guidance and/or over a guidewire, to a position within a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. that is to be stented. Thereafter, when the stent 768 is positioned at the location to be stented, the sheath 762 is withdrawn, allowing the self-expanding stent 768 to spring or self expand to a radially expanded configuration in which it frictionally engages the surrounding anatomical structure. Thereafter, the remainder of the system 760 is removed, leaving the stent 768 implanted in the body. The stent 768 may perform dilation and scaffolding and/or substance delivery function (s) as described hereabove with respect to the pressure expandable stent 748 of FIG. 5P.

[0191] FIG. 5S shows a snare apparatus 780 comprising a flexible catheter 782 having a lumen 784 extending therethrough. A snare 786 having a general loop shape is advanceable out of the lumen 784 of the device 780. In some embodiments, the snare 786 may optionally be charged with electrical current or otherwise heated so that it performs a cauterization function as it cuts through tissue. Additionally or alternatively, in some embodiments, the snare 786 may be of variable diameter (e.g., a noose that

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may be tightened or loosened by the operator). Also, optionally, a scope or side lumen 788 may be located on the catheter 782 and a stationary or moveable endoscope may be permanently embodied in or temporarily inserted into (or through) such side lumen 788 to enable the operator to view the distal portion of the device 780 and the area of the snare 786. Also, in embodiments where the scope or side lumen 780 comprises a side lumen, such side lumen 788 may be employed as a guidewire lumen to permit the device 780 to be advanced over a guidewire. Alternatively, multiple lumens may run through catheter 782 such that they can accommodate a snare, a guidewire and/or an endoscope. In routine operation, the snare 786 is initially retracted within lumen 784 and the device 780 is advanced under endoscopic guidance and/or over a guidewire, to a position within a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. where a polyp or other matter to be snared or cut away is located. The snare 786 is advanced out of lumen 784 and positioned around the polyp or other matter and, thereafter, the snare may be pulled or moved, heated (if equipped for heating) and/or tightened (if equipped for tightening) so as to sever or cut the polyp or other matter. In some cases, the severed polyp or other matter bay be suctioned through the lumen 784. In other cases, a separate catheter or device may be introduced to retrieve the severed polyp or other matter. After completion of the procedure, the snare 786 may be retracted into lumen 784 and the device 780 may be removed. Also, in some embodiments, the snare 786 may be replaced by a basket, bag or other retrieval receptacle that is useable to capture and retrieve tissue or other matter and to withdraw it into the lumen of the catheter 782.

[0192] FIG. 5T shows a forceps device 790 which comprises a flexible shaft 792 having jaws or forceps 794 thereon. The jaws or forceps 794 may be volitionally opened and closed by the operator. A scope or side lumen 796 may be located on the flexible shaft 792, as shown. In embodiments where the scope or side lumen 792 comprises a scope, such scope may be fixed or moveable and may be used to observe or view the advancement of the device 790 and/or the use of the forceps 794. In embodiments where the scope or side lumen 796 comprises a side lumen, a stationary or moveable endoscope may be permanently embodied in or temporarily inserted into (or through) such side lumen 796 to enable the operator to view the distal portion of the device 790 and the area of the forceps 794. Also, in embodiments where the scope or side lumen 796 comprises a side lumen, such side lumen 796 may be employed as a guidewire lumen to permit the device 790 to be advanced over a guidewire. In routine operation, the device 790 is advanced, either alone or through the lumen of a catheter, and possibly under endoscopic guidance and/or over a guidewire, to a position within a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. where matter is to be grasped by the forceps. Thereafter, under optional endoscopic guidance and observation, the forceps 794 are used to grasp the intended matter. In some embodiments, a distal portion of the flexible shaft 792 may be bendable or steerable as indicated by doted lines on the example of FIG. 5T. In some embodiments, the jaws of the forceps 794 may be designed to sever and retain a specimen of tissue for biopsy or other tissue sampling applications or the forceps 794 may comprise scissors for cutting tissue, cartilage, bone, etc. Alternatively, a lumen may pass through flexible shaft 792 and exit through or next to the forceps 794 and allow the passage of a guidewire or endoscope through such lumen.

[0193] FIGS. 5U and 5U' show a telescoping system 800 comprising a flexible catheter 802, a flexible scope 804 and a guidewire 806. The flexible scope 804 comprises a plurality of light transmitting pathways 808 (e.g., optical fibers) that transmit light in the distal direction from a light source (not shown) and out of the distal end of the scope

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804 such that the light is cast onto the object or anatomical structure to be viewed. Also, the scope comprises an image transmitting pathway 810 (e.g., optical fiber and lens) that carries reflected light from distal end of the scope to an eyepiece or monitor on which the image may be viewed. The scope also has a guidewire lumen 805 extending therethrough and opening through its distal end. The scope 804 is advanceable through the flexible catheter 802 and a guidewire 806 that is advanceable through a guidewire lumen 805 of the scope, as shown. In routine operation, the telescoping system 800 may be inserted into the nose and the scope 804 may be utilized to view an anatomical structure, such as the ostium of a paranasal sinus, and facilitate advancement of the guidewire into that anatomical structure. Thereafter, the scope may be advanced over the guidewire and into the anatomical structure (e.g., though the ostium and into the interior of the paranasal sinus). The scope may then be used to examine the anatomical structure (e.g., to view the condition of the mucosa lining the paranasal sinus and to look for signs of infection, tumors, etc.) The catheter 802 may then be advanced over the scope 804 and into the anatomical structure (e.g., the catheter tip may be advanced through the ostium and into the paranasal sinus). Thereafter, the scope 804 may be removed and a diagnostic or therapeutic substance as defined hereabove may be infused through the catheter 802 and/or another working device, including but not limited to the working devices shown in FIGS. 5A-5T and 5V-5Y"", may be advanced through the catheter 802 and into the anatomical structure where it is used to perform a diagnostic or therapeutic function.

[0194] FIG. 5V shows a side port suction/cutting device 820 which comprises a flexible outer tube 822, a flexible inner tube 830 is disposed coaxially and rotatably mounted within the outer tube 822. One or more bearings 834 (e.g., a helical bearing or a series of individual cylindrical bearings) may be disposed between the outer tube 822 and inner tube 830, as shown. Alternatively, one or both apposing tube surfaces may be made of, lined with, or be coated by etc. a lubricious material such as silicone or PTFE to facilitate movement. A rotating cutter 832 is positioned on the distal end of the inner tube 830. A side opening 828 is formed in the outer tube 822 and the cutter 832 is positioned proximal to the side opening 828. Optionally, a tapered atraumatic distal tip 824 may be formed on the distal end of the outer tube 822 and the side opening 828 may be configured to form a ramp or chute through which matter may pass into the area immediately distal to the cutter 832. Also optionally, an opening may be formed in the distal end of the distal tip such that a guidewire or scope 826 may pass through the lumen of the inner tube 830 and out of the opening in the distal tip, as shown. In operation, the device 820 is advanced to a position where the side opening 828 is near a polyp, tissue or other obstructive matter to be removed. The inner tube 830 and cutter 832 are rotated. Suction may be applied through the lumen of the inner tube 830 and/or through the lumen of the outer tube 822 to draw the obstructive matter into the side opening 828 and into contact with the rotating cutter 832. As the obstructive matter is severed by the rotating cutter 832, the severed obstructive matter or pieces thereof may be suctioned through the lumen of the inner tube 830 and/or through the lumen of the outer tube 822. Of course, as in any of the working devices described in this patent application, a scope or side lumen of any size or length, into which a scope may be inserted (not shown in FIG. 5U but shown in various other figures such as FIGS. 50, 5P, 5Q, 5R, 5S and 5T) may be attached to the outer tube 822 at a position which allows a scope to be used to view the side opening 828 and matter entering the side opening 828. Alternatively, the catheter may incorporate a deflectable tip or a curved distal end which may force the side opening of the catheter against a lumen wall or into the direction of a polyp or other tissue to be removed.

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[0195] In some applications of the invention, it may be desirable to break bone, such as the thin bone that forms the periphery of a sinus ostium. FIGS. 5W-5X"" show devices that may be used to break bones at specific locations. For example, FIGS. 5W-5W" show a device 840 that comprises a flexible catheter 842 having a rigid cylindrical member 847 located on the distal end thereof. An advanceable and retractable member 846 extends through the catheter 842 and is connected to a distal tip member 844. The distal tip member 844 has a cylindrical proximal end 849 that is sized to be received within the cylindrical member 847. As shown in FIGS. 5W' and 5W", in routine operation, the advanceable and retractable member 846 is advanced to separate the distal tip member 844 from the rigid cylindrical member 847. The device 840 is advanced to a position adjacent to a bony structure, such as a structure formed by bone B covered with mucosal tissue M. The device is positioned such that the bony structure is between the cylindrical proximal end 849 of the distal tip member 844 and the cylindrical member 847. The advanceable and retractable member 846 is then retracted, pulling the distal tip member 844 in the proximal direction and capturing the bony structure between the cylindrical proximal end 849 of the distal tip member 844 and the cylindrical member 847, thereby breaking the bone B. The shape or configuration of the distal tip member 844 and/or cylindrical member 847 may be varied depending on the shape and pattern of break desired to be made in the bone B, In this regard, FIGS. 5X-5X"" show alternative constructions or configurations that may be used to produce different shapes and patterns of bone breaks. FIG. 5X' shows an assembly 850 comprising a distal tip member 852 that has three (3) projections on its proximal side and a proximal member 854 that has three (3) notches in its distal surface, such notches being configured to receive the three projections of the distal tip member 852 when the distal tip member 852 is retracted. FIG. 5W" shows an assembly 860 comprising a distal tip member that forms a pincher for breaking bone. FIG. 5X"' shows an assembly 870 comprising a collapsible distal tip member 872 and a cylindrical proximal member 874. The distal tip member 872 may be initially deployed in a collapsed configuration that allows it to be advanced through an opening such as the ostium of a sinus. Then, it may be expanded to a size that is too large in diameter to pass through that opening, thereby causing it to strike the periphery of the opening as it is retracted in the proximal direction. In this manner, the assembly 5X"' may be used to break bone B all the way around an ostium or aperture. FIG. 5X"" shows another assembly 880 comprising a distal tip 882 that has two projections on its proximal side and a proximal member 884 that has one projection on its distal side. The projection on the distal side of the proximal member 884 is received between the projections formed on the proximal side of the distal member 882 when the distal member 882 is retracted in the proximal direction.

[0196] FIGS. 5Y'-5Y""" show various substance delivery implants that may be implanted into the nasal cavities, paranasal sinuses, middle or inner ear, nasopharynx, etc. to deliver a diagnostic or therapeutic substance as defined herein. These devices may be formed of permanent or bio-absorbable material. In many instances, these devices will be formed of a polymer (e.g., Hydron, hydrogel, collagen, etc.) within which the diagnostic or therapeutic substance is contained or a polymer or metal that is coated with or otherwise contains the substance. FIG. 5Y' shows an implant 1070 that comprises a bead or pellet. FIG. 5Y" shows an implant 1072 that comprises a wafer. FIG. 5Y"' shows an implant 1074 that comprises a brad or staple. FIG. 5Y"" shows an implant 1076 that comprises a screw or helical coil. FIG. 5Y""' shows an implant 1078 that comprises a strand or coil, another example of which is shown in FIG. 7E and described herebelow.

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[0197] D. Pre-Shaped Guide Catheters

[0198] FIGS. 6A-6E show various guide catheters that may be used in the methods of the present invention.

[0199] FIG. 6A shows a sphenoid sinus guide catheter 120 that incorporates three preformed curves 122, 124, 126. The three dimensional shape of the catheter 120 is such that, when advanced through a nasal cavity, the distal end of the catheter 120 will tend to enter the ostium of the sphenoid sinus.

[0200] FIG. 6B shows a frontal sinus guide catheter 128 that incorporates two preformed curves 130, 133. The shape of the catheter 128 is such that, when advanced through a nasal cavity, the distal end of the catheter 128 will tend to enter the ostium of the frontal sinus.

[0201] FIG. 6C shows a maxillary sinus guide catheter 136 that incorporates three preformed curves 138, 140, 142. The three dimensional shape of the catheter 136 is such that, when advanced through a nasal cavity, the distal end of the catheter 136 will tend to enter the ostium of the maxillary sinus.

[0202] FIG. 6D shows an ethmoid sinus guide catheter 144that incorporates two preformed curves 146, 148. The three dimensional shape of the catheter 144 is such that, when advanced through a nasal cavity, the distal end of the catheter 144 will tend to enter the ostium of the ethmoid sinus.

[0203] In some of the methods of the invention, it will be desirable to plug the ostium of a sinus or another opening such as the nasolacrimal duct or the nasopharyngeal opening into the Eustachian tube. Thus, any of the above-described guide catheters 120, 128, 136, 144 may be equipped with a plug on its distal tip such that when its distal end enters the sinus ostium it will plug the sinus thereby preventing fluid from exiting the sinus through the ostium. An example of one such procedure is shown in FIG. 7B and described herebelow.

[0204] FIG. 6E shows a plug guide catheter 149 that is useable for temporarily plugging the opening into a nasolacrimal duct. This plug guide catheter 149 has two preformed curves 150, 152 and a plug 154 at its distal tip. The three dimensional configuration of this catheter 149 is such that, when advanced through a nasal cavity the distal tip plug 154 will tend to enter the opening into the nasolacrimal duct. The plug may consist of, but is not limited to, a semi-rigid plug or a balloon on the end of the catheter. It will be appreciated that a different shaped plug guide catheter (not shown) may be used to plug the Eustachian tube.

[0205] E. Devices and Methods for Treatment Within Paranasal Sinuses:

[0206] FIGS. 7A-7G provide examples of devices and methods for performing diagnostic or therapeutic procedures within the paranasal sinuses. In the methods of the prior art, rigid or flexible scopes are sometimes used to visualize the ostia of sinuses but, typically, such scopes have not actually been advanced into the interior of the sinuses. As described hereabove, the present invention does provide devices and methods for placing endoscopes inside the paranasal sinuses and such methods may or may not be used in conjunction with any of the diagnostic or therapeutic devices and methods shown in FIGS. 7A-7G.

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[0207] FIG. 7A shows an electrode network delivery device 168 being used to deliver radiofrequency or electrical current to the lining of the sphenoid sinus SS. This device 168 comprises a flexible catheter 168 that has been inserted through the sphenoidal sinus ostium SSO. An expandable electrode network such as a cage 170 is advanced out of the distal end of the catheter 169. Electrodes 172 are positioned at spaced apart locations on the cage. As the cage 170 expands, it places the electrodes in contact with the lining of the sinus SS. Current is delivered to the electrodes 172 to ablate all mucous producing tissue within the sinus in preparation for the sinus to be functionally isolated or embolized, or to ablate tumors or polyps located within the sinus.

[0208] FIG. 7B shows a procedure where a flowable substance, such as a diagnostic or therapeutic substance as defined above, is introduced into the sphenoid sinus SS and the ostium SSO has been plugged by a sphenoid sinus plug guide catheter device 174. This device 174 comprises a flexible catheter 176 having the shape shown in FIG. 6A and described above and a plug member 178 at its distal tip. The fluid is maintained in the sphenoid sinus SS until the plug catheter device 174 is removed, allowing the fluid to then drain through the sphenoid sinus ostium SSO. This procedure may be particularly useful when it is desired to fill a sinus with radiographic contrast agent to visualize the entire sinus or to apply a therapeutic agent to the entire lining of the sinus by entirely filling the sinus with the agent and maintaining such fully filled state for a desired period of time to allow the agent to act on the entire lining of the sinus. Imaging materials may be mixed with visous agents so that they simulate mucous or if simple structural imaging is desired it may be preferable to have substances of lower viscosity. It may be also desirable to use imaging agents which bind with the surface of the mucosa to minimize the amount of injected contrast.

[0209] FIG. 7C shows a balloon catheter device 180 which comprises a flexible catheter 182 having a balloon 184 that is positioned in the sphenoid sinus ostium SSO and inflated to hold the catheter 182 in position while a quantity of a diagnostic or therapeutic substance 186 (as defined above) is introduced into the interior of the sinus SS. This therapeutic substance may be one or more of any of the drug delivery materials and drugs selected from the previous list, or may additionally include a sclerotic agent such as alcohol to uniformly kill all the tissues within the cavity. Other materials such as capasian or other neuro-toxic substances may be considered to eliminate the pain and other sensation within the caity.

[0210] FIG. 7D shows a sensor equipped catheter device 190 that comprises a flexible catheter 192 having a sensor 194 thereon for 3 dimensional mapping or navigation. This procedure may be used to map the precise configuration of the interior of the sphenoid sinus SS. Examples of the construction and use of such sensor 194 and associated systems/computers are found in U.S. Pat. Nos. 5,647,361; 5,820,568; 5,730,128; 5,722,401; 5,578,007; 5,558,073; 5,465,717; 5,568,809; 5,694,945; 5,713,946; 5,729,129; 5,752,513; 5,833,608; 5,935,061; 5,931,818; 6,171,303; 5,931,818; 5,343,865; 5,425,370; 5,669,388; 6,015,414; 6,148,823 and 6,176,829, the entirities of which are expressly incorporated herein by reference.

[0211] FIG. 7E shows an implant delivery device 196 which comprises a flexible catheter 198 that is inserted through the sphenoid sinus ostium SSO and into the sphenoid sinus SS and is being used to implant a coil 200 within the sphenoid sinus. Such coil 200 may comprise an elongate fiber or other elongate member that may contain a diagnostic or therapeutic substance as defined herein. This coil 200 may be

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constructed to embolize the sinus for the purpose of to permanently close off the sinus and to prevent any further mucous production, trapping of secretions or infection and/or to deliver a diagnostic or therapeutic substance to the tissues lining the sinus. For example, a coil for sustained delivery of an antimicrobial agent may be implanted in a sinus to treat an acute or chronic infection of that sinus. In some cases, the coil may be bioabsorbable.

[0212] FIG. 7F shows an over-the-wire endoscopic system 240 being used to view the interior of the sphenoid sinus SS. A flexible catheter 242 is positioned in or near the sphenoid sinus ostium SSO and a guidewire 248 is advanced through the sphenoid sinus ostium SSO and into the sphenoid sinus SS. An over-the-wire endoscope 246 (such as a 2.2 mm over-the-wire scope available commercially as Model # AF-28C from Olympus America, Melville, N.Y.) is advanced over the guidewire 248 and is used to examine the interior of the sphenoid sinus SS.

[0213] FIG. 7G shows a biopsy system 250 being used to obtain a biopsy specimen from a lesion L within the sphenoid sinus SS. A flexible catheter 242 is positioned in or near the sphenoid sinus ostium SSO and an endoscope 246 is advanced through the catheter 242 and into the interior of the sinus SS. A biopsy instrument 252 is inserted through a working channel of the endoscope 246 and is used, under endoscopic visualization and guidance, to obtain a specimen of the lesion L.

[0214] F. General Examples Of Interventions Using the Occluder & Access Devices and/or Working Devices

[0215] FIGS. 8A-8D show two of many possible examples of methods wherein the occluder & access devices 10, 12 of FIGS. 2A and 2B and/or various working devices such as those shown in FIGS. 5A-5Y" " are used to perform diagnostic and/or therapeutic procedures within the nose, nasopharynx or paranasal sinuses.

[0216] In general, diagnostic interventions in accordance with this invention may include: a) anatomic studies where obstructions, sizes, parameters or abnormalities in anatomy are visualized and/or identified, b) dynamic studies where gas, mucous or fluid is introduced into the nose, sinus, nasal cavity, nasopharynx, Eustachian tube, inner or middle ear, etc and the movement of such materials is monitored to asses drainage or gas flow issues and c) perturbation studies where an agent (e.g., an allergen, irritant, agent that induces mucous production, etc.) is introduced into the nose, sinus, nasal cavity, nasopharynx, Eustachian tube, inner or middle ear, etc., and the patient's response and/or flow of the endogenously produced mucous or other secretions is assessed. Examples of procedures that may be used to perform these types of diagnostic interventions include, but are not limited to, the following:

[0217] 1. Gaining Access To Sinus: Access to one of more of the paranasal sinuses is gained by advancement of catheter(s) into the sinus or sinuses of interest. A guidewire may be inserted into the sinus first and the catheter may then be advanced over the guidewire and into the sinus. In some cases, a sinus ostium guide catheter of the type shown in FIGS. 6A-6E may be inserted into the ostium of the sinus and a smaller catheter may be advanced through the guide catheter. One or more scopes may be used to visualize the sinus ostium and to guide the guidewire and/or catheter into the sinus ostium. In some cases, a steerable guidewire, catheter and/or scope may be used to gain entry into the sinus. In some cases, occlusion & access device(s) such as those shown in FIGS. 2A-2R, may be inserted and the guidewire(s), catheter(s) and/or

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scope(s) used to access the sinus may be inserted through a device insertion port on the occluder & access device.

[0218] 2. Mucous Flow Study: Optionally, after catheter access to the sinus has been gained, an imageable contrast substance or radioactive material such as microbeads or a flowable contrast medium (e.g., an iodinated contrast solution with or without a thickening agent to adjust its viscosity to that of mucous) that may have a consistency similar to that of mucous may be injected into the sinus. An imaging or scanning technique (e.g., X-ray, fluoroscopy, CT scan, ultrasound, MRI, radiation detector, gamma camera, etc.) may then be used to observe the flow of the contrast medium through and out of the sinus. In some cases a fluoroscope with a C-arm may be used in a fashion similar to that used in coronary artery catheterization and angiography procedures to allow the clinician to view the movement of the contrast medium from different vantage points or angles. To facilitate flow of the contrast medium from the sinus, the previously inserted catheter(s) and/or guidewires and/or scope(s) may be backed out of the sinus and ostium or removed completely, to allow normal flow to occur. The patient's head and/or other body parts may be repositioned to observe different postural drainage effects. In this manner, the clinician may specifically locate and identify which anatomical structures are obstructing or interfering with normal mucous flow from the sinus.

[0219] 3. Air Flow Study: Optionally, after access to the sinus has been gained as described in No. 1 above, an imageable or traceable gas, such as a radiolabled gas, radiopaque gas or a gas with imageable or radioactive microbeads therein, may be injected through a catheter and into the sinus. An imaging device or tracing device (e.g., radiation detector, gamma camera, X-ray, fluoroscopy, CT scan, ultrasound, MRI) may then be used to observe subsequent movement or dissipation of the gas as it passes out of the sinus and/or equilibrates with other sinus cavities. In this manner, the clinician may determine whether normal gas exchange in the sinus is occurring and may locate and identify any anatomical structures or irregularities that are obstructing or interfering with normal gas flow and/or gas exchange.

[0220] 4. Anatomic Dimension Study: An entire paranasal sinus or other anatomical passageway or structure may be filled with an imageable substance or otherwise measured to determine its actual dimensions and/or configuration. In some such studies, access to a paranasal sinus will be gained as described in No.1 above and the sinus may be filled with an imageable substance (e.g., contrast medium). A suitable imaging technique (e.g., X-ray, fluoroscopy, CT scan, ultrasound, MRI, radiation detector, gamma camera, etc.) may then be used to determine the size and shape of the sinus. Again, in such procedure, a moveable imaging apparatus such as a fluoroscope with a C-arm may be used to view and measure the contrast filled sinus from different vantage points or angles. One example of such a procedure is shown in FIG. 7B and described hereabove.

[0221] 5. Endoscopic Study: A flexible and/or steerable endoscope, as described above, may be inserted into the nose, sinus, nasal cavity, nasopharynx, Eustachian tube, inner or middle ear, etc and used to visually examine the anatomy and/or to observe a treatment and/or to assess the efficacy or completeness of a previously rendered treatment. In cases where it is desired to view the interior of a paranasal sinus, access to the sinus may be gained as described in No. 1 above and the endoscope may be advanced into the interior of the sinus either directly or over a guidewire.

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[0222] 6. Transillumination Study: A flexible light emitting instrument (e.g., a catheter having a powerful light emitting apparatus at its distal end) may be advanced into the nose, paranasal sinus, nasal cavity, nasopharynx, Eustachian tube, inner or middle ear, etc and used to illuminate anatomical structures. Direct or endoscopic observation may then be made from outside the body and/or from other locations within the nose, sinus, nasal cavity, nasopharynx, Eustachian tube, inner or middle ear, orbit, cranial vault, etc. to observe anatomical structures and/or to detect aberrant openings or leaks through which the light passes. In cases where the light emitter and/or the viewing instrument (e.g., endoscope) is/are positioned within paranasal sinus(es) access to the sinus(es) may be gained as described in No. 1 above and the light emitter and/or viewing instrument may then be advanced into the sinus(es) either directly or over guidewire(s).

[0223] 7. Other Imaging Studies: Other imaging techniques such as MRI, CT, etc. in combination with any of the modalities set forth in Nos. 1-6 above and modifications may be made to any of those techniques to adjust for sinus anatomy or other pathology.

[0224] After any or all of the elected diagnostic studies have been completed, one or more working devices, such as the flexible devices described herein and shown in FIGS. 5A-5Y"", may be inserted and used to perform therapeutic procedure(s).

[0225] As shown in the example of FIG. 8A, an anterior/posterior occluder & access device 10 is inserted through the right nasal cavity NC. The device's anterior occluder 14 is positioned to occlude the nostril on the right side while its posterior occluder (not seen in FIGS. 8A-8E) occludes the posterior choanae or nasopharynx. An anterior occluder & access device 12 is inserted into the left nasal cavity and its occluder 40 occludes the left nostril. In this manner, a sealed operative field is established between the posterior occluder positioned in the posterior choanae or nasopharynx and the anterior occluders 14, 40 positioned in the right and left nostrils or anterior nasal cavities.

[0226] FIGS. 8B-8C show an example of a method for performing a diagnostic and/or therapeutic procedure in the right frontal sinus FS in the patient in whom the occluder & access devices 10, 14 have been inserted. In FIG. 8B, a frontal sinus guide catheter 128 is inserted into the working device insertion port 30 and advanced through tube 16 and out of outlet aperture 22. The guide catheter 128 is then advanced to a position where its distal end is in the right frontal sinus ostium.

[0227] In FIG. 8C, a working device 202 is inserted through the guide catheter 128 and into the frontal sinus FS. This working device 202 may comprise any of the devices shown in FIGS. 5A-5Y"" or 7A-7G. In some procedures, it may be desired to initially introduce a contrast agent into the frontal sinus FS and pull back the guide catheter 128 to allow the contrast agent to drain from the sinus. Imaging of the draining contrast agent may be used to diagnose drainage impairment and to identify the specific anatomical structures that are causing the impairment of drainage. Thereafter, the guide catheter may be reinserted into the frontal sinus ostium and the working device (s) 202 may be used to modify the structures that have been identified and impairments to drainage. Thereafter, the contrast injection and imaging steps may be repeated to assess whether the procedure(s) performed have overcome or corrected the drainage problem that had been initially diagnosed. A suction device 206 is connected by way of suction line 204 to port 36 to suction blood, other fluid or debris from the operative field

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during the procedure.

[0228] FIGS. 8D and 8E show an example of a treatment rendered to the left maxillary sinus MS, in the same patient in whom the occluder & access devices 10, 14 have been inserted. In FIG. 8D, a guide catheter 136 is inserted into device insertion aperture 44 and advanced through tube 41 to a position where the distal end of the guide catheter 136 is positioned in the ostium of the maxillary sinus MS.

[0229] Thereafter, as shown in FIG. 8E, a working device 202 is inserted through the guide catheter 136 and into the maxillary sinus MS. This working device 202 may comprise any of the devices shown in FIGS. 5A-Y"" or 7A-7G. In some procedures, it may be desired to initially introduce a contrast agent into the maxillary sinus MS by the same procedure described above in reference to FIGS. 8B and 8C.

[0230] After all of the desired procedures have been completed, the anterior occluders 14, 40 and posterior occluder (not shown on FIGS. 8A-8E) are collapsed (e.g., deflated) and the occluder & access devices as well as the guide catheters and working devices are removed (except for implants such as stents, embolic coils, substance delivery implants, etc.).

[0231] G. Cochlear Implant Procedure

[0232] FIGS. 9A-9C show a procedure for installation of a cochlear implant in accordance with the present invention. In this procedure, the nasopharyngeal opening into the Eustachian tube ET is located and a guidewire is initially advanced into the Eustachian tube ET. A catheter 900 is advanced over the guidewire to a location where the distal end of the catheter 900 is in or near the tympanic cavity TC of the middle ear. Thereafter, if deemed necessary, a forceps device 790 and/or other devices are advanced through the catheter 900 and used to remove the small bones of the sear (i.e., the malleus, incus and stirrup) as shown in FIG. 9A. This optional removal of the bones of the middle ear may be done under endoscopic visualization using an endoscope equipped device such as the endoscope equipped forceps device 790 shown in FIG. 5T and described above. As shown in FIG. 9B, a cochlear guide catheter 904 having a "J" shaped distal tip 905 is advanced through the catheter 900 to a position where the tip 905 of the cochlear guide catheter 904 is directed into or inserted into the cochlea C. In some applications, the cochlear guide catheter 904 may be configured to advance into the round window of the cochlea and through the secondary tympanic membrane that covers the round window. If necessary, a penetrator such as a needle, drill or cutter may be advanced through or formed or positioned on the distal end of the cochlear guide catheter 904 to penetrate through the secondary tympanic membrane. In other applications, the cochlear guide catheter 904 may be positioned adjacent to the cochlea and a cochleostomy device (e.g., a penetrator such as a drill, needle or cutter) may be advanced through or formed or positioned on the distal end of the cochlear guide catheter 904 and used to form a cochleostomy through which the distal end of the guide catheter 904 is advanced into the cochlea C. Thereafter, a cochlear electrode array 906 is advanced through the cochlear guide catheter 904 and into the cochlea, as seen in FIG. 9B. One example of a commercially available cochlear electrode array is the Nucleus 24 Countour device manufactured by Cochlear Corporation.

[0233] Thereafter, a sound receiving device or transducer 908 is advanced through the catheter 900 and positioned in the tympanic cavity TC. The sound receiving device or

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transducer 908 may be of any type that is a) sufficiently small to pass through the Eustachian tube ET and into the tympanic cavity TC and b) useable to perform the desired function of converting sound waves to electrical impulses and delivering such electrical impulses to the cochlear electrode array 906. A microphone/power/electronics device 910 may be positioned in the outer ear canal, as shown in FIG. 9C or may be implanted subcutaneously or in any other way that is acceptable. Certain non-limiting examples of devices 906, 908, 910 that may be useable for this procedure are set forth in PCT International Patent Publication No. WO 2004/018980 A2 designating the United States, the entirety of which is expressly incorporated herein by reference.

[0234] It is to be appreciated that the invention has been described hereabove with reference to certain examples or embodiments of the invention but that various additions, deletions, alterations and modifications may be made to those examples and embodiemnts without departing from the intended spirit and scope of the invention. For example, any element or attribute of one embodiment or example may be incorporated into or used with another embodiment or example, unless to do so would render the embodiment or example unsuitable for its intended use. All reasonable additions, deletions, modifications and alterations are to be considered equivalents of the described examples and embodiments and are to be included within the scope of the following claims.

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Espacenet

Claims: JP2007537784 (A) — 2007-12-27

Devices, systems and methods for diagnosing and treating sinusitus and other disorders of the ears, nose and/or throat

Claims not available for JP2007537784 (A)
Claims of corresponding document: US2005240147 (A1)

A high quality text as facsimile in your desired language may be available amongst the following family members:

AU2005249376 (B2) CA2563711 (A1) EP1744708 (A2) ES2591282 (T3) US2005240147 (A1) WO2005117755 (A2) EP2638871 (A1) US2008097295 (A1) US2008154250 (A1) US2008275483 (A1) US2010100181 (A1) US2010210901 (A1) US2017071625 (A1) US2017164965 (A1) US2019388113 (A1) US2020022717 (A1) US2021007762 (A1)

- Original claims
- Claims tree

The EPO does not accept any responsibility for the accuracy of data and information originating from other authorities than the EPO; in particular, the EPO does not guarantee that they are complete, up-to-date or fit for specific purposes.

1. A method for diagnosing and/or treating sinusitis or another disorder affecting the nose, paranasal sinuses or other anatomical structures of the ear, nose or throat, said method comprising the steps of:
(A) placing a port device in the nostril or nasal cavity on at least one side of the intranasal septum, said port device comprising a device insertion port and a valve that is operative to allow a working device to be inserted through said device insertion port while preventing blood or other fluid from backflowing out of the device insertion port at least when no working device is inserted therethrough;
(B) advancing at least one working device through the port device to a location within the nose, nasopharynx or paranasal sinus; and
(C) using the working device to perform a diagnostic or therapeutic procedure

2. A method according to claim 1 wherein the working device is used to perform a procedure selected from the group consisting of:
i) delivering an imageable or traceable substance;
ii) delivering a therapeutically effective amount of a therapeutic substance;
iii) implanting a stent, tissue remodeling device, substance delivery implant or other therapeutic apparatus;
iv) cutting, ablating, debulking, cauterizing, heating, lasing, dilating or otherwise modifying tissue;
v) grafting or implanting cells or tissue;

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vi) reducing, setting, screwing, applying adhesive to, affixing, decompressing or otherwise treating a fracture;
vii) delivering a gene or gene therapy preparation;
viii) cutting, ablating, debulking, cauterizing, heating, lasing, forming an osteotomy in or otherwise modifying bony or cartilaginous tissue within paranasal sinus or elsewhere within the nose;
ix) remodeling or changing the shape, size or configuration of a sinus ostium or other anatomical structure that affects drainage from one or more paranasal sinuses;
x) removing puss or aberrant matter from the paranasal sinus or elsewhere within the nose; and
xi) scraping or otherwise removing cells that line the interior of a paranasal sinus;
xii) removing all or a portion of a tumor;
xiii) removing a polyp; and
xiv) delivering histamine, an allergen or another substance that causes secretion of mucous by tissues within a paranasal sinus to permit assessment of drainage from the sinus.

3. A method according to claim 1 wherein a port device positioned in Step A comprises an anterior nasal occluder and access device that comprises an occluder and a working device insertion port.

4. A method according to claim 3 wherein Step A further comprises deploying the anterior nasal occluder and access device such that its occluder occludes the nostril or nasal cavity on one side of the nasal septum and wherein Step B comprises inserting the working device through the working device insertion opening and advancing the working device to a location within the nose, nasopharynx or paranasal sinus.

5. A method according to claim 4 wherein a first anterior nasal occluder and access device is positioned on one side of the nasal septum and a second anterior nasal occluder and access device is positioned on the other side of the nasal septum.

6. A method according to claim 1 comprising the steps of:
providing a posterior occluder device that is configured to occlude the posterior choanae, nasopharynx or pharynx at a location that is posterior to the intranasal septum and superior to the glotis; and
positioning the posterior occluder device such that it does occlude the posterior choanae, nasopharynx or pharynx posterior to the intranasal septum and superior to the glottis, thereby deterring fluid from draining into the patient's esophagus or trachea during the performance of the method.

7. A method according to claim 1 comprising the steps of:
providing an anterior/posterior nasal occluder and access device that comprises an anterior occluder member, a working device insertion port and a posterior occluder member; and
deploying the anterior/posterior nasal occluder and access such that; its anterior occluder occludes a nostril or nasal cavity on one side of the nasal septum and its posterior occluder occludes the posterior choanae, nasopharynx or pharynx posterior to the intranasal septum and superior to the glottis; and
wherein Step B comprises:
inserting the working device through the working device insertion opening and advancing the working device to a location within the nose, nasopharynx, middle ear or paranasal sinus.

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8. A method according to claim 7 further comprising the step of:
providing an anterior nasal occluder device; and
and positioning the anterior nasal occluder device such that it occludes the other nostril or nasal cavity on the other side of the nasal septum.

9. A method according to claim 7 further comprising the step of:
providing an anterior nasal occluder and access device that comprises an occluder member and a working device insertion port; and
positioning the anterior nasal occluder and access device such that its occluder occludes the other nostril or nasal cavity on the other side of the nasal septum.

10. A method according to claim 9 further comprising the step of:
inserting a working device through the working device insertion port of the on the anterior nasal occluder and access device and advancing that working device to a location within the nose, nasopharynx or paranasal sinus.

11. A method according to claim 7 wherein the anterior/posterior occlusion and access device comprises 1) a tube having an anterior end, a posterior end and at least one lumen; ii) an anterior occluder at a first location on the tube; iii) a posterior occluder at a second location on the tube, said second location being posterior to said first location; iv) a working device insertion opening located anterior to the anterior occluder; and v) a working device exit opening located between the anterior occluder and the posterior occluder and placing said anterior/posterior nasal occlusion and access device such that its anterior occluder occludes the nostril or nasal cavity on one side of the intranasal septum and its posterior occluder occludes the nasopharynx at a location posterior to the intranasal septum and superior to the glottis.

12. A method according to claim 11 wherein Step B comprises inserting a working device through the working device insertion opening and advancing the working device out of the working device exit opening to a location within the nose, nasopharynx or paranasal sinus.

13. A method according to claim 1 further comprising the step of:
suctioning fluid from the nose, nasopharynx or paranasal sinus.

14. A method according to claim 11 wherein the anterior/posterior nasal occlusion and access device comprises a suction lumen and a suction opening formed in said tube between the anterior occluder and the posterior occluder and wherein the method further comprises the step of:
applying suction to the suction lumen to suction matter through the suction opening and through the suction lumen.

15. A method according to claim 1 wherein Step B comprises:
inserting a guide catheter; and, thereafter,
inserting another working device through the guide catheter.

16. A method according to claim 1 wherein:
Step B comprises advancing a tube through the port device to a location within a paranasal sinus; and
Step C comprises delivering a flowable contrast agent into a paranasal sinus through the tube and subsequently imaging the flowable contrast agent to assess the manner in

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which the flowable contrast agent drains from the paranasal sinus.

17. A method according to claim 16 wherein the flowable contrast agent has a viscosity similar to the viscosity of mucous.

18. A method according to claim 16 wherein the imaging is carried out using an imaging apparatus that is moveable and wherein the imaging apparatus is moved to different positions to different vantage points relative to the patient's anatomy.

19. A method according to any of claim 1 wherein Step B comprises inserting a scope into the nose or paranasal sinus and wherein Step C comprises using the scope to visualize structures within the nose and/or paranasal sinuses.

20. A method according to claim 19 wherein the scope is used to guide, facilitate or verify positioning of another working device.

21. A method according to claim 19 wherein the scope is used to guide, facilitate or verify positioning of a guide catheter and wherein another working apparatus is then advanced through the guide catheter after the guide catheter has been positioned.

22. A method according to claim 1 wherein Step C comprises implanting a stent.

23. A method according to claim 22 wherein the stent is positioned at least partially within the ostium of a paranasal sinus.

24. A method according to claim 22 wherein the stent comprises a substance eluting stent.

25. A method according to claim 24 wherein the substance eluting stent elutes a therapeutically effective amount of at least one substance selected from the group consisting of:
an antibiotic;
an antifungal;
an antiparacytic;
an antimicrobial;
a steroid;
a vasoconstrictor;
a leukotriene inhibitor;
an IgE inhibitor;
an anti-inflammatory;
a mast cell stabilizer;
an antihistamine;
an imunomodulator;
a chemotherapeutic agent;
an antineoplastic agent;
a mucolytic agent;
an agent that thins or otherwise changes the viscosity of mucous;
a substance that facilitates remodeling of soft tissue and/or bone and/or cartilage.

26. A method according to claim 1 wherein Step C comprises implanting a device that will change the size, shape, configuration or position of soft tissue, bone or cartilage.

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27. A method according to claim 26 wherein the implanted device can be adjusted one or more times after implantation and wherein the method further comprises the step of adjusting the implanted device at least one time subsequent to implantation.

28. A method according to claims 1 wherein Step C comprises enlarging or modifying a sinus ostium, nasal meatus, or other passage way within the nose or nasopharynx.

29. A method according to claim 1 wherein Step C comprises introducing a diagnostically or therapeutically effective amount of a diagnostic or therapeutic substance to a location within the nose, nasopharynx or paranasal sinus.

30. A method according to claim 29 wherein the substance is contained in a substance delivery implant and wherein Step C comprises implanting the substance delivery implant at a location within the nose, nasopharynx or paranasal sinus.

31. A method according to claim 29 wherein Step C comprises injecting the substance at a location within the nose, nasopharynx or paranasal sinus.

32. A method according to claim 29 wherein the substance is selected from the group consisting of:
an imageable contrast agent;
a diagnostic indicator agent;
an antibiotic;
an antifungal;
an antiparacytic;
an antimicrobial;
a steroid;
a vasoconstrictor;
a leukotriene inhibitor;
an IgE inhibitor;
an anti-inflammatory;
a mast cell stabilizer;
an antihistamine;
an imunomodulator;
a chemotherapeutic agent;
an antineoplastic agent;
a mucolytic agent;
an agent that thins or otherwise changes the viscosity of mucous; and
a substance that facilitates remodeling of soft tissue and/or bone and/or cartilage.

33. An anterior/posterior occlusion and access device for use in the diagnosis and/or treatment of sinusitis or a disorder of the ear, nose or throat, said device comprising:
a tube having an anterior end, a posterior end and at least one lumen;
an anterior occluder at a first location on the tube;
a posterior occluder at a second location on the tube, said second location being posterior to said first location;
a working device insertion opening located anterior to the anterior occluder; and
a working device exit opening located between the anterior occluder and the posterior occluder; and
at least one additional element selected from the group consisting of a) a valve that is operative to allow a working device to be inserted through said device insertion port while preventing blood or other fluid from backflowing out of the device insertion port at

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least when no working device is inserted therethrough, b) at least one moveable suction port for suctioning blood, fluid or debris from a plurality of locations between the anterior occluder and posterior occluder and/or c) separate infusion and suction lumens such that fluid may be infused into a location between the anterior and posterior occluders at the same time that fluid is being suctioned from a location between the anterior and posterior occluders.
said nasal access and occlusion device being deployable such that i) the anterior occluder occludes the nostril or nasal cavity on one side of the intranasal septum ii) the posterior occluder occludes the nasopharynx at a location posterior to the intranasal septum and iii) a working device may be inserted through the working device insertion opening and advanced out of the working device exit opening to a location within the nose, nasopharynx or paranasal sinus.

34. A device according to claim 33 wherein the anterior occluder comprises a balloon.

35. A device according to claim 33 wherein the posterior occluder comprises a balloon.

36. A device according to claim 33 which includes at least first and second working device exit openings such that a working device may be selectively advanced out of either the first or second working device exit opening.

37. A system that comprises a nasal access and occlusion device according to claim 33 in combination with at least one working device selected from the group consisting of:
a guidewire;
a guide catheter;
a guide catheter shaped to advance into the ostium of a paranasal sinus;
a balloon catheter,
apparatus for delivery of a stent;
apparatus for delivery of a substance-eluting stent;
implantable apparatus for exerting pressure on bone or soft tissue to cause reshaping of the bone or soft tissue;
apparatus for cutting tissue;
apparatus for ablating tissue;
apparatus for debulking tissue;
apparatus for cauterizing tissue;
apparatus for dilating a passageway;
apparatus for delivering a cryogen;
apparatus for delivering a radiographic contrast agent,
apparatus for delivering a diagnostic or therapeutic substance;
a cannula;
an endoscope;
a sensor;
a light;
a diagnostic device;
a therapeutic device.

38. A device according to claim 33 further comprising at least one suction port located on the tube between the anterior occluder and the posterior occluder such that fluid or debris may be aspirated though the aspiration port and through a lumen of the tube.

39. A system comprising a device according to claim 33 in combination with an anterior

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nasal occlusion and access device that is positionable on the other side of the nasal septum, said anterior nasal occlusion and access device comprising:
an anterior occluder for occluding the nostril or nasal cavity on one side of the nasal septum; and
a working device insertion opening through which a working device may be inserted and advanced past the anterior occluder to a location within the nose, nasopharynx or paranasal sinus.

40. A system according to claim 39 wherein the anterior occluder of the anterior nasal occlusion and access device comprises a balloon.

41. A device according to claim 33 further comprising a valve associated with the working device insertion opening, said valve being configured to prevent backflow out of the working device opening when no working device is inserted through said working device insertion opening.

42. A system according to claim 39 further comprising a valve associated with the working device insertion opening of the anterior nasal occlusion and access device that is positionable on the other side of the nasal septum, said valve being configured to prevent backflow out of the working device opening when no working device is inserted through said working device insertion opening.

43. A nasal access and anterior occlusion device for use in the diagnosis and/or treatment of sinusitis or a disorder of the ear, nose or throat, said device comprising:
an anterior occluder for occluding the nostril or nasal cavity on one side of the nasal septum; and
a working device insertion port through which a working device may be inserted and advanced past the anterior occluder to a location within the nose, nasopharynx or paranasal sinus; and
at least one valve that allows a working device to be inserted through said working device insertion port and prevents blood or other fluid from backflowing out of the working device insertion port, at least when no working device is inserted therethrough.

44. A device according to claim 43 wherein the anterior occluder comprises a balloon.

45. A system that comprises an anterior nasal occlusion and access and access device according to claim 43 in combination with at least one working device selected from the group consisting of:
a guidewire;
a guide catheter;
a guide catheter shaped to advance into the ostium of a paranasal sinus;
a balloon catheter,
apparatus for delivery of a stent;
apparatus for delivery of a substance-eluting stent;
implantable apparatus for exerting pressure on bone or soft tissue to cause reshaping of the bone or soft tissue;
apparatus for cutting tissue;
apparatus for ablating tissue;
apparatus for debulking tissue;
apparatus for cauterizing tissue;
apparatus for dilating a passageway;
apparatus for delivering a cryogen;

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apparatus for delivering a radiographic contrast agent,
apparatus for delivering a diagnostic or therapeutic substance;
a cannula;
an endoscope;
a sensor;
a light;
a diagnostic device;
a therapeutic device.

46. A device according to claim 43 further comprising a valve associated with the working device insertion opening, said valve being configured to prevent backflow out of the working device opening when no working device is inserted through said working device insertion opening.

47. A method for diagnosing or locating an obstruction that impedes drainage from a paranasal sinus or for assessing the efficacy of previously rendered treatment intended to improve or modify drainage from a paranasal sinus, said method comprising the steps of:
A. introducing a flowable medium into the paranasal sinus; and,
B. monitoring the flow or diffusion of the flowable medium from the paranasal sinus.

48. A method according to claim 47 further comprising the step of occluding the nasopharynx posterior to the nasal septum but superior to the glottis so as to deter drainage of the flowable medium into the esophagus or trachea.

49. A method according to claim 47 further comprising the step of occluding the nostril or nasal cavity on at least one side of the intranasal septum to deter drainage of the flowable medium out of the nostril.

50. A method according to claim 47 wherein Step A comprises inserting a catheter into the paranasal sinus and infusing the flowable medium through the catheter and into the paranasal sinus.

51. A method according to claim 47 further comprising the steps of:
providing an anterior nasal occlusion and access device that comprises an anterior occluder and a device insertion passageway;
positioning the anterior nasal occlusion and access device such that its occluder occludes the nostril or nasal cavity on one side of the intranasal septum; and
wherein Step A comprises inserting a catheter through the device insertion passageway, advancing the catheter to or through the ostium of the paranasal sinus and infusing the contrast medium through the catheter and into the paranasal sinus.

52. A method according to claim 51 wherein the anterior nasal occlusion and access device comprises an anterior occluder for occluding the nostril or nasal cavity on one side of the nasal septum and a working device insertion port through which a working device may be inserted and wherein:
Step A comprises i) inserting a catheter through the working device insertion port, ii) advancing the catheter to or through the ostium of the paranasal sinus and iii) infusing the contrast medium through the catheter and into the paranasal sinus.

53. A method according to claim 47 further comprising the steps of:
providing an anterior/posterior nasal occlusion and access device that comprises an

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anterior occluder, a posterior occluder and a device insertion passageway; and positioning the anterior/posterior nasal occlusion and access device such that its anterior occluder occludes the nostril or nasal cavity on one side of the intranasal septum and its posterior occluder occludes the nasopharynx posterior to the intranasal septum and superior to the glottis; and
wherein Step A comprises advancing a catheter through the device insertion passageway to or through the ostium of the paranasal sinus and infusing the contrast medium through the catheter and into the paranasal sinus.

54. A method according to claim 47 wherein the flowable medium is an imageable contrast medium and wherein Step B of the method comprises imaging the imageable contrast medium.

55. A method according to claim 47 wherein Step B is carried out using a moveable imaging device and comprises obtaining images from a plurality of vantage points.

56. A method according to claim 55 wherein the movable imaging device comprises a radiographic imaging device and a C-arm and wherein Step B comprises moving the C-arm to obtain images from a plurality of vantage points.

57. A method according to claim 47 wherein the flowable medium is a radioactive or radiolabled fluid and wherein Step B of the method comprises tracing the radioactive or radiolabled fluid using a device that detects radioactivity.

58. A method for diagnosing or locating an obstruction that impedes drainage from a paranasal sinus or for assessing the efficacy of previously rendered treatment intended to improve or modify drainage from a paranasal sinus, said method comprising the steps of:
(A) introducing into the paranasal sinus a substance that causes tissues lining the paranasal sinus to secrete mucous or other secretions; and,
(B) monitoring the flow of the mucous or other secretions from the paranasal sinus.

59. A method according to claim 58 wherein the substance introduced in Step A comprises histamine.

60. A method according to claim 58 wherein the substance introduced in Step A comprises an allergen to which the patient is allergic.

61. A method according to claim 58 wherein the drainage of the mucous or other secretions is assessed visually using an endoscope.

62. A method according to claim 58 wherein Step A further comprises causing a contrast agent to be combined with the mucous or other secretions and wherein the drainage of mucous or other secretions is assessed by imaging the contrast agent.

63. A device for removing polyps or other tissue from the nose, nasopharynx or paranasal sinus, said device comprising:
a flexible catheter having a distal end and a lumen;
a flexible tube having an open distal end and a lumen extending therethrough, said flexible tube being rotatably disposed within a lumen of the catheter such that the flexible tube may rotate while the catheter does not rotate;
a rotating cutter on the distal end of the flexible tube; and

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an opening formed in the catheter such that matter may be received through the opening and cut by the rotating cutter.

64. A device according to claim 63, further comprising a connector for connecting the lumen of the flexible tube to a source of negative pressure such that matter that is cut by the rotating cutter will be suctioned though the open distal end and through the lumen of the flexible tube.

65. A device according to claim 63 wherein the opening in the catheter is an opening in the distal end of the catheter.

66. A device according to claim 63 wherein the opening in the catheter is a side opening formed in a side of the catheter.

67. A device according to claim 63 wherein there is at least one bearing disposed between the catheter and the flexible tube.

68. A device according to claim 63 further comprising a scope which is useable to view the distal end of the catheter while the device is inserted in the body of a patient.

69. A device according to claim 68 wherein the scope extends through the lumen of the flexible tube.

70. A device according to claim 68 wherein the scope is attached to the exterior of the catheter.

71. A device according to claim 70 wherein the scope is disposed in a lumen on one side of the catheter.

72. A device according to claim 70 further comprising a side lumen on the catheter.

73. A system comprising a device according to claim 72 in combination with a scope positioned in the side lumen.

74. A system comprising a device according to claim 72 in combination with a guidewire positioned in the side lumen.

75. A device according to claim 66 further comprising moveable retractor apparatus that is operative to retract matter that has entered the opening into contact with the rotating cutter.

76. A device according to claim 75 wherein the moveable retractor apparatus comprises an elongate member having a retractor head, said elongate member being advanceable in a distal direction to move the retractor head to a location distal to the side opening and retractable in the proximal direction to move the retractor head in the proximal direction such that the retractor head will propel matter that has entered the opening into contact with the rotating cutter.

77. A device according to claim 66 wherein the catheter has a closed distal tip.

78. A device according to claim 77 further comprising a lumen that extends through the flexible tube and through an opening formed in the distal tip of the catheter.

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79. A system comprising a device according to claim 78 in combination with a scope positioned within the lumen that extends through the flexible tube and through an opening formed in the distal tip of the catheter.

80. A system comprising a device according to claim 78 in combination with a guidewire positioned within the lumen that extends through the flexible tube and through an opening formed in the distal tip of the catheter.

81. A method for treating deafness or hearing impairment in a human or veterinary patient having a Eustachian tube, a cochlea, a tympanic cavity and an outer ear, said method comprising the steps of:
(A) inserting a flexible catheter through the patient's nose and into the Eustachian tube;
(B) providing a cochlear implant system comprising a cochlear electrode array, a transducer and a power source;
(C) advancing the cochlear electrode array through the catheter that is inserted in the Eustachian tube and into the cochlea; and
(D) communicating the cochlear electrode array to the transducer and power source such that the cochlear implant system delivers sound-associated electrical impulses to the cochlea.

81. A method according to claim 81 wherein Step A comprises using a scope to visualize the Eustachian tube and guiding said catheter into the Eustachian tube.

83. A method according to claim 81 wherein Step C comprises inserting a cochlear guide through the catheter that is positioned in the Eustachian tube and advancing the electrode array over or through the cochlear guide and into the cochlea.

84. A method according to claim 81 wherein Step C comprises advancing the cochlear electrode array through the round window of the cochlea.

85. A method according to claim 81 wherein Step C further comprises penetrating the secondary tympanic membrane.

86. A method according to claim 81 wherein Step C comprises creating a cochleostomy and advancing the cochlear electrode through the cochleostomy.

87. A method according to claim 81 further comprising the step of passing the transducer through the Eustachian tube and implanting the transducer in the tympanic cavity.

88. A method according to claim 87 wherein the method further comprises the step of removing bones from the tympanic cavity prior to implantation of the transducer in the tympanic cavity.

89. A method according to claim 81 further comprising the step of placing the power supply in the outer ear canal.

90. A method according to claim 7 further comprising the step of adjusting the distance between the anterior occluder member and the posterior occluder member.

91. An anterior/posterior occlusion and access device according to claim 33 wherein

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the distance between the anterior occluder and posterior occluder is adjustable.

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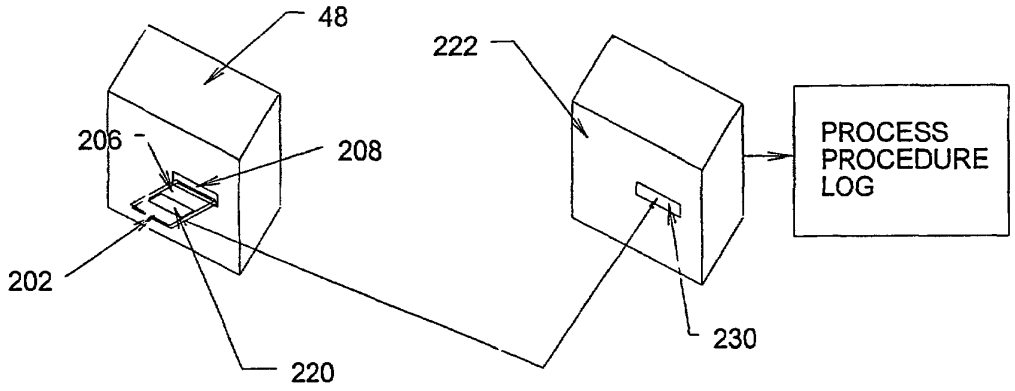
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(57) Abstract: A device for treating a tissue region is supplied with a separate usage key card (202). The usage key card (202) comprises a storage medium (204), which is formatted to contain an identification code unique to the usage key card (202). The usage key card (202) is adapted to be read by a remote reader (48), to download the identification code for processing by a controller (54) for the device. Processing of the identification code by the controller (54) either enables or disables operation of the device according to prescribed criteria. A viewable image is generated on a display screen (420) that changes in response to processing of the identification code.

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GRAPHICAL USER INTERFACE FOR MONITORING AND CONTROLLING USE OF MEDICAL DEVICES

RELATED APPLICATION

This application is a continuation-in-part of co-pending United States Patent Application Serial Number 09/026,296, filed February 19, 1998, and entitled "Method for Treating Sphincter." This application is also a continuation-in-part of co-pending United States Patent Application Serial Number 09/495,390, filed January 31, 2000 and entitled "Systems and Methods for Monitoring and Controlling Use of Medical Devices." This application is also a continuation-in-part of co-pending provisional United States Patent Application Serial Number 60/152,749, filed September 8, 1999 and entitled "Systems and Methods for Monitoring and Controlling Use of Medical Devices."

FIELD OF THE INVENTION

The invention is directed to systems and methods for monitoring and controlling use of medical devices.

BACKGROUND OF THE INVENTION

Use of medical devices intended to treat or diagnose conditions of the body can sometimes generate stress on the material or materials from which the devices are made. The material stress can alter the physical characteristics of the devices, making future performance of the devices unpredictable.

In addition, exposure to blood and tissue during use can entrap biological components on or within

many medical devices. Despite cleaning and subsequent sterilization, the presence of entrapped biological components can lead to unacceptable pyrogenic reactions.

The effects of material stress and damage caused during a single use of a medical device, coupled with the possibility of pyrogen reactions even after resterilization, reasonably justify imposing a single use restriction upon many medical devices.

SUMMARY OF THE INVENTION

The invention provides systems and methods for monitoring and controlling use of medical devices. The systems and methods employ a controller to control operation of the device and a reader to download information to the controller. The systems and methods also include a usage key card adapted to be handled separate from the device and comprising a storage medium formatted to contain an identification code unique to the usage key card. Upon reading by the reader, the identification code is downloaded to the controller. The controller includes a processing function for processing the identification code to either enable or disable operation of the device according to prescribed criteria. The systems and methods further include a display screen and an operating system to generate a viewable image on the display screen that changes in response to processing of the identification code by the processing function.

In one embodiment, the processing function causes the controller to create a table by registering unlike identification codes in memory as they are downloaded by the reader. The controller enables operation of the device when a new identification code is registered in the table. In this arrangement, the operating system displays a first image to prompt input to create the table for the device using the processing function.

In one embodiment, the processing function causes the controller to disable operation of the device when the given identification code matches an identification code in the table. In this arrangement, the operating system displays a second image, different than the first image, to prompt exchange of the device when operation of the device is disabled as a result of the processing function.

In one embodiment, the processing function causes the controller to register in the table, a time period of use of the device. In this arrangement, the processing function causes the controller to disable operation of the device when the time of use exceeds a prescribed period. The operating system displays a second image, different than the first image, to prompt exchange of the device when operation of the device is disabled as a result of the processing function.

In one embodiment, the device applies radio frequency energy to the tissue region.

Features and advantages of the inventions are set forth in the following Description and Drawings, as well as in the appended Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a diagrammatic view of a system for treating body sphincters and adjoining tissue regions, which embodies features of the invention;

Fig. 2 is a perspective view, with portions broken away, of a device usable in association with the system shown in Fig. 1 having an operative element for contacting tissue shown in a collapsed condition;

Fig. 3 is a perspective view, with portions broken away, of the device shown in Fig. 2, with the operative element shown in an expanded condition;

Fig. 4 is a perspective view, with portions broken away, of the device shown in Fig. 2, with the

operative element shown in an expanded condition and the electrodes extended for use;

Fig. 5 is an enlarged view of the operative element shown in Fig. 4, with the electrodes extended for use;

Fig. 6 is a perspective view of a kit containing a device, such as shown in Figs. 2 to 5, and a usage key card;

Fig. 7 is an enlarged, mainly schematic view of the usage key card shown in Fig. 6, embodied as a floppy disk, and also showing the pre-formatted files it contains;

Fig. 8 is a schematic view of a controller, which the system shown in Fig. 1 incorporates, showing the pre-programmed rules by which information contained on the usage key card shown in Figs. 6 and 7 is read and processed;

Fig. 9 is a schematic view of another processing device that reads information from the usage key card for further processing;

Fig. 10 is a left perspective views of an integrated generator/controller apparatus for use in association with a disposable treatment device, the apparatus including a graphical user interface (GUI) that aids in monitoring and controlling the incidence of use of the disposable treatment device;

Fig. 11 is a representative SETUP display that can be implemented by the GUI shown in Fig. 10 as part of monitoring and controlling the incidence of use of the disposable treatment device;

Fig. 12 is a representative EXCHANGE display that can be implemented by the GUI shown in Fig. 10 as part of monitoring and controlling the incidence of use of the disposable treatment device; and

Fig. 13 is a flow chart showing the various

states and modes that the apparatus shown in Fig. 10 employs in implementing the GUI in monitoring and controlling the incidence of use of the disposable treatment device.

The invention may be embodied in several forms without departing from its spirit or essential characteristics. The scope of the invention is defined in the appended claims, rather than in the specific description preceding them. All embodiments that fall within the meaning and range of equivalency of the claims are therefore intended to be embraced by the claims.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1 shows one embodiment of a system 10, which monitors and controls the use of an operative element 12. The system 10 is well adapted for association with single use, catheter-based devices. Therefore, in the illustrated embodiment, the operative element 12 is part of a catheter-based treatment device 26. It should be appreciated, however, that the system 10 is also adaptable for use with devices and methods that are not necessarily catheter-based.

I. The Treatment Device

In the illustrated embodiment, the device 26 includes a handle 28 made, e.g., from molded plastic. The handle 28 is sized to be conveniently held by a physician, to introduce the catheter tube 30 into the targeted tissue region.

The handle 28 carries a flexible catheter tube 30. The catheter tube 30 can be constructed, for example, using standard flexible, medical grade plastic materials. The catheter tube 30 has a distal end 34, which carries the operative element 12.

The operative element 12 can support, for example, a device for imaging body tissue, such as an endoscope, or an ultrasound transducer. The operative element 12

can also support a device to deliver a drug or therapeutic material to body tissue. The operative element 12 can also support a device for sensing a physiological characteristic in tissue, such as electrical activity, or for transmitting energy to stimulate or form lesions in tissue.

In the illustrated embodiment, the device 26, in use, is intended to treat dysfunction of sphincters and adjoining tissue regions in the upper gastrointestinal tract, e.g., in the lower esophageal sphincter and adjacent cardia of the stomach, as well as in the lower gastrointestinal tract, e.g., in the intestines, rectum and anal canal. Still, it should be appreciated that the system 10 can be used in association with other devices and methods used to treat other dysfunctions elsewhere in the body, which are not necessarily sphincter-related. For example, the various aspects of the invention have application in procedures requiring ablation of tissue throughout the body, or treatment of hemorrhoids, or restoring compliance to or otherwise tightening interior tissue or muscle regions.

In the illustrated embodiment, one function that the operative element 12 is to perform is to apply energy in a selective fashion to a targeted body region, which, for the purpose of illustration, can be the lower esophageal sphincter, or cardia, or both. The applied energy creates one or more lesions, or a prescribed pattern of lesions, below the mucosal surface of the esophagus or cardia. The subsurface lesions are formed in a manner that preserves and protects the mucosal surface against thermal damage.

It has been discovered that natural healing of the subsurface lesions leads to a physical tightening of the sphincter and/or adjoining cardia. The subsurface lesions can also result in the interruption of aberrant

electrical pathways that may cause spontaneous sphincter relaxation. In any event, the treatment can restore normal closure function to the sphincter.

The structure of the operative element 12 to achieve this result can vary. A representative embodiment is shown in Figs. 2 to 4, in which the operative element 12 comprises a three-dimensional basket 56. The basket 56 includes one or more spines 58, and typically includes from four to eight spines 58, which are assembled together by a distal hub 60 and a proximal base 62.

In the illustrated embodiment, an expandable structure 72 comprising a balloon is located within the basket 56. The balloon structure 72 can be made, e.g., from a Polyethylene Terephthalate (PET) material, or a polyamide (non-compliant) material, or a radiation cross-linked polyethylene (semi-compliant) material, or a latex material, or a silicone material, or a C-Flex (highly compliant) material.

The balloon structure 72 presents a normally, generally collapsed condition, as Fig. 2 shows. In this condition, the basket 56 is also normally collapsed about the balloon structure 72, presenting a low profile for deployment into the esophagus 10.

The catheter tube 30 includes an interior lumen, which communicates with the interior of the balloon structure 72. A fitting 76 (e.g., a syringe-activated check valve) is carried by the handle 28. The fitting 76 communicates with the lumen. The fitting 76 couples the lumen to a syringe 78 (see Fig. 3). The syringe 78 injects fluid under pressure through the lumen into the balloon structure 72, causing its expansion.

Expansion of the balloon structure 72 urges the basket 56 to open and expand (see Fig. 3). The force exerted by the balloon structure 72, when expanded, is sufficient to exert an opening force upon the tissue

surrounding the basket 56.

Each spine 58 carries an electrode 66 (see Fig. 4). In the illustrated embodiment, each electrode 66 is carried within the tubular spine 58 for sliding movement. Each electrode 66 slides from a retracted position, withdrawn in the spine 58 (shown in Fig.3) and an extended position, extending outward from the spine 58 (see Fig. 4) through a hole in the spine 58. A push-pull lever 68 on the handle 28 is coupled by one or more interior wires to the sliding electrodes 66. The lever 68 controls movement electrodes between the retracted position (by pulling rearward on the lever 68) and the extended position (by pushing forward on the lever 68). The electrodes 66 have sufficient distal sharpness and strength, when extended, to penetrate a desired depth into tissue the smooth muscle of the esophageal or cardia 20 wall. The desired depth can range from about 4 mm to about 5 mm.

In this arrangement (see Fig. 1), the system 10 includes a generator 38 to supply the treatment energy to the electrodes 66. In the illustrated embodiment, the generator 38 supplies radio frequency energy, e.g., having a frequency in the range of about 400 kHz to about 10 mHz. Of course, other forms of energy can be applied, e.g., coherent or incoherent light; heated or cooled fluid; resistive heating; microwave; ultrasound; a tissue ablation fluid; or cryogenic fluid.

A cable 40 extending from the proximal end of the handle 28 terminates with an electrical connector 42. The cable 40 is electrically coupled to the operative element 12, e.g., by wires that extend through the interior of the handle 28 and catheter tube 30. The connector 42 plugs into the generator 38, to convey the generated energy to the operative element 12.

The electrodes 66 are formed of material that

conducts radio frequency energy, e.g., nickel titanium, stainless steel, e.g., 304 stainless steel, or a combination of nickel titanium and stainless steel.

In the illustrated embodiment (see Fig. 5), an electrical insulating material 70 is coated about the proximal end of each electrode 66. When the distal end of the electrode 66 penetrating the smooth muscle of the esophageal sphincter 18 or cardia 20 transmits radio frequency energy, the material 70 insulates the mucosal surface of the esophagus 10 or cardia 20 from direct exposure to the radio frequency energy. Thermal damage to the mucosal surface is thereby avoided. The mucosal surface can also be actively cooled during application of radio frequency energy, to further protect the mucosal surface from thermal damage.

In the illustrated embodiment (see Fig. 5), at least one temperature sensor 80 is associated with each electrode. One temperature sensor 80 senses temperature conditions near the exposed distal end of the electrode 66, a second temperature sensor 80 is located on the corresponding spine 58, which rests against the muscosal surface when the balloon structure 72 is inflated.

The system 10 (see Fig. 1) can also include certain auxiliary processing equipment, e.g., an external fluid delivery apparatus 44 for supplying cooling liquid to the targeted tissue, e.g., through holes in the spines, and an external aspirating apparatus 46 for conveying liquid from the targeted tissue site, e.g., through other holes in the spine or elsewhere on the basket 56.

The system 10 also includes a controller 52. The controller 52, which preferably includes a central processing unit (CPU), is linked to the generator 38, the fluid delivery apparatus 44, and the aspirating apparatus 46. Alternatively, the aspirating apparatus 46 can comprise a conventional vacuum source typically present

in a physician's suite, which operates continuously, independent of the controller 52. The controller 52 governs the delivery of processing fluid and, if desired, the removal of aspirated material.

The controller 52 also governs the power levels, cycles, and duration that the radio frequency energy is distributed to the electrodes 66, to achieve and maintain power levels appropriate to achieve the desired treatment objectives. The controller 52 can condition the electrodes 66 to operate in a monopolar mode. In this mode, each electrode 66 serves as a transmitter of energy, and an indifferent patch electrode (not shown) serves as a common return for all electrodes 66. Alternatively, the controller 52 can condition the electrodes 66 to operate in a bipolar mode. In this mode, one of the electrodes comprises the transmitter and an other electrode comprises the return for the transmitted energy. The bipolar electrode pairs can electrodes 66 on adjacent spines, or electrodes 66 spaced more widely apart on different spines.

The controller 52 includes an input/output (I/O) device 54. The I/O device 54 allows the physician to input control and processing variables, to enable the controller to generate appropriate command signals. The I/O device 54 also receives real time processing feedback information from the temperature sensors 80, for processing by the controller 52, e.g., to govern the application of energy and the delivery of processing fluid. The I/O device 54 also includes a graphical user interface (GUI), to graphically present processing information to the physician for viewing or analysis.

II. Monitoring and Control of Reuse

The handle 28 and the catheter tube 30 form an integrated construction intended for a single use and subsequent disposal as a unit. Alternatively, the handle

28 can comprise a nondisposable component intended for multiple uses. In this arrangement, the catheter tube 30, and components carried at the end of the catheter tube 30 comprise a disposable assembly, which the physician releasably connects to the handle 28 at time of use and disconnects and discards after use. The catheter tube 30 can, for example, include a male plug connector that couples to a female plug receptacle on the handle 28.

To protect patients from the potential adverse consequences occasioned by multiple use, which include disease transmission, or material stress and instability, or decreased or unpredictable performance, the controller 54 includes a module 48 that controls use of the device 26.

In the illustrated embodiment (see Fig. 6), the device 26 is supplied as part of a kit 200 that includes, together with the device 26, a usage key card 202. The kit 200 packages the device 26 and usage key card 202 as a unitary, single use item in a sterile fashion within peripherally sealed sheets of plastic film material that are torn or peeled away at the instance of use.

The presence of the device 26 and user key card 200 packaged together in the kit 200 verifies to the physician or user that device 26 is sterile and has not be subjected to prior use. The physician or user is thereby assured that the device 26 meets established performance and sterility specifications. No unused device 26 is supplied in the kit 200 without a usage key card 202, and vice versa.

The usage key card 202 incorporates a storage medium 204 that is readable by the module 48. The storage medium 204 contains information that enables at least two use control and monitoring functions.

The first use control and monitoring function of the

usage key card 202 occurs prior to use of the device 26 in association with the generator 38. To enable use of the generator 38 in association with the device 26, the physician must first present the usage key card 202 for reading by the module 48. To enable use of the device 26, the controller 54 must then find that the usage key card 202 meets the criteria necessary for its registration by the controller 54. The criteria are designed to indicate the absence of a prior use, either in absolute terms or in terms of a period of use outside a predetermined time period. If the criteria are not met, the controller 54 will not register the usage key card 202, and the controller 54 will also not enable use of the generator 38 in association with the device 26. Further details of the registration function of the controller 54 will be described later.

The second use control and monitoring function of the usage key card 202 occurs if the criteria are met and registration of the usage key card 202 occurs. During permitted use of the device 26 in association with the generator 38, the storage medium 204 of the usage key card 202 remains in the module 48 and receives, via the module 48, data generated by the controller 54 recording operating parameters and performance of the device 26. The storage medium 204 of the usage key card 202 retains and organizes the data for further off-line storage and processing. Further details of the data retention function will be described later.

The usage key card 202 can be variously configured. In the illustrated embodiment (see Fig. 7), the usage key card 202 comprises a computer-readable storage medium 204 housed within a conventional 3.5 inch floppy disk 206. In this arrangement, the module 48 comprises a conventional floppy disk drive 208 (see Fig. 8) capable of reading data from and downloading data to the storage

medium 204 of the disk 206.

Alternatively, the usage key card 202 can take the form of a PC card, flash memory device, or magnetic card. In these alternative embodiments, the module 48 comprises a data reading and writing device compatible with the storage medium of the card 202.

As Fig. 7 shows, the storage medium 204 of the usage key card 202 contains at least two pre-formatted files 210 and 212. The first file 210 contains a unique identification code 214 capable of being read by the module 48 and registered by the controller 54. The second file 212 is formatted to receive and retain operational and performance data generated by the controller 54 to create from it a procedure log 220.

The identification code 214 contained in the first file 210 is created to be unique to the particular usage key card 202. That is, each usage key card 202 contains its own unique identification code 214. No two usage key cards share the same identification code 214. The unique identification code 214 can comprise, e.g., a serial number uniquely assigned to the particular device 26 found in the kit 200, or any other unique code that is not repeated for any other usage key card 202. The code 214 itself can comprise letters, numbers, or combinations thereof.

As Fig. 8 shows, the module 48 reads the identification code 214 off the usage key card 202 for input to the controller 54. This identification code will be called the "instant identification code."

Following pre-programmed rules, the controller 54 constructs and maintains in non-volatile memory a use table 216. The use table 216 contains all prior identification codes that meet the criteria to be registered by the controller 54. These identification codes will be called the "registered identification

codes."

Following pre-programmed rules, the controller 54 compares the instant identification code 214 to all registered identification codes contained in the table 216. In the absence of a match between the instant identification code and any registered identification code, the controller 54 updates the table, i.e., the controller registers the instant identification code by adding it to the table 216. Upon registering the usage key card 202, the controller 54 also enables use of generator 38 in association with the device.

The presence of a match between the instant identification code and any registered identification code indicates the usage key card 202 has been previously read by the module 48, which reflects a prior use of the device 26 or another device not packaged with the card 202. In this circumstance, the controller 54 does not add the duplicative identification code to the table 216 and does not enable use of the generator 38 in association with any device 26. Preferably, the controller 54 outputs to the GUI notice of prior use.

In an alternative arrangement, the controller 54 maintains for each registered identification code in the table 216 a time record 218. The time record 218 contains a value reflecting the period of time during which energy was applied by the generator 38 during the previous permitted use. In this embodiment, when a match occurs between the instant identification code and a registered identification code, the controller 54 ascertains whether the time period of previous use contained in the record 218 is less than a prescribed maximum time period, e.g., 45 minutes. If so, the controller 54 enables a subsequent operation of the generator 38 in association with the device 26, but only for the time period remaining. The controller 54 updates

the time record 218 as further use occurs. The controller 54 preferably outputs to the GUI the time period of permitted use remaining.

If the controller 54 ascertains that the time period of previous use equals or exceeds the prescribed maximum time period, the controller 54 does not enable use of the generator 38. Preferably, the controller 54 outputs to the GUI notice of prior use.

As Fig. 9 shows, the second file 212 contained on the storage medium 204 of the usage key card 202 is formatted to receive, via the module 48, data that is generated by the controller 54 during permitted use of the device 26 in association with the generator 38. The file 212 retains the data in a formatted array according to pre-programmed rules to create a procedure log 220.

The content of the formatted log 220 can vary. For example, the log 220 can document, by date of treatment and number of treatments, the coagulation level (i.e., the depth at which the electrodes are inserted), the time duration of energy application, the magnitude of energy delivered by each electrode, and the coolant flow rate. The procedure log 220 can also record at pre-established intervals (e.g., every 5 seconds) the temperatures of the electrodes and surrounding tissue, along other parameters, e.g., sensed impedance and power delivered by each electrode.

The procedure log 220 preferably records these values in a pre-formatted data base format, to enable import of the values as data base items for storage, processing, and retrieval by an off-line data processing device 222 having a compatible data base processing application. The off-line data processing device 222 reads processing log data from the usage key card 202 (via a floppy disk drive 230 or otherwise compatible reading device).

The device 222 can process the data in various ways according to the rules of the data processing application. The device 222 can, e.g., create a print-formatted record of the procedure log 220 for printing in a hard copy version. The device 222 can also, e.g., process the procedure logs for multiple devices and patients, to create historical patient treatment records, patient reimbursement records, and the like for storage or retrieval. The device 222 thereby makes possible the establishment and maintenance of an archival patient data base by processing individual procedure logs.

As Fig. 6 shows, the kit 200 can also include a label 224 that is pre-applied or that can be applied by the physician to the usage key card 202. The label 224 receives manually transcribed, visually readable information pertaining to the usage key card 202, e.g., the name of the patient being treated by the device 26, the date of treatment, and the like. In this way, usage key cards 202 can itself be physically stored and indexed.

As Fig. 6 also shows, the kit 200 can also include instructions 232 for using the usage key card 202 in the fashion described. For example, the instructions 232 can instruct the physician as to the need for having the usage key card 202 read by the module 48, in order to enable use of the device 26 in association with the generator 38. The instructions 232 can also instruct the physician regarding the content of the procedure log and the subsequent off-line processing options that are available.

As Fig. 7 shows, the storage medium 204 of the usage key card 202 can also contain at least one additional formatted file 226 that provides device information 228, which characterizes the device 26 supplied in the kit 200. For example, the device information 228, when read

by the module 48, can identify the type of device 26 in terms of its operational characteristics, the inclusion of temperature sensing, and reuse criteria (e.g., no reuse after a single use, or multiple uses permitted up a prescribed maximum number of uses, or multiple uses permitted up to a maximum time period of use, or multiple uses permitted up to a maximum application of RF energy). The file 226 can also condition the GUI to display the desired images and data formats, which change depending upon the treatment procedure using the device (e.g, treatment of GERD, fecal incontinence, or urinary incontinence). In one arrangement, the controller 54 can compare the device characteristics with the operational characteristics of the controller 54 and generator 38, and disable operation of the device 26 should the characteristics of the device 26 be incompatible with the characteristics of the controller 54 and/or generator 38.

III. Graphical User Interface (GUI) For Monitoring and Controlling Reuse

In the illustrated embodiment (see Fig. 10), the radio frequency generator 38, the controller 52 with I/O device 54, and the fluid delivery apparatus 44 (e.g., for the delivery of cooling liquid) are integrated within a single housing 400. The I/O device 54 includes input connectors 402, 404, and 406. The connector 402 accepts an electrical connector 408, to which the connector 42 of the selected treatment device 26 is electrically coupled for use. The connector 404 accepts an electrical connector 410 coupled to a patch electrode 412 (for mono-polar operation). The connector 406 accepts an pneumatic connector 414 coupled to a conventional foot pedal 416, when, when depressed, causes the delivery of radio frequency energy to the electrodes 66 on the device 26. These connectors 402, 404, and 406 couple these external devices to the controller 52.

The I/O device 54 also couples the controller 54 to an array of membrane keypads 422 and other indicator lights on the housing 400, for entering and indicating parameters governing the operation of the controller 52.

The I/O device 54 also couples the controller 52 to a display microprocessor 474. In the illustrated embodiment, the microprocessor 474 comprises, e.g., a dedicated Pentium®-based central processing unit. The controller 52 transmits data to the microprocessor 474, and the microprocessor 474 acknowledges correct receipt of the data and formats the data for meaningful display to the physician. In the illustrated embodiment, the dedicated display microprocessor 474 exerts no control over the controller 52.

In the illustrated embodiment, the controller 52 comprises an 68HC11 processor having an imbedded operating system. Alternatively, the controller 52 can comprise another style of processor, and the operating system can reside as process software on a hard drive coupled to the CPU, which is down loaded to the CPU during system initialization and startup.

The display microprocessor 474 is coupled to a graphics display monitor 420 in the housing 400. The controller 52 implements through the display microprocessor 474 the graphical user interface, or GUI, which is displayed on the display monitor 420.

The GUI can be realized, e.g., as a "C" language program implemented by the microprocessor 474 using the MS WINDOWS™ or NT application and the standard WINDOWS 32 API controls, e.g., as provided by the WINDOWS™ Development Kit, along with conventional graphics software disclosed in public literature.

The display microprocessor 474 is also itself coupled to the floppy disk drive 208, previously described. The display microprocessor 474 can also be

coupled to a keyboard, printer, and include one or more parallel port links and one or more conventional serial RS-232C port links or Ethernet™ communication links.

Upon boot-up of the CPU (see Fig. 13), the operating system implements the START-UP function 510 for the GUI 424. The GUI 424 displays an appropriate start-up logo and title image (not shown), while the controller 52 performs a self-test.

Upon completion of the START-UP function (see Fig. 13), the controller 54 conducts a CHECK function 512. The function 512 checks for the presence of a usage key card 202 in the floppy disk drive 208. As before described, a valid usage key card 202 is a prerequisite for using a given treatment device 26.

The absence of a usage key card 202 causes the controller 54 to command the display microprocessor 474 to generate a SETUP prompt 500 on the graphics display monitor 420. Fig. 11 shows a representative SETUP prompt 500. When graphically implemented, as shown in Fig. 11, the SETUP prompt 500 leads the operator in a step-wise fashion through the tasks required to enable use of the generator 38. A first graphic field displays one or more icons and/or alpha-numeric indicia 502 that prompt the operator to connect the electrical connector 42 of the treatment device 26 to the connector cable 408. A second graphic field displays one or more icons and/or alpha-numeric indicia 504 that prompt the operator to insert a valid user key card 202 (i.e., floppy disk). A third graphic field displays one or more icons and/or alpha-numeric indicia 506 that prompt the user to select the standby-ready button 430 on the housing 400 (see Fig. 10).

With the treatment device 26 connected and a user key card 202 inserted in the floppy disk drive 208, the actuation of the standby-ready button 430 causes the

controller 52 to enter the STAND-BY mode 508(see Fig. 13). In the STAND-BY mode 508, the controller 52 executes the REGISTRATION function 514, to determine whether the user key card 202 inserted in the drive 208 contains a valid identification code 214.

The identification code 214 will not be deemed valid when the code already exists in the use table 216 of the controller 52 with a time record 218 equal to or greater than the prescribed maximum, thereby indicating a completed prior use of the device 26. When the identification code 214 is not valid, the REGISTRATION function 514 commands the display microprocessor 474 to generate an EXCHANGE prompt 516 on the graphics display monitor 420. Fig. 12 shows a representative EXCHANGE prompt 516. When graphically implemented, as shown in Fig. 12, the EXCHANGE prompt 516 leads the operator in a step-wise fashion through the tasks of replacing the previously used device 26 and its key card 202 with a new device 26 and its associated key card 202.

As shown in Fig. 12, a first graphic field displays one or more icons and/or alpha-numeric indicia 518 that prompt the operator to disconnect the electrical connector 42 of the previously used treatment device 26 and to connect a new treatment device 26. A second graphic field displays one or more icons and/or alpha-numeric indicia 520 that prompt the operator to remove the old user key card 202 and insert the new key card 202 that accompanied the new treatment device 26 in the kit 200. A third graphic field displays one or more icons and/or alpha-numeric indicia 522 that prompt the user to again select the standby-ready button 430 on the housing 400.

With the new treatment device 26 connected and the new user key card 202 inserted in the floppy disk drive 208, selection of the standby-ready button 430 causes the

controller 52 to again enter the STAND-BY mode 508, and again execute the REGISTRATION function 514 (see Fig. 13).

The presence of a valid identification code 214 on the user card 202 causes the controller 52 to enter the READY mode 524. The operator deploys the treatment device 26 to the intended treatment site. The operator locates the electrodes 66 in the desired orientation. When delivery of radio frequency energy is desired, the operator depresses the foot pedal 416 (or selects the standby-ready button 430). In the illustrated embodiment, the controller 52 executes a prescribed PAUSE state 528 (e.g., 8 seconds), and then commands the generator 38 to apply radio frequency energy through the electrodes 66 carried by the treatment device 26.

The controller 52 includes an UPDATE function 526 (see Fig. 13). The UPDATE function 526 registers the time period during which radio frequency energy is applied using the device 26. The time is entered into the time record 218 of the use table 216 maintained by the controller 52. After a prescribed maximum period of use is registered (e.g., sixty minutes), the UPDATE function 526 interrupts application of radio frequency energy to the electrodes 66, and prevents further delivery by the generator 38 to the particular device 26.

In this circumstance, the UPDATE function 526 causes the controller 52 to generate the EXCHANGE prompt 516. As previously described, the EXCHANGE prompt 516 requires the operator to replace the existing device 26 and its key card 200 with a new device 26 and its associated key card 200.

In the illustrated embodiment, while radio frequency energy is being applied during the READY mode 524, the controller 52 preferably monitors impedance and/or temperature conditions at the treatment site. The

controller 52 enters a DEFAULT mode 530 and returns to the PAUSE state 528 when certain localized impedance and/or temperature conditions are sensed, e.g., when impedance is outside a prescribed range (for example, less than 50 ohms or greater than 1000 ohms); or electrode tip temperature exceeds 100 degrees C; or tissue surface temperature exceeds 50 degrees C. In the PAUSE state 528, the controller 52 prevents the application of radio frequency energy through the electrodes 66 for a prescribed period of time (e.g., 8 seconds), after which operation of the generator 38 using the foot pedal 416 or standby-ready button 430 is restored.

Other details of the GUI during operation of the device 26 can be found in co-pending United States Patent Application Serial No. 09/305,123, filed May 4, 1999 and entitled "Graphical User Interface for Association with an Electrode Structure Deployed in Contact with a Tissue Region," which is incorporated herein by reference.

Various features of the invention are set forth in the following claims.

We Claim:

1. A system for controlling use of a device for treating a tissue region comprising

a controller to control operation of the device,

a reader to download information to the controller,

a usage key card adapted to be handled separate from the device and comprising a storage medium formatted to contain an identification code unique to the usage key card that, upon reading by the reader, is downloaded to the controller,

the controller including a processing function for processing the identification code to either enable or disable operation of the device according to prescribed criteria,

a display screen, and

an operating system to generate a viewable image on the display screen that changes in response to processing of the identification code by the processing function.

2. A system according to claim 1

wherein the processing function causes the controller to create a table by registering unlike identification codes in memory as they are downloaded by the reader and to enable operation of the device when a new identification code is registered in the table, and

wherein the operating system displays a first image to prompt input to create the table for the device using the processing function.

3. A system according to claim 2

wherein the processing function causes the controller to disable operation of the device when the given identification code matches an identification code in the table, and

wherein the operating system displays a second image, different than the first image, to prompt exchange of the device when operation of the device is disabled as a result of the processing function.

4. A system according to claim 2

wherein the processing function causes the controller to register in the table, a time period of use of the device.

5. A system according to claim 4

wherein the processing function causes the controller to disable operation of the device when the time period of use exceeds a prescribed period, and

wherein the operating system displays a second image, different than the first image, to prompt exchange of the device when operation of the device is disabled as a result of the processing function.

6. A system according to claim 1

wherein the device applies radio frequency energy to the tissue region.

7. A method for controlling use of a device for treating a tissue region comprising the steps of

providing a usage key card for the device adapted to be handled separate from the device and comprising a storage medium formatted to contain an identification code unique to the usage key card,

reading the usage key card by a reader separate from the device to download the identification code to a controller for the device,

causing the controller to process the identification code by pre-programmed rules to either enable or disable operation of the device, and

generating a viewable image on a display screen that changes in response to processing of the identification code according to the pre-programmed rules.

8. A method according to claim 7

wherein the viewable image generating step generates a first image to prompt input to process the identification code for a given device according to the pre-programmed rules and a second image, different than the first image, to prompt exchange of the device when operation of the device is disabled by the pre-programmed rules.

9. A method according to claim 7

wherein the pre-programmed rules register a time period of use of the device.

10. A method according to claim 9

wherein the pre-programmed rules causes the controller to disable operation of the device when the time period of use exceeds a prescribed period.

11. A method according to claim 7

wherein the device, during use, applies radio frequency energy to the tissue region.

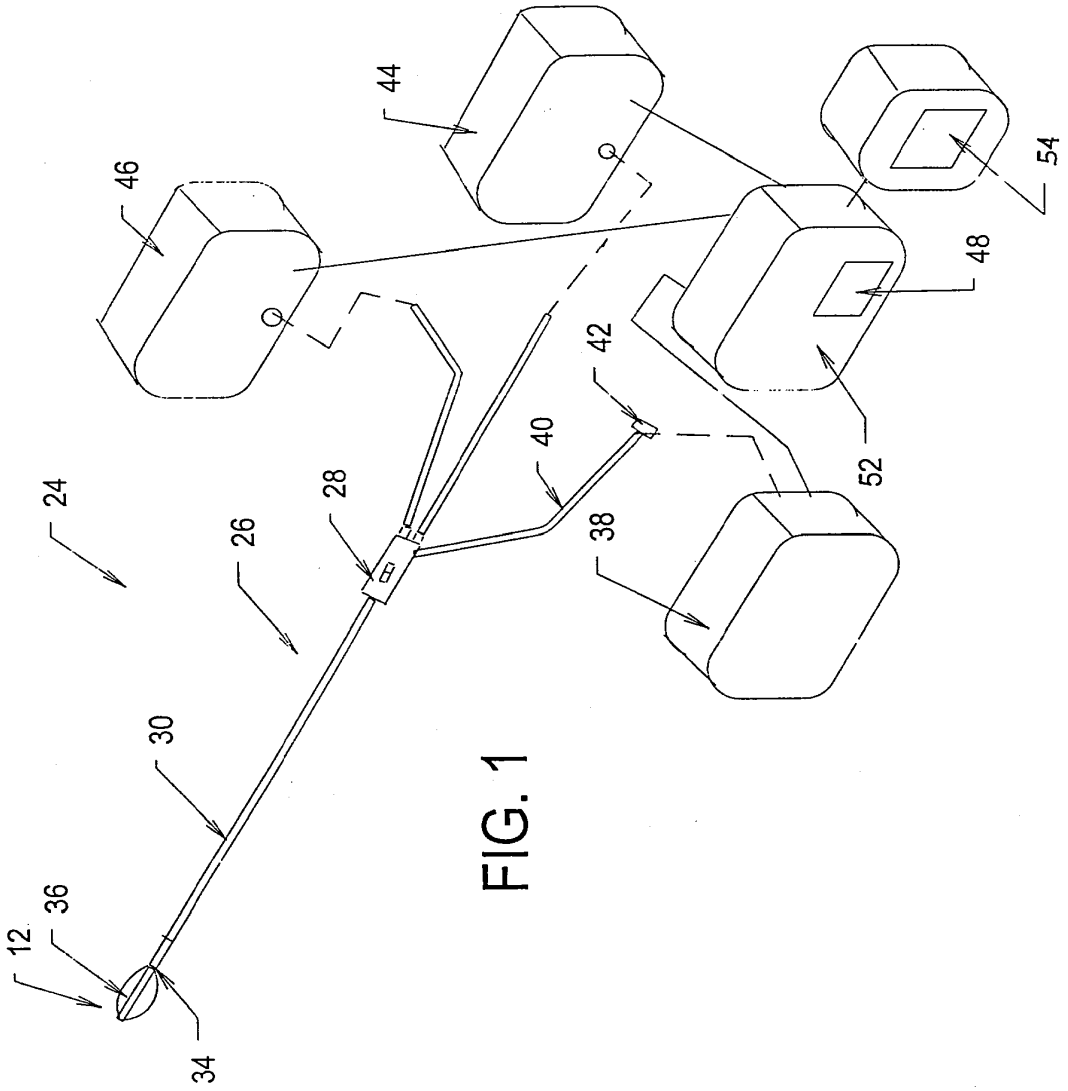


FIG. 1

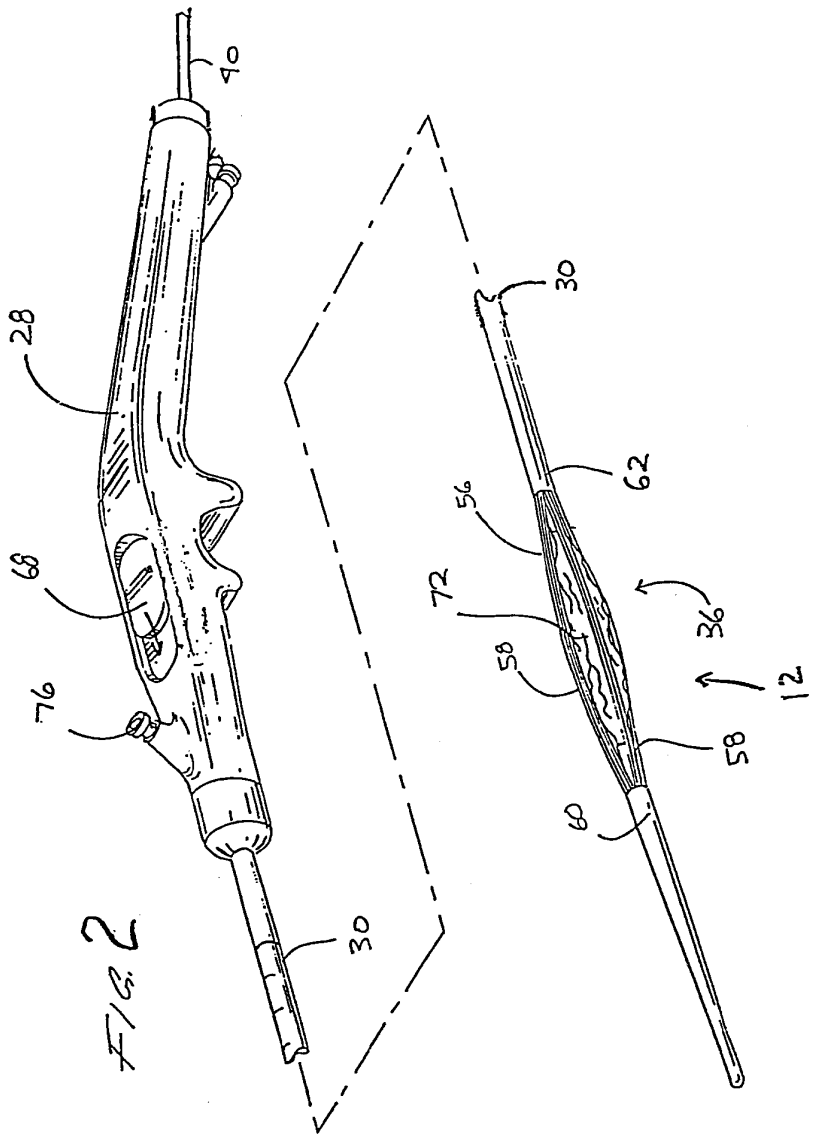


FIG. 2

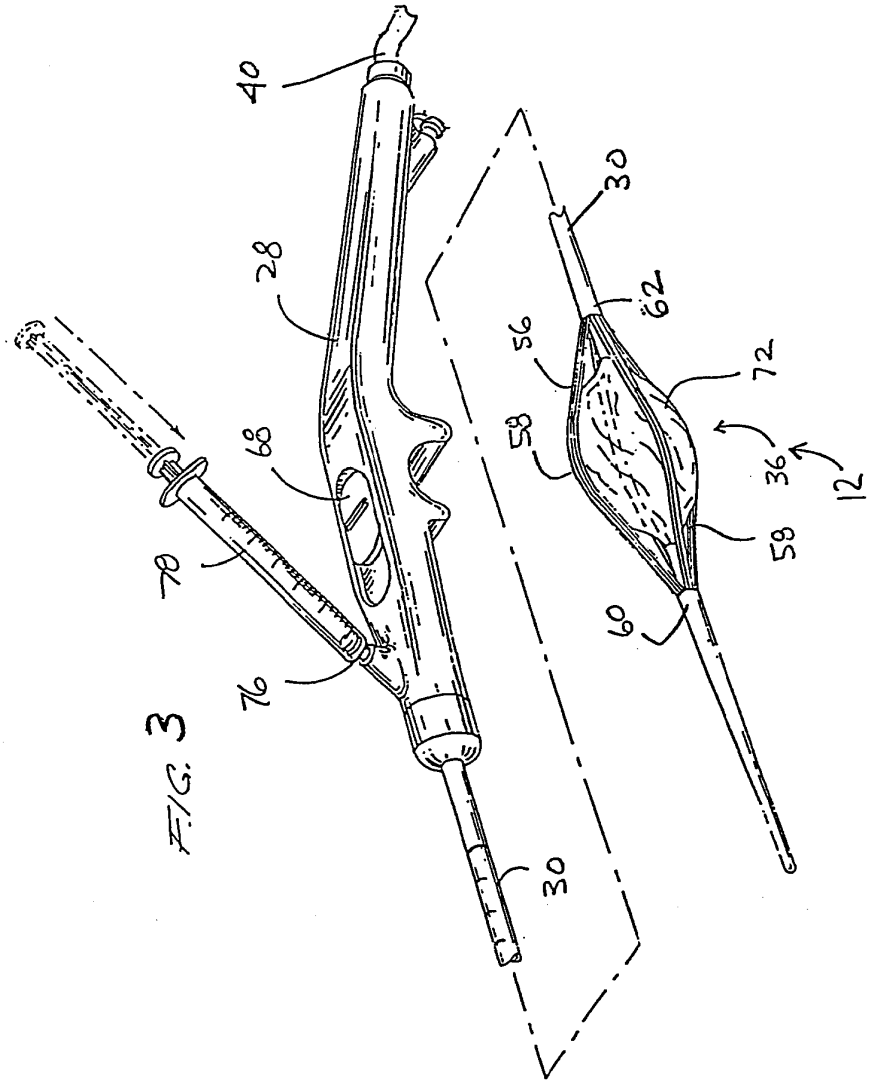


FIG. 3

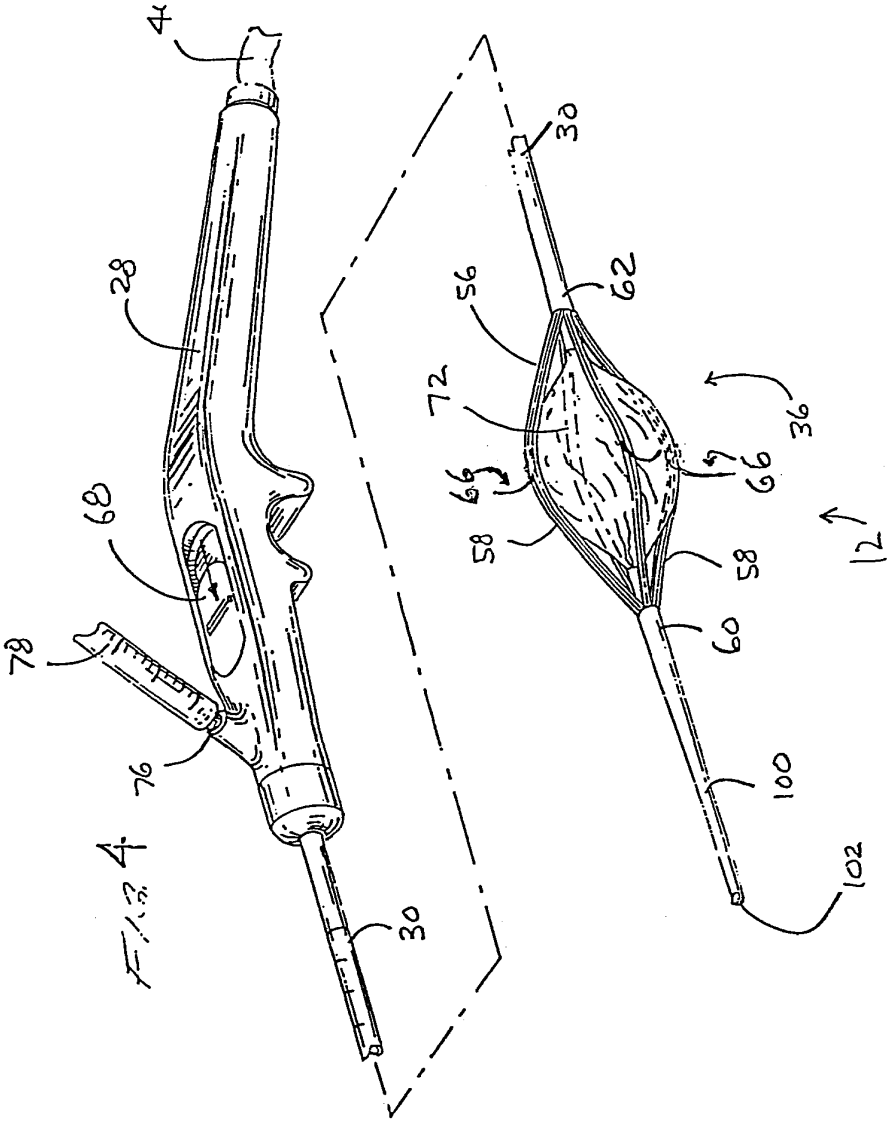


Fig. 4

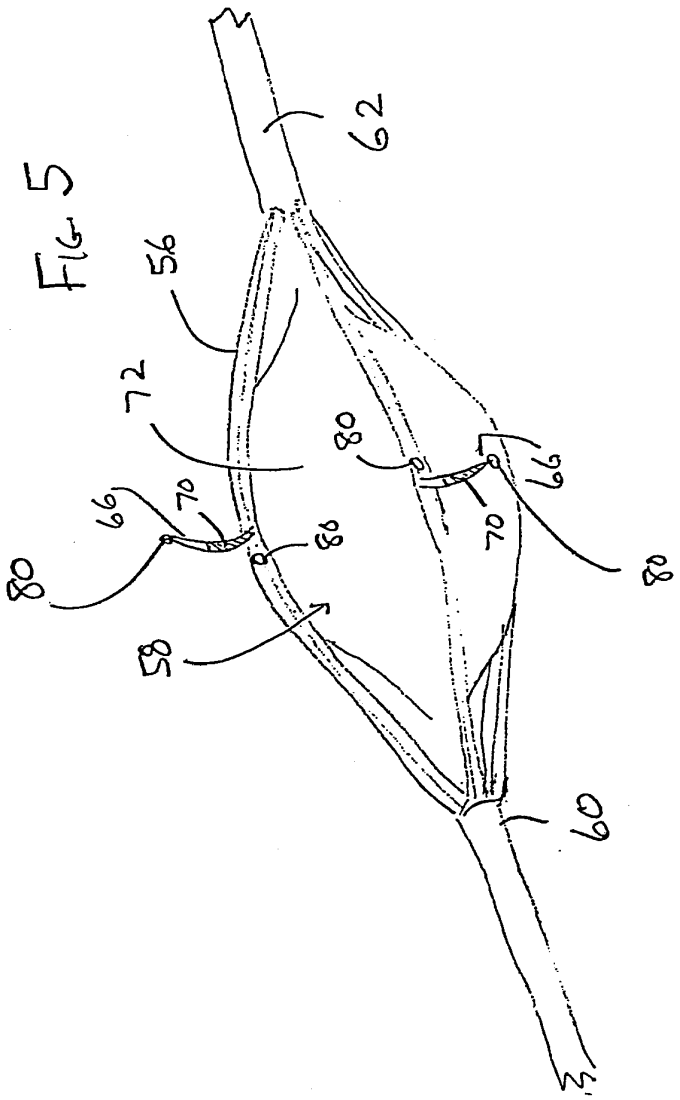


Fig. 5

FIG. 6

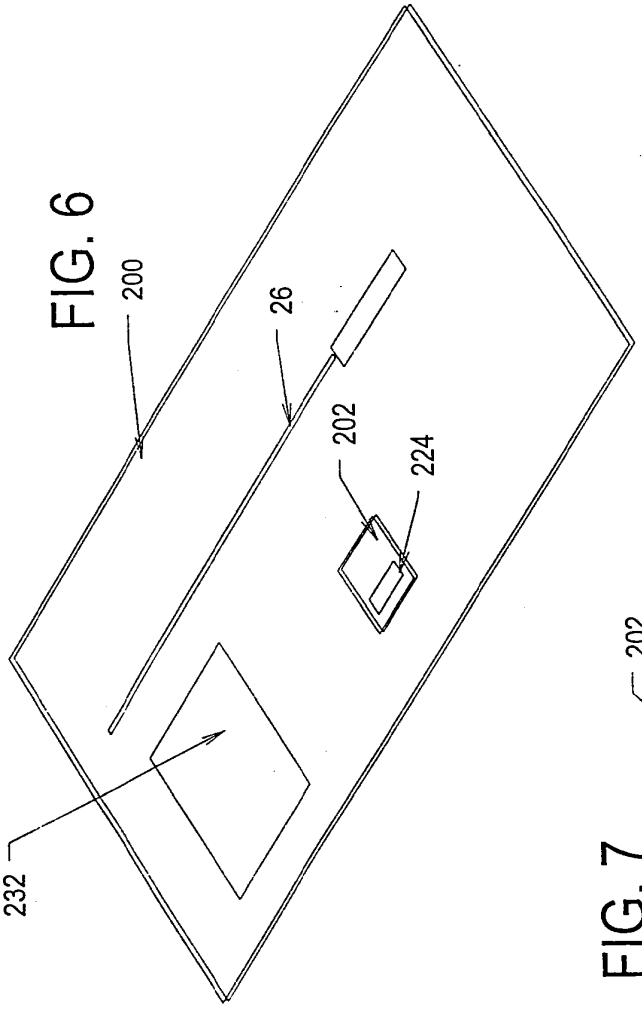
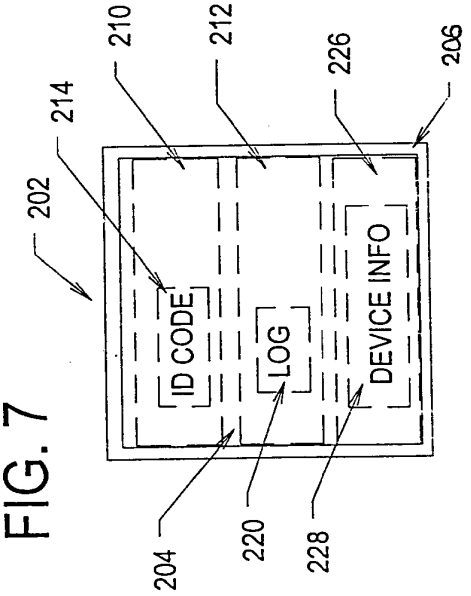

200
26
202
224
232

FIG. 7


210
212
226
206
214
202
ID CODE
LOG
DEVICE INFO
204
220
228

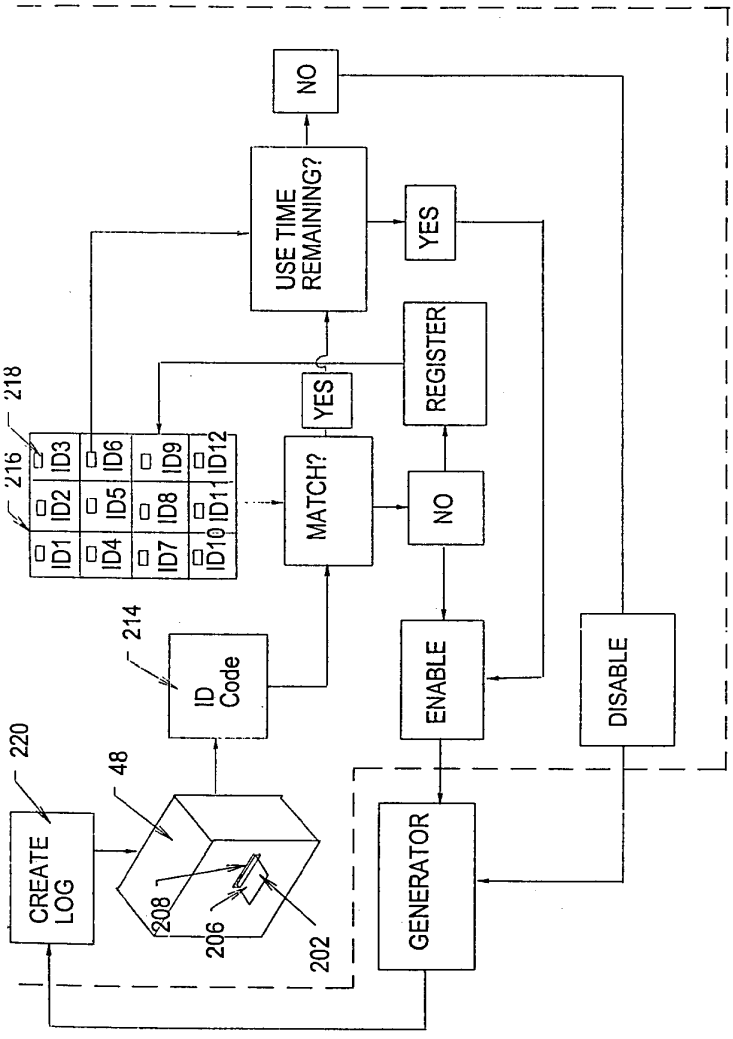
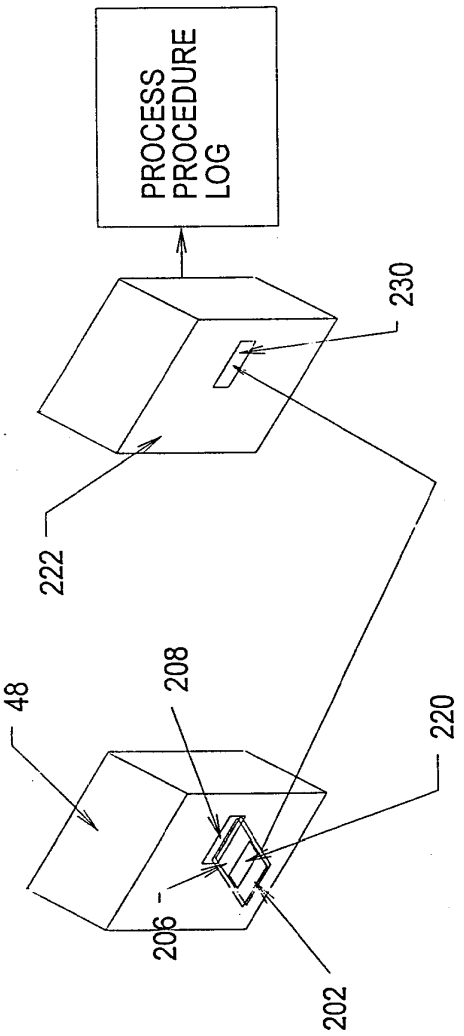

NO
USE TIME REMAINING?
YES
REGISTER
YES
218
216
ID1 ID2 ID3
ID4 ID5 ID6
ID7 ID8 ID9
ID10 ID11 ID12
MATCH?
NO
214
ID Code
ENABLE
DISABLE
220
48
CREATE LOG
208
206
202
GENERATOR

FIG. 8

FIG. 9



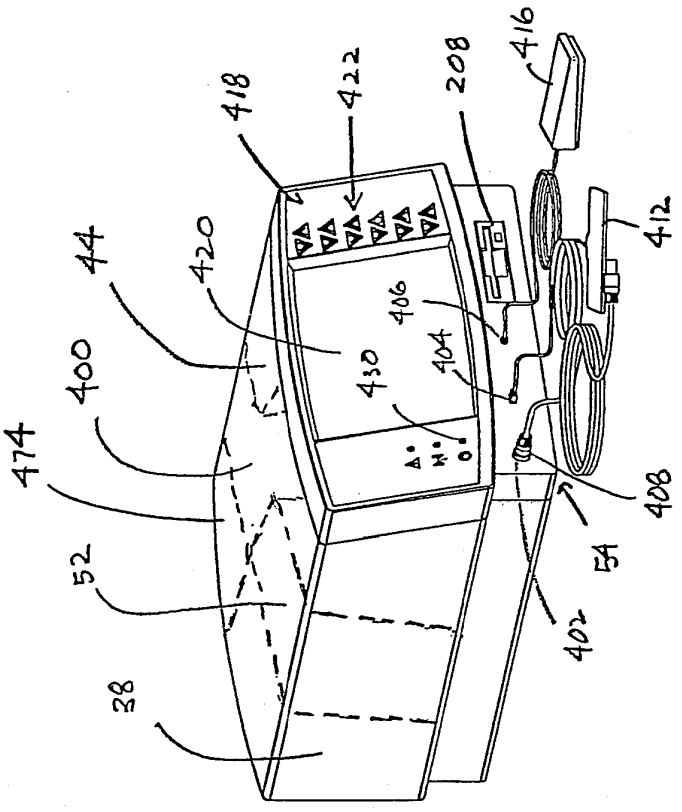


Fig. 10

Fig. 11

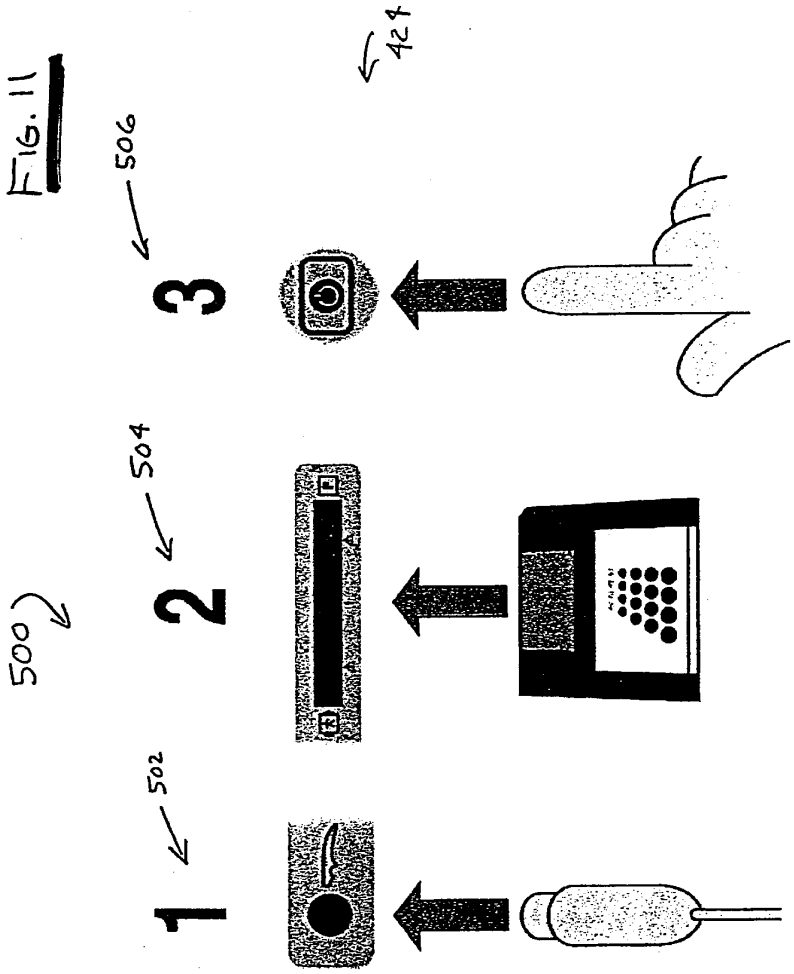
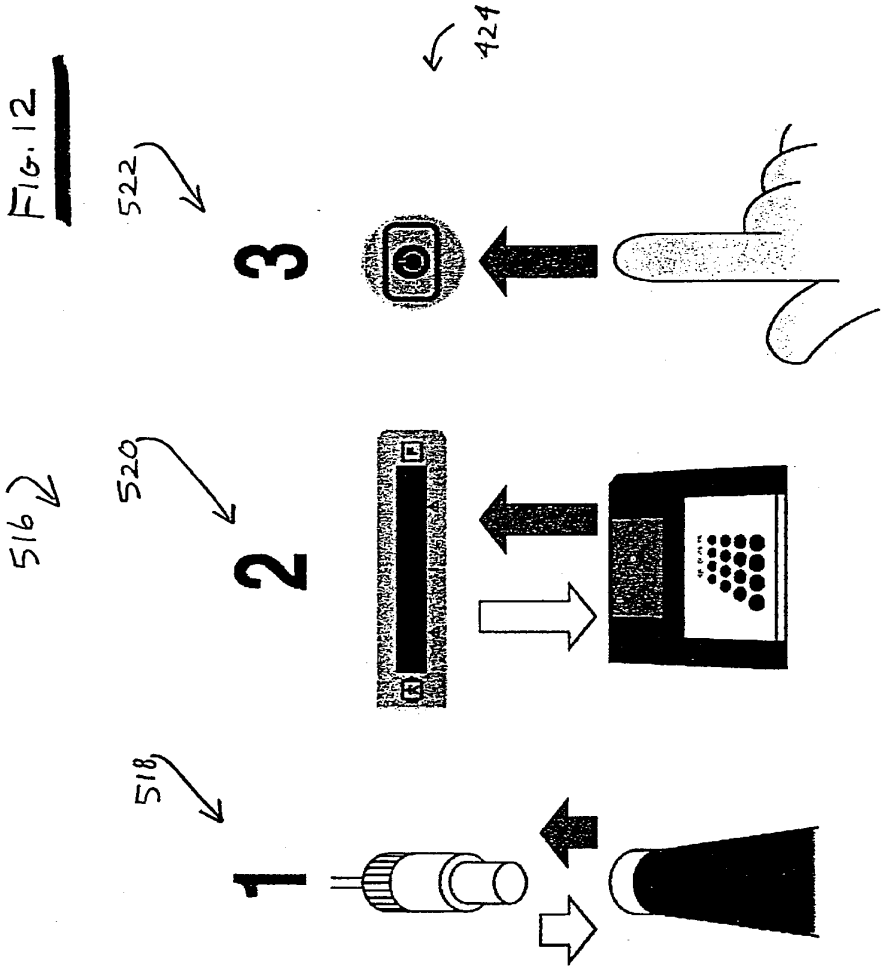


Fig. 12



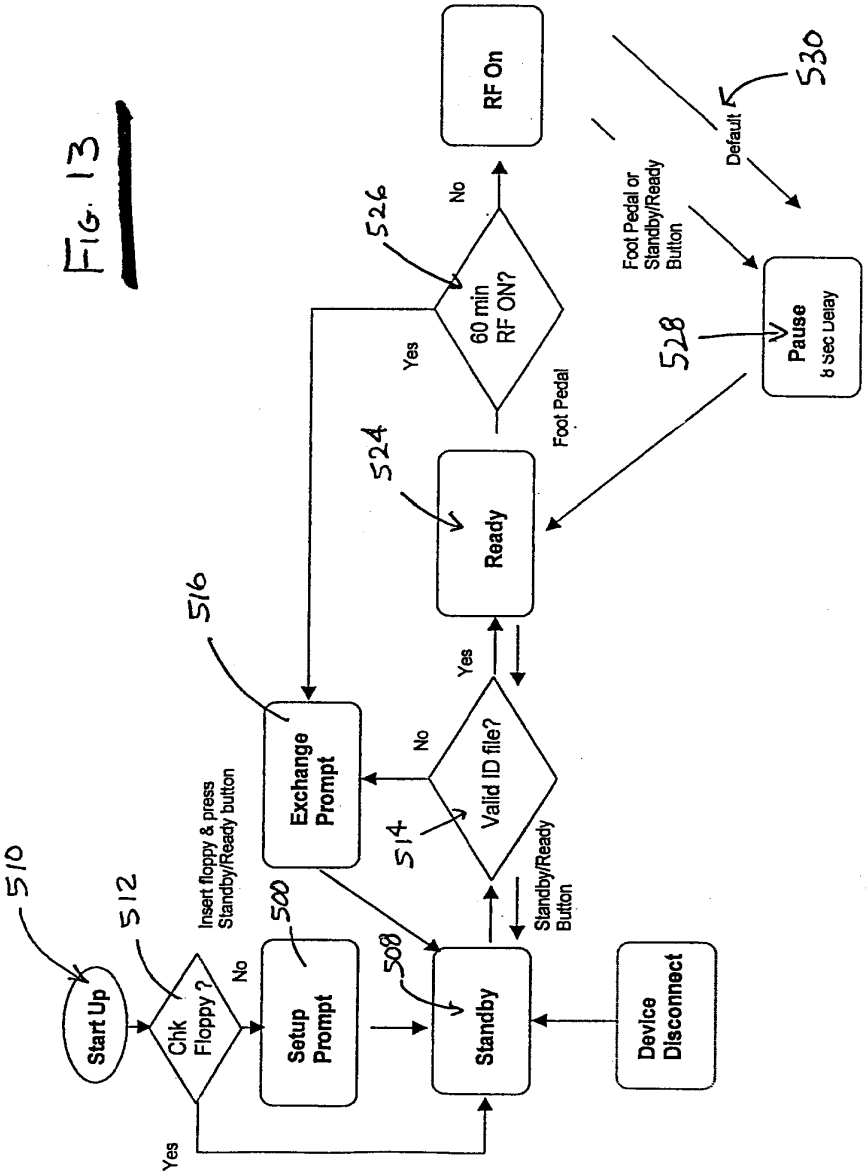

Start Up
510
Chk Floppy ?
512
No
Yes
Insert floppy & press Standby/Ready button
Setup Prompt
500
Exchange Prompt
516
No
Valid ID file?
514
Yes
Standby/Ready Button
Standby
508
Device Disconnect
Ready
524
Foot Pedal
60 min RF ON?
526
No
Yes
RF On
Foot Pedal or Standby/Ready Button
Pause
6 sec Delay
528
Default
530

Fig. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/24461

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61B 18/18
US CL :606/41

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/34,41,42; 607/101,102; 600/300,372,374; 128/920; 345/10,11,24,27,156

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST

search terms: key card, identification code, surgical, GUI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,848,969 A (Panescu et al) 15 Dec 1998, whole document	1-11
Y	US 5,742,718 A (Harman et al) 21 April 1998, whole document	1-11
A,P	US 6,106,460 A (Panescu et al) 22 Aug 2000, whole document	1-11

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 09 NOVEMBER 2000	Date of mailing of the international search report 22 JAN 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL PEFFLEY Telephone No. (703) 308-0858

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Published:

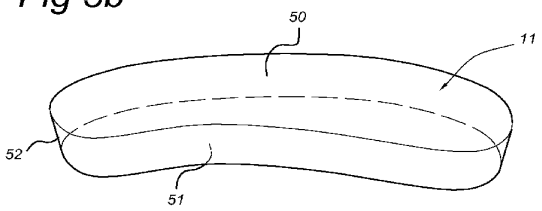
— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2009/154456 A1

(54) **Title**: A flexible electronic system for producing a stimulation signal to the human body.

Fig 3b



(57) **Abstract**: An implantable electronic system has electronics (12), a detection device (16) and a stimulation device (17) within a casing (11). The electronics (12) receive detected parameter values from the detection device (16) relating to one or more functions of a human body. A controller (20) processes the parameter values and generates a control signal for the stimulation device (17) based on the detected parameter values in accordance with the predetermined function. The casing (11) is made of a flexible material.The casing (11) is made of a flexible biocompatible material, and has an upper surface (50) and a lower surface (51) which are substantially parallel to one another and connected to one another by means of a side surface (52).

A flexible electronic system for producing a stimulation signal to the human body.

Field of the invention

The invention relates to a flexible electronic system for producing a stimulation signal to the human body.

Background of the invention

The present invention relates to a flexible implantable stimulation device.

Many implantable devices are available these days, among which pacemakers and defibrillators. Such devices have been described in a wide variety of documents. Using flexible implantable devices have been disclosed in, for instance, CA 2 507 142 A1 and US 2006/0217779 A1. However, the flexible devices shown in these prior art documents are shaped like a hose and not suitable to be placed in every location in the human body where a stimulation device should be located.

One important location where a stimulation device can be implanted is in the pharyngeal area of the human body to provoke an induced aspiration reflex by a resuscitating stimulation of the respiratory area of the human brain stem, as described in PCT/NL2006/000599, which has not been published prior to the claimed priority date of the application relating to the present invention. Embodiments of the devices described in PCT/NL2006/000599 relate to implantable devices. However, this document is silent as to how such implantable devices may be constructed.

It is observed that auto-optimization of stimulation devices is known as such from WO 2007/146213.

Summary of the invention

To that end, the invention provides an electronic system as claimed in claim 1.

The advantage of using a flexible casing as defined in claim 1 is that it adapts itself to the form of the body where the casing is implanted. Thus, it does not, or hardly, perform any mechanical pressure to the human body after implantation, which would cause discomfort or even undesired stimulation by pressure.

When stimulating a predetermined point of the human body in the course of time, irritation of that point may occur. Moreover, the stimulation effect may reduce in the course of time when stimulation is always applied to the same point. This is especially true for stimulating an area of the pharynx where it is not easy to identify the best location for stimulation and which can be damaged by the stimulation over time easily. Therefore, it is an object of an embodiment of the present invention to provide an improved implantable device with stimulation device that can be used to generate a stimulus to a human brain via an area in the pharynx.

To that end, in an embodiment, the invention provides an electronic system with a stimulation matrix.

The advantage of using a stimulation matrix is that the stimulus can be spread over an area instead of being applied to a point. This reduces irritation when used during longer time periods. Moreover, the applied stimulus pattern can be changed, thus avoiding adaptation of the body to and reduced efficiency of the stimulus. Moreover, integrating the stimulation matrix in the casing of the implantable device saves space and provides a device that can be implanted more easily. Also, stimulation waves of all kinds can be applied from one point to one or more of the other points on the matrix. This can be employed to produce more complex stimulation patterns.

Brief description of the drawings

The invention will be explained in detail with reference to some drawings that are only intended to show embodiments of the invention and not to limit the scope. The scope of the invention is defined in the annexed claims and by its technical equivalents.

Figure 1 is a schematic cross section of a part of the human head and neck.

Figure 2 is a detail from figure 1.

Figure 3a shows a schematic block diagram of an electronic system.

Figures 3b and 3c show alternative shapes of a casing of an implantable device.

Figure 4 shows an example of electronics that can be used in the present invention.

Figure 5 shows a substrate with stimulation units arranged in the form of a matrix.

Figure 6 shows an electronic arrangement according to the invention.

Figure 7 shows a flexible substrate with some electronic components on top of it.

Figure 8 shows a portion of a flexible casing with sensors and stimulation electrodes.

Description of embodiments.

The following detailed specification will explain the invention with reference to a stimulation device being implantable in the pharyngeal area of a subject, although application of the present invention is not restricted to this as will be explained further below.

The brainstem contains a number of central mechanisms regulating a number of vital physiological functions. Disorders in the regulation of the cardio-pulmonary system can result in a number of pathological conditions some of which may be potentially life threatening.

People suffering from sleep apnoea have cardio-pulmonary disorders manifesting with breathing irregularities and even frequent stops of breathing (apnoea), particularly during sleep, but also during the day. The apnoeic episodes during the day-time are less dangerous, because they can be self-managed by conscious actions, apnoeas during the night are more dangerous. Patients can feel very sick in everyday life, due to oxygen deprivation. During episodes of apnoea, blood pressure can collapse and subsequently the heart may stop its function, resulting in inadequate brain perfusion, loss of consciousness and even sudden death. At least 4% of the adult population in developed countries suffers from sleep apnoea.

There are several types of apnoea. One type, central apnoea, involves a dysfunction of the respiratory muscles (including the diaphragm) for lack of command from the

respiratory centre in the brainstem. This is the type occurring in approximately 10 percent of the cases. Another type, obstructive apnoea, occurs in 80% of cases, when in spite of respiratory movements there is no supply of air to the lungs, due to collapse of the upper airways. The third type, a mixed apnoea, occurs in the rest of the patients.

It is known, that apnoea can be counteracted by stimulation of the patient in various ways. In infants shaking is usually enough to arouse the baby from sleep and restart the process of automatic breathing and even provoke gasps, which induces resuscitation from asphyxia. Adults suffering from sleep apnoea now sleep with a mask, tightly connected to the facial contours, so a slight over-pressure of air from a device can continuously be applied (Continuous Positive Airway Pressure- CPAP). This keeps the airways open and allows air supply by spontaneous breathing. In any case these patients have to sleep attached to their breathing apparatus, limiting their freedom of movement during sleep. For patients with sleep apnoea travelling means carrying the breathing apparatus with them. For patients suffering from central sleep apnoea or mixed type sleep apnoea, treatment with CPAP is showing limited success. Modulating the air pressure (BIPAP) offers only a slightly better success rate.

Research in cats has shown that breathing can be stopped by inhalation of anoxic mixtures for over 1 minute, with subsequently a severe drop in blood pressure and heart rate. Mechanical or electrical stimulation of the nasopharynx can induce a sniff- and gasp-like "aspiration reflex" (Tomori and Widdicombe, 1969, Beňačka & Tomori, 1995, Tomori et al. 1995, 1998, 2000). Due to resuscitation effects, the blood pressure returns to normal, heart rhythm normalizes, respiration and neuro-behavioral functions return to normal. The anesthetized cat seems to be in good condition, even after as long as three minutes without adequate blood pressure, heart rate and breathing. This experiment can be repeated over 10 times on the same cat, without any noticeable negative consequences.

Provocation of such an aspiration reflex has been indicated as a possible means for interruption of apnoea in cats (Tomori et al., 1991, 1995, Beňačka & Tomori, 1995, Jakus et al., 2004). Alternatively, similar resuscitation may be induced by (electro)-

acupuncture, (electro)-acupressure or mechanical stimulation of the nasal philtre in cats, inducing spasmodic inspiration (Beňačka & Tomori, 1997).

The present invention relates to devices that are, among others, suitable for inducing autoresuscitation in a subject in need thereof. The term autoresuscitation should be understood to comprise resuscitation by activation of natural compensatory mechanisms of the human organism via inducing a sniff- and/or gasp-like aspiration reflex, or its alternative forms in various species, similar to that provided by means of spontaneous gasping autoresuscitation observed in non-human animals and human infants (Sridhar et al., 2003; Xie et al., 2004). When referring to induction of autoresuscitation in this specification the term resuscitation may be used. Subjects that may benefit from induction of autoresuscitation are subjects suffering from and/or having a predisposition for functional disorders, such as hyper and hypo-function of the: a) respiratory system, b) cardiovascular system, c) neurobehavioral changes and d) psychiatric disorders. These include one or more of apnoea, transient ischemic attacks (TIA), bronchospasm also in asthmatics, laryngospasm, hiccup, tremor associated with Parkinson's disease, epileptic seizure, absence type epilepsy, migraine, hypotension, syncope, haemorhagic shock (loss of blood), alternating hemiplegia, Alzheimers disease, depression, anorexia nervosa, bulimia, autism, psychiatric disorders, sleep paralysis, insomnia, comatose states.

It is believed that the "aspiration reflex", via strong activation of the inspiratory centre, causes the controlling functions of the brainstem to be reset, similar to activation of brainstem centres during autoresuscitation induced by gasping. In rapid and strong inspiratory efforts during a gasp or a provoked aspiration reflex, activation of the inspiratory centre in the brainstem resets the failing centres of other vital functions, including the centres controlling cardiac activity, blood pressure, as well as various neuropsychic and somato-motor functions.

As indicated in PCT/NL2006/000599 referred to in the introduction of the present document, without wishing to be bound by any theory, it is believed that inducing the aspiration reflex may be helpful in relation to the following 5 groups of disorders of the human body.

1. In patients with apnoea and hypopnoea caused by transient inactivity of the inspiratory neurons in the brainstem, induction of the aspiration reflex can reverse the apnoea or hypopnoea and restore spontaneous breathing. In patients with obstructive apnoea, the stimulation of the inspiratory centre in the brainstem may reverse the closure of the airways and restore normal breathing.
2. In patients with Transient Ischemic Attack (TIA), syncope, hypotension, migraine and hemorrhagic shock the aspiration reflex activates, via the respiratory centre, the brainstem vasomotor centre to evoke peripheral vasoconstriction and vaso-dilatation in the brain and heart, resulting in increase of blood pressure and consequently increased brain and heart perfusion, interrupting, terminating or at least alleviating the pathological condition.
3. Bronchospasm, laryngospasm, hiccup, epileptic seizures, and tremor in Parkinson's disease may be inhibited by impulses from the inspiratory centre via the reticular formation, transmitted through interneurons providing inhibitory influence to the relevant control centres in the brainstem and elsewhere.
4. In alternating hemiplegia, sleep paralysis and absence type epilepsy: stimulation via the inspiratory centre and interneurons activates the descending part of the reticular formation, which activates motoneurons, terminating, or at least alleviating the attack.
5. In comatose states, depression, insomnia, Alzheimers disease, anorexia nervosa, bulimia, and autism, stimulation via the inspiratory centre and interneurons influences the ascending part of the reticular formation. This inhibits or provides relief in depression, bulimia, anorexia nervosa and increases concentration and other cognitive functions. This improves some comatose states, may inhibit the development of Alzheimer's disease and autism and has a positive influence on insomnia and psychiatric disorders.

Resuscitating stimulation of the inspiratory neurons of the brainstem should be understood to mean stimulation of the human body such that the aspiration reflex or its

alternatives are induced, which will influence various brainstem centres. Through such stimulation other parts of the brain relevant for the conditions treatable with the device are influenced. The aspiration reflex and its alternatives have as a common feature strong and short inspiratory efforts comparable to that occurring before or during one or more of gasp, sniff, sigh or augmented breath.

In accordance with a first embodiment of the present invention, the device is designed to provide resuscitating stimulation in the area of the pharynx. As shown in figure 1 the pharynx of the human body is situated from the underside of the skull to the level of cervical vertebra C6. The pharynx may be divided in three compartments, the nasopharynx (roughly situated behind the nasal cavity between arrows 1 and 2), the oropharynx (roughly situated behind the oral cavity between arrows 2 and 3) and the laryngopharynx (roughly situated behind the larynx between arrows 3 and 4).

Figure 2 shows the preferred location of resuscitating stimulation of the pharynx. Resuscitating stimulation is preferably administered in the area of the nasopharynx enclosed by reference marks A, B, C, D surrounding the tuba auditiva 5. More preferably resuscitating stimulation is administered in the direct proximity of the tuba auditiva 5 indicated by the hatched lines in figure 2.

Figure 3a shows a schematic overview of an implantable device 10 with a casing 11. Enclosed in the casing 11 is a battery 13 which is connected to electronics 12. The battery 13 may comprise lithium iodine with nanocrystaline cathode components, as generally used in cardiac pacemakers. The electronics 12 are connected to a detection device 16 via suitable wires 14, as well as to a stimulation device 17 via suitable wires 15.

Figure 3b shows a first physical embodiment of the casing 11 of the present invention. The casing 11 is made of a flexible biocompatible polymer like silicone. However, the invention is not restricted to silicone. Other such flexible biocompatible materials known to persons skilled in the art or still to be developed may be used instead. The form of the casing 11 is box shaped. I.e., casing 11 has an upper surface 50 and a lower surface 51 which are substantially parallel and connected to one another via a side

surface 52. The casing is designed such that it is flexible in three dimensions. The embodiment shown in figure 3b is shaped such that the upper surface 50 and lower surface 51 are either circular or oval.

Figure 3c shows an alternative embodiment in which the upper surface 50 and lower surface 51 have rectangular shape.

It is observed that the invention is not restricted to the shapes shown in figures 3b and 3c. Every box shaped form of casing 11 is considered to fall within the scope of the present invention where the box has substantially parallel upper and lower surfaces. Moreover, side surface 52 need not be flat but may be curved seen in a cross sectional view in a direction perpendicular to upper surface 50 and lower surface 51.

Is will be evident to persons skilled in the art, the flexible casing 11 as proposed by the present invention is very suitable to be used in an implantable device 10 to be implanted in body areas as volatile as a (human) pharynx. Due to the flexibility, its form adapts itself to the surrounding tissue thus causing less irritation and health problems than in cases where a non-flexible casing is used.

The electronics 12 may be implemented by means of an analogue circuit, a digital circuit or a computer arrangement with a processor instructed by a suitable computer program, or any combination thereof. Figure 4 shows an embodiment based on a computer arrangement.

As shown in figure 4, the electronics 11 comprise a controller, e.g., in the form of a microprocessor 20 which is connected to a memory 21. Moreover, the microprocessor 20 is connected to a wave function generator 23 via suitable wires 22, which has an output connected to the wires 15 that are connectable to stimulation device 17.

The memory 21 may be implemented as several memory units of different types (RAM, ROM, etc.). The memory 21 stores instructions of a program to allow the microprocessor 20 to perform one or more functions. Optionally, memory 21 stores a number of detected parameter values as obtained from detection device 16. The

memory 21 may be any suitable memory for storing a predetermined function such as a computer readable memory. The predetermined function may be a mathematical function or correlation. Suitable functions may be functions that are suitable for determining whether a determined parameter value is equal to, greater than or smaller than a predetermined threshold value. Based on his knowledge the skilled person will be able to determine suitable functions on the basis of which a response is required as a function of determined parameter values of parameters sensed by the detection device 16. E.g. the function may relate the absence of certain parameter values below a certain threshold value to a certain time frame. Such a function may be determined to detect the absence of breathing during a certain time period e.g. 2 seconds and longer, 5 seconds and longer or 10 seconds and longer.

Based on the program as stored in the memory 21, the microprocessor 20 is able to process the number of detected parameter values as obtained from the detection device 16 in said function. For this, the detected parameter values are loaded into the microprocessor 20 either directly from the detection device 16 or alternatively from the memory 21 into which the detected parameter values were previously loaded. The function is loaded in the microprocessor 20 from the memory 21 or in an alternative embodiment the predetermined function may be embedded in said microprocessor 20. In the latter embodiment at least one memory is (partially) integrated in the microprocessor 20.

The detection device 16 may be any suitable device for detecting a number of parameter values. In the present specification, a "number" shall mean one or more unless explicitly stated otherwise. In use, the detection device 16 provides an output signal on wire 14, representing determined parameter values in response to determined parameter values. The determined parameter values are values of a parameter as measured/determined by the detection device 16 within a certain time frame. The parameter may be any parameter on the basis of which it may be determined whether a subject is in need of induction of autoresuscitation.

Parameters suitable for determining whether a subject is in need of resuscitation are parameters corresponding to electrical activity recorded from, for instance, the pharynx

indicating a level of cerebral activity. Suitable devices for detecting electrical activity from the surface of the pharynx are conductive patches connected to a suitable amplifier and filter. Alternatively, sensors may be anchored inside the nasopharynx. The microprocessor 20 is arranged to, as instructed by a suitable program stored in memory 21, receive values of such parameters from the detection device 16 and establish whether or not the subject is in need of autoresuscitation. However, the detection device may, alternatively, be arranged to detect at least one of a gas flow, a gas composition, a gas pressure, a gas temperature, a body temperature, a body part movement and sound. Signals delivered by detecting device 16 may, thus, be a measure of breathing activity, EEG data, EMG data, ECG data, or neural activity.

The stimulation device 17 is arranged to provide a response as a function of the number of processed parameter values as instructed by a suitable control signal received from electronics 12. The stimulation device 17 comprises a number of stimulation units which may be designed to provide resuscitating stimulation in order to stimulate and/or reactivate the inspiratory centre of the brainstem. The primary preferred stimulation as provided by the stimulation device 17 goes from the upper airways, preferably the pharynx, to the inspiratory centre in the brainstem. In the brainstem there are other controlling centres, such as the vasomotor centre and the neurons controlling cardiac activity, which will as a result also be influenced secondarily to the stimulation of the inspiratory centre. Furthermore, the inspiratory centre is connected by interneurons to the reticular formation (RF). The descending part of the RF connects to the peripheral nervous system, such as various motor and sensory neurons; the ascending part connects to higher centres controlling e.g. sensation, perception and cognitive functions.

Stimulation of certain locations distant from the brainstem, like in the pharynx, results in induction of resuscitation because in certain locations of the mammalian body afferent nerves connected to the inspiratory centre of the brainstem are present. Stimulation of such afferent nerves or their receptive zones results in activation of the inspiratory centre of the brainstem and through this in influencing of the other centres in the brainstem and other parts of the brain such that resuscitation and/or autoresuscitation may be induced.

Stimulation of the nasopharynx, more preferably the part of the nasopharynx in the proximity of the tubae auditivae, is a suitable option as it provides the strongest resuscitation effect with induction of the aspiration reflex.

The stimulation device 17 may be a mechanical or an electrical stimulation device. The electrical stimulation device may include a separate power source. A suitable power source may be an array of charged capacitors connected to a battery, allowing voltage selection for the stimulation, in case spikes are used. This separate power source may, alternatively, be absent in which case the stimulation device 17 will be connected to the battery 13 within casing 11 via wiring 15. The wave generator 23 as shown in figure 4 may be part of the stimulation device 17. In combination with such a power source, the wave generator 23 is arranged to produce a desired control signal for the stimulation device 17, for instance in the form of block waves, sinus waves or spikes of different length, frequency and amplitude, or combinations thereof.

Figure 5 shows a stimulation matrix 40 which is used in an embodiment of the invention. The stimulation matrix 40 is connected to the stimulation device 17. As shown in figure 5, the stimulation matrix 40 has a substrate 42 provided with a plurality of stimulation units 43(i), i = 1, 2, 3, …, I. The stimulation units 43(i) are arranged in a matrix form. The arrangement shown comprises stimulation units 43(i) in a regular matrix pattern. However, the invention is not restricted to this arrangement. Irregular patterns may be used instead.

In an embodiment, the stimulation units are stimulation electrodes 43(i) for delivering an electrical stimulation to the body of the subject. Such electrodes 43(i) receive suitable stimulation signals via wires 41 from electronics 44 within stimulation device 17 based on the control signal received from the electronics 12 via wire 15. Electrodes 43(i) may be mono-polar or multipolar, including bipolar electrodes, and may, in use, be placed on the surface of the pharynx. For stimulation of the pharynx the electrodes may be anchored in the subject's pharynx.

By using a plurality of stimulation electrodes 43(i) arranged in the form of a two dimensional matrix more complex stimulation currents can be provided to the body. This also provides the possibility of precise definition of the area to be stimulated. There is some distance between the electrodes 43(i). Due to this distance the electrical current will travel over that distance through the subject's body. This may enhance the stimulatory effect. It also allows to let the device auto-optimise the stimulation position, by optimising the effect as measured by the detection devices, as explained hereinafter.

If spikes are used for the control signal, variations in the amplitude and duration of the spikes, i.e. the amount of energy can be made, apart from trains of spikes over an extended period of time (seconds) (Beňačka and Tomori, 1995). Sinus waves of various frequencies and duration, block waves, spikes, spike trains and any combination of these can be used. It is preferred to not just transfer energy, but to stimulate the targeted response centres more complexly to elicit the desired physiological response.

In an embodiment, the microprocessor 20 is designed to activate the wave function generator 23 if an EMG as detected by detection device 16 does not satisfy a predetermined criterion, such as a lack of normal EMG activity for >10 sec (central apnoea) or extremely strong EMG activity accompanied by stop of airflow (obstructive apnoea) as detected by detection device 16. Then, upon activation the wave function generator 23 may generate the control signal in the form of a predetermined wave, such as a sinus wave, block wave, spike train or any combination in a suitable frequency, duration and amplitude that is guided through electrical wires 41 to its stimulation electrode.

In an embodiment, the stimulation units 43(i) are mechanical stimulation units arranged to provide a mechanical stimulus to the human body. Such mechanical stimulation units 43(i) may be formed by electrostriction components which produce a mechanical movement when excited by an electrical current. Such mechanical stimulation units 43(i) may have the form of needles.

An implantable device 10 according to the invention may be a fully integrated implantable device. Such a fully integrated implantable device is shown in figure 6 in which like components as in figure 3 are indicated with the same reference numbers, however provided with a prime. As shown in figure 6, the casing 11' of such a device 10', then, accommodates all components including the detection device 16', the electronics 12', the battery 13' and the stimulation device 17'. The battery 13' is shown to be connected to the electronics 12' but may equally well be connected to the detection device 16' and the stimulation device 17'.

Moreover, the casing 11' is shaped and made like casing 11.

The casing 11' may be partly conductive. For instance, the casing 11' may be provided with sensors 33 in the form of conductive areas, for instance in the form of conductive pads on the casing 11'of the detection device 16' and operating as sensors to detect electric activity of the human body e.g. for the detection of an EEG. The sensors 33 may be formed by providing suitable conductive coating portions on casing 11'. If the casing itself is also conductive, or in part conductive, then, sensors 33 should be electrically isolated from the casing 11'. However, the invention is not restricted to this embodiment. Cf. for instance figure 8. It is observed that one or more of the sensors could be arranged such as to be usable as stimulators too. This also holds for other embodiments explained here.

In an alternative embodiment, the detection device 16' is connected to one or more small microphones to sense sound, small piezo-electric sensors to convert mechanical pressure into electric signals, or strain gages, etc. that are integrated in or placed on top of the casing 11'.

Alternatively, the detection device 16' is connected to a sensor to measure oxygen saturation in the blood of the subject. This can be done in any way known to a person skilled in the art. In the embodiment where the apparatus is implanted in the pharyngeal area this is possible with a sensor having a light source directed to a blood vessel, as is evident to persons skilled in the art. Measuring oxygen saturation is a good indication of whether or not apnoea is present.

Sensors arranged in a matrix arrangement may especially be suitable to measure EMG or neural activity.

The casing 11' is also provided with the stimulation units 43(i) connected to the stimulation device 17' which may be arranged in the form of a matrix and used to guide an electric stimulation current to the part of the pharynx in its direct proximity. The stimulation units 43(i) may also be formed by providing suitable conductive coating portions on casing 11'. If the casing itself is also conductive, then, sensors 33 should be electrically isolated from the casing 11'. However, the invention is not restricted to this embodiment. Cf. for instance figure 8.

Both the sensors 33 and the stimulation units 43(i) may be provided on a separate, insulating, flexible substrate 42 (cf. figure 5) which is attached to the outside of the casing 11'. The wirings to the detection device 16' and stimulation device 17', respectively, are then guided through suitable through holes in casing 11'.

The sensors 33 may also be arranged in a two dimensional matrix. The sensors 33 and the stimulation units 43(i) may be arranged in matrices separate from one another. However, they may be arranged in a single mixed matrix arrangement with a plurality of electrically conductive areas where some of the electrically conductive areas are connected as sensors 33 and the others as stimulation units 43(i).

In an embodiment, the device 10' is designed to be implanted in the pharyngeal area of the human body where electric stimulation may suitably be applied to obtain resuscitating stimulation of the respiratory area of the brainstem with an induction of an aspiration reflex, e.g. in the nasopharyngeal area.

To that effect the flexible casing 11' of the device will easily adapt to the local form of the pharyngeal area of the body concerned. The area on the casing 11' where the sensors 33 and the stimulation units 43(i) are located is arranged to cover the pharyngeal area A-B-C-D as indicated in figure 2, and preferably at least the area in the

direct proximity of the tuba auditiva 5, for instance within a distance of 5 mm from the tuba auditiva 5.

The flexible casing 11' may be designed to be implantable in or behind the nasopharynx. In an embodiment, the casing 11, 11'is sized and designed such that it may be implanted in or behind the nasopharynx via a human nose or throat.

As indicated above, the casing 11' that accommodates electronics 2' and battery 13' is made of a flexible material. A suitable material is silicone since that is found to be well tolerated by the human body. However, other flexible biocompatible materials tolerated by the human body may be used instead.

The advantage of using a flexible casing 11' is that it can well be used in implantable devices: it adapts itself to the form of the body where the casing 11' is implanted. Thus, it does not, or hardly, perform any mechanical pressure to the human body after implantation, which would cause discomfort or even undesired stimulation by pressure.

In an embodiment, the battery 13' may be made flexible too. Alternatively, many small batteries may be joined to form a virtually flexible battery pack. From cardiac pacemakers it is known that the battery life can be as long as 10 years. With devices for resuscitating stimulation of the inspiratory neurons of the brainstem the battery life can be expected to be much longer, or the device can be made much smaller, as it does not have to stimulate as often as a cardiac pacemaker. In cardiac pacemakers, approximately 70% of the pacemaker's volume is taken up by the battery and connectors.

The electronics 12' may be made of flexible components as well or at least electronic components may be provided on a flexible substrate, e.g., a flexible printed circuit board 30. Figure 7 shows such a flexible substrate 30 having electronic components 31 located on at least one surface of the substrate 30.

As shown in figure 6, the stimulation device 17' is located inside the casing 11' too and is made of electronic components on a flexible substrate too. Then, the stimulation device 17' may be arranged as shown in figure 7 as well.

The electronic components of the electronics 12' may be arranged on a first flexible substrate and the stimulation device 17' may be arranged on a second flexible substrate. However, these first and second substrates may be a single substrate. The battery 13' may be provided on that substrate too.

As also shown in figure 6, the detection device 16' is located inside the casing 11' too and is made of electronic components on a third flexible substrate. Then, the detection device 16' may be arranged as shown in figure 7 as well. The substrates with the electronic components of the electronics 12', the detection device 16' and the stimulation device 17' may be separate substrates. Alternatively, however, they may be one single substrate.

In the embodiment where the casing is made of silicone and the stimulation units are stimulation electrodes 43(i), these stimulation electrodes 43(i) can be made as electrically conductive silicone portions in the silicone casing 11, 11'. This can be done by providing silicone portions of the casing 11, 11' with doping materials like titan or platina. Such an embodiment is shown in Figure 8. Figure 8 shows a portion of a cross section of the flexible casing 11, 11' with sensors 33 and stimulation electrodes 43(i). In this embodiment, both the casing 11, 11' and the sensors 33 and the stimulations electrodes 43(i) are made of silicone. They are all produced from a silicone substrate in which predetermined portions are doped with a suitable doping material like titan or platina to become sensors 33 and stimulation electrodes 43(i). Suitable conductive wirings are connected to these latter portions for electrically connecting the sensors 33 to the detection device 16, 16'and the stimulation electrodes 43(i) to the stimulation device 17, 17'.

Such a device can be made auto-optimizing. The electronics 12, 12' can be arranged to perform a feedback measurement, such that stimulation can be performed at a point where the aspiration reflex can be elicited best. In one embodiment the electronics will,

through a suitable sensor, register the strength of the aspiration reflex; this can for example be performed by measuring airflow through the nose or mouth, measuring sound, heart rate, blood pressure etc. Impedance of the stimulation point may be a guide for finding the optimal point. In this case the device may use impedance measurement to find suitable points for stimulation.

The electronics 12, 12' can be arranged to send different types of stimulation signals to the stimulation units 43(i), either in form or in amplitude or both. The effect of the different stimulation signals per stimulation unit 43(i) can be measured by detection device 16, 16' and be evaluated by electronics 12, 12'. Electronics 12, 12' can be programmed to amend these stimulation signals by amending its control signal as output to the stimulation device 17, 17'.

Moreover, the electronics 12, 12' can be programmed to randomly vary its generated control signal such that the stimulation signals produce random stimuli over the area of the pharynx stimulated by the stimulation units 43(i). This could reduce adaptation of the pharynx to the generated stimuli and, thus, enhance efficiency of the device 10, 10'.

The method according to the invention is suitable for the treatment of several disorders including one or more of but not limited to apnoea, such as central apnoea or obstructive apnoea, transient ischemic attacks (TIA), hypotension, syncope, haemorhagic shock (loss of blood), bronchospasm, laryngospasm, hiccup, tremor associated with Parkinson's disease, epileptic seizure, absence type epilepsy, migraine, alternating hemiplegia, Alzheimers disease, depression, anorexia nervosa, bulimia, autism, psychiatric disorders, insomnia, sleep paralysis, comatose states. As used in this specification the term treatment should be construed to encompass alleviation of discomfort or provide reversal of life threatening functional disorders. Depending on the application concerned, the microprocessor 20 is programmed to analyse received signals from sensors 33 and establish from them whether or not the subject concerned is in need of autoresuscitation. If so, the microprocessor 20 will produce suitable control signals and send them to the stimulation device 17, 17' which, then, produces suitable stimulation signals for the stimulation units 43(i).

It should be understood that the embodiments presented in the examples above are solely intended to illustrate the present invention and are not intended to limit the scope of the invention which is only limited by the annexed claims and its technical equivalents.

For instance, the device as presented above, can be used in a pacemaker arrangement where at least the electronics 12 are located within the flexible casing 11 but the stimulation device 17 is outside casing 11. If so, the sensors may located outside the casing 11 as well or on top of or in casing 11 to sense parameters indicating whether or not the subject concerned is in need of a pacemaker stimulation signal. The stimulation device 17 may have any form suitable to provide the heart with a suitable pacing signal, as known from the prior art. In that case, the detecting device 16, 16' is at least arranged to sense an ECG signal from some part of the subject's body. Sensing and pacing may be done by one single electrode located in the heart wall as is known to a person skilled in the art.

Moreover, the device 10, 10' may be implanted at other locations in the subject to stimulate one or more predetermined nerves, etc.

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Claims

1. Implantable electronic system comprising:
   - a casing (11; 11'),
   - a detection device (16; 16') connected to at least one sensor (33),
   - a stimulation device (17; 17') connected to at least one stimulation unit (43(i)),
   - electronics (12; 12') arranged within said casing (11; 11') and arranged to receive one or more detected parameter values from said detection device (16; 16') relating to one or more functions of a subject, and comprising a controller (20) for processing the number of detected parameter values and to generate a control signal for said stimulation device (17') based on said detected parameter values in accordance with said predetermined function,

wherein said casing (11; 11') is made of a flexible biocompatible material, and has an upper surface (50) and a lower surface (51) which are substantially parallel to one another and connected to one another by means of a side surface (52).

2. Implantable electronic system according to claim 1, wherein the upper and lower surfaces (50, 51) have a shape selected from a circular shape, an oval shape and a rectangular shape.

3. Implantable electronic system according to claim 1 or 2, wherein the detection device (16') is located within said casing (11'), the at least one sensor (33) being arranged either embedded in or provided on at least one of said lower, upper and side surfaces of the casing (11').

4. Implantable electronic system according to claim 1, 2 or 3, wherein the stimulation device (17') is located within said casing and connected to a plurality of stimulation units (43(i)) arranged in a matrix arrangement either embedded in or provided on at least one of said lower, upper and side surfaces of said casing (11').

5. Implantable electronic system according to any of the preceding claims, wherein the casing (11') is designed to be implantable in a human pharyngeal area.

6. Implantable electronic system according to claim 1, wherein the detection device (16') is located within said casing (11'), the at least one sensor (33) being arranged either embedded in or provided on at least one of said lower, upper and side surfaces of the casing (11'), the stimulation device (17') is located within said casing and connected to a plurality of stimulation units (43(i)) arranged in a matrix arrangement either embedded in or provided on one of said lower, upper and side surfaces of said casing (11'), and the system is designed to be implantable in a human pharyngeal area via either a human nose or a human throat.

7. Implantable electronic system according to claim 4 or 6, wherein the stimulation units (43(i)) are located on a flexible substrate (42) attached to said casing (11').

8. Implantable electronic system according to claim 4 or 6, wherein said casing (11') is a silicone casing and said stimulation units (43(i)) are electrodes which are electrically conductive silicone portions in said silicone casing (11').

9. Implantable electronic system according to claim 4, 6, 7 or 8, wherein said system is arranged as an auto-optimizing system, and said stimulation system is arranged to identify a best location to provide a stimulus based on feedback signals from the detection device.

10. Implantable electronic system according to any of the preceding claims, wherein said electronics (12; 12') comprise electronic components (31) on a further flexible substrate (30).

11 Implantable electronic system according to claim 3 or 6, wherein said casing (11') is a silicone casing and said at least one sensor (33) comprises one or more electrically conductive silicone portions in said silicone casing (11').

12. Implantable electronic system according to any of the preceding claims, wherein the detector device (16') is one of a cerebral activity sensor arranged to sense EEG signals, an EMG sensor, an ECG sensor, a sensor to measure temperature, a sensor to measure pressure, a sensor to measure neural activity and a sound sensor.

13. Implantable electronic system according to any of the preceding claims, wherein the controller (20) and the stimulation device (17') are arranged to generate randomly varying stimulation signals.

14. Implantable electronic system according to any of the preceding claims, wherein the at least one sensor (33) comprises a plurality of sensors arranged in a matrix arrangement.

15. Implantable electronic system according to claim 1, wherein the at least one sensor comprises a plurality of sensors (33) and the at least one stimulation unit comprises a plurality of stimulation units (43(i)), the plurality of sensors and the plurality of stimulation units being arranged in a mixed matrix arrangement.

16. Implantable electronic system according to any of the preceding claims, wherein the controller (20) is arranged to establish whether said subject is suffering from at least one of a set of disorders including apnoea, such as central apnoea or obstructive apnoea, heart failure, transient ischemic attacks (TIA), hypotension, syncope, haemorhagic shock, bronchospasm, laryngospasm, hiccup, tremor associated with Parkinson's disease, epileptic seizure, absence type epilepsy, migraine, alternating hemiplegia, Alzheimers disease, depression, anorexia nervosa, bulimia, autism, psychiatric disorders, insomnia, sleep paralysis, comatose states.

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Fig 1

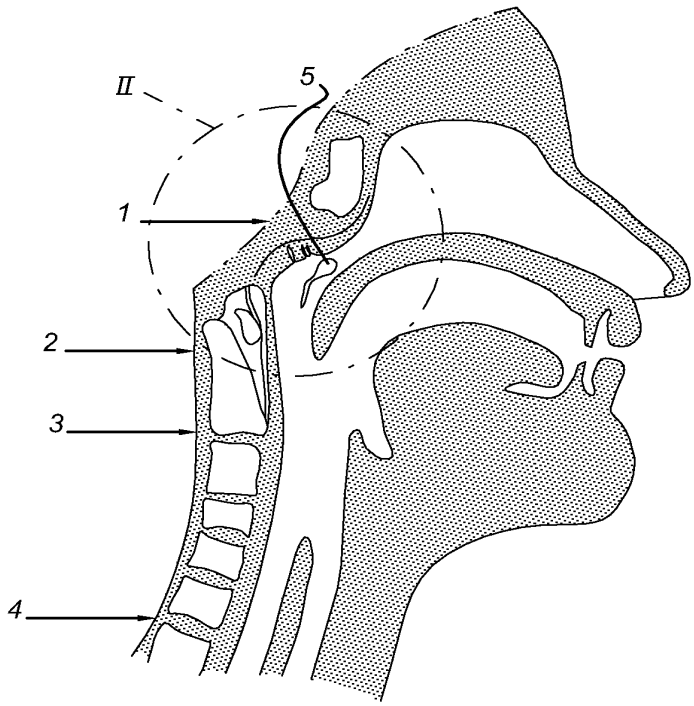


Fig 2

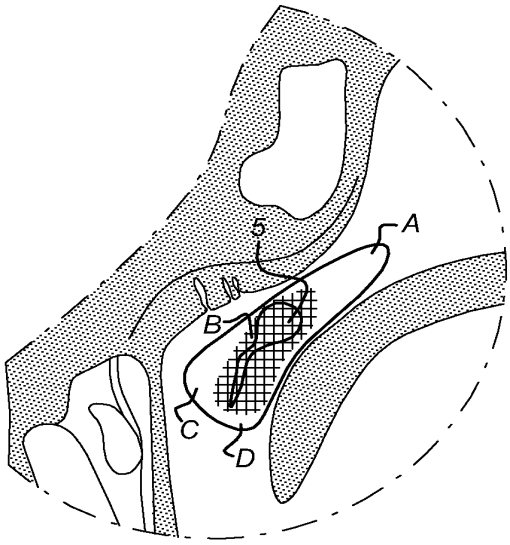


Fig 3a

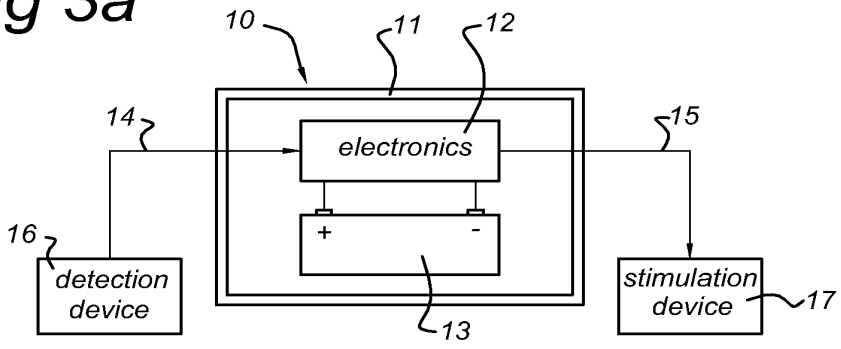


Fig 3b

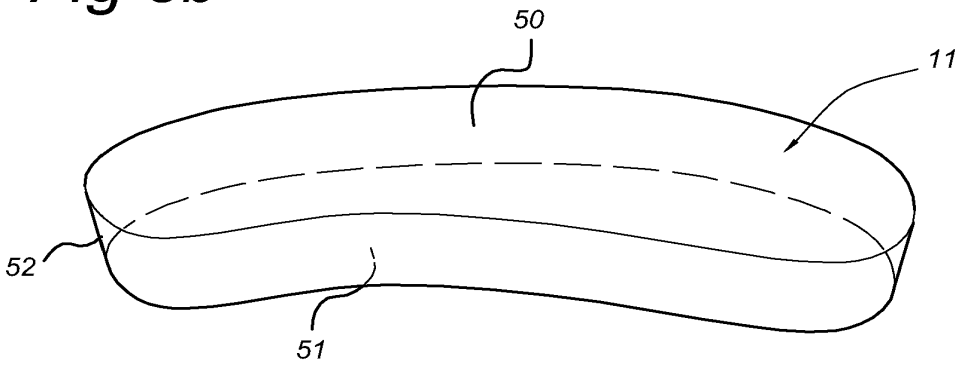


Fig 3c

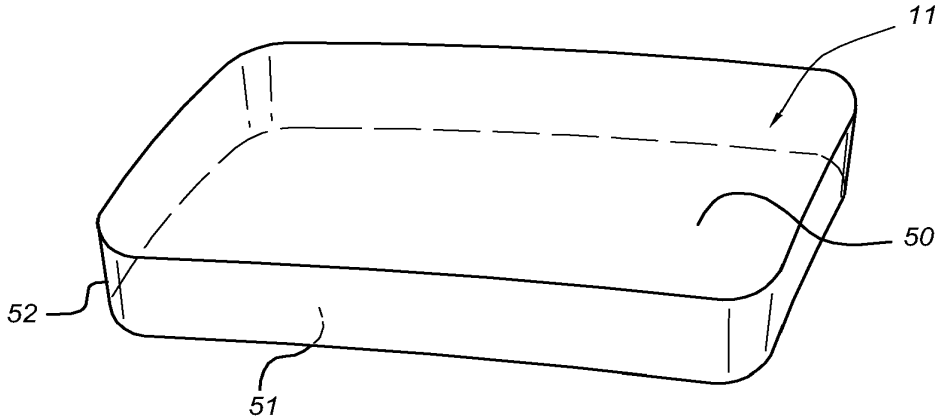


Fig 4

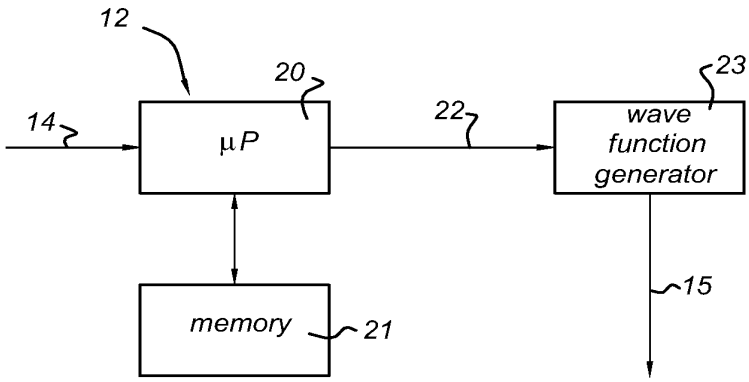


Fig 5

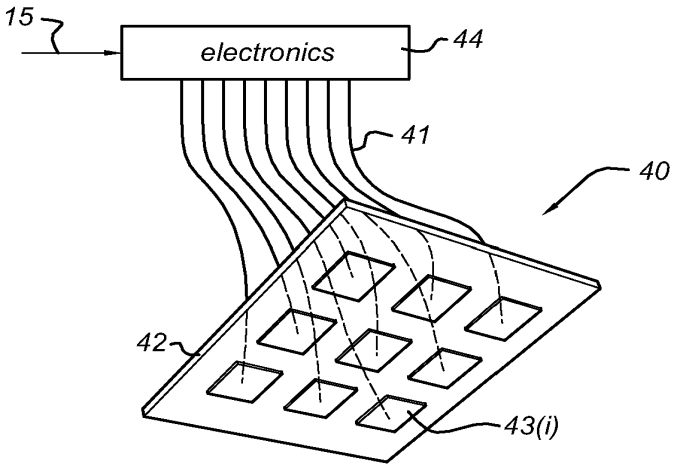


Fig 6

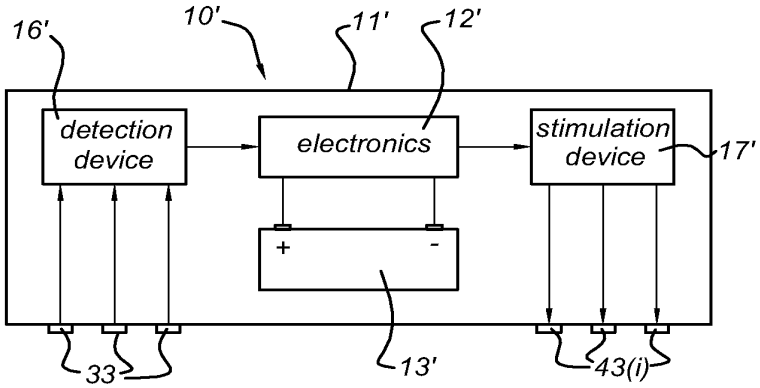


Fig 7

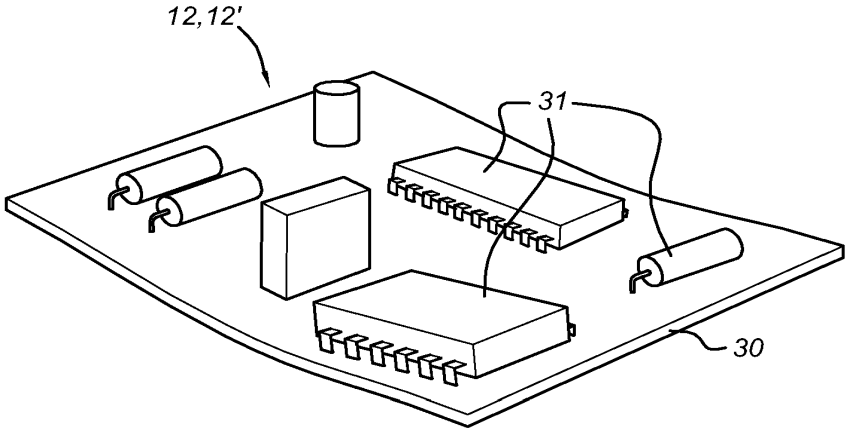
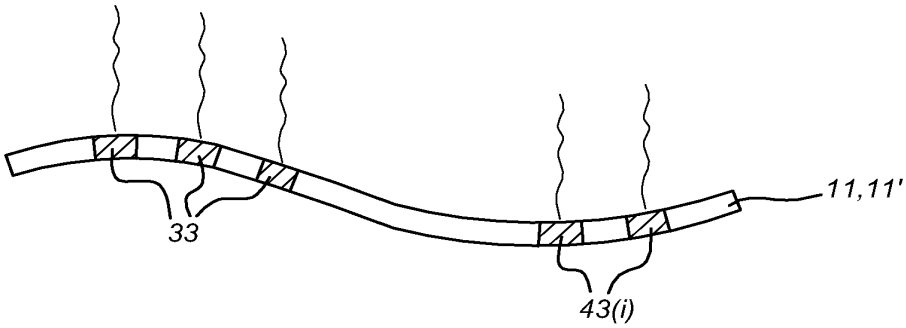


Fig 8



INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2009/050356

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00 A61N1/375 A61N1/05

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2008/157435 A (NORTHSTAR NEUROSCIENCE NC [US]; SLOAN LEIF R [US]; FOWLER BRAD [US]) 24 December 2008 (2008-12-24) page 2, line 13 pages 9,10,11 page 12, line 9 page 13, line 21 page 15, lines 1,2,8,9 page 17, line 25 page 18, line 15 page 19, lines 12,18 figures 2A,5	1-4,6-8, 11-16
X	US 2004/176673 A1 (WAHLSTRAND CARL D [US] ET AL) 9 September 2004 (2004-09-09)	1,2
Y	paragraphs [0042], [0048], [0051], [0052], [0054], [0070]; figures 3,5,7B	5,9,10
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 July 2009	16/10/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Visser, Rogier

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2009/050356

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	TOMORI ET AL: "Hypoxic apnoea induced by N2 inhalation can be reversed by the aspiration reflex in anaesthetized cats" RESPIRATORY MEDICINE, BAILLIERE TINDALL, LONDON, GB, vol. 85, 1 January 1991 (1991-01-01), pages 61-65, XP022012786 ISSN: 0954-6111 page 61, column 2	5,16
Y	US 2008/103545 A1 (BOLEA STEPHEN L [US] ET AL) 1 May 2008 (2008-05-01)	5
A	paragraphs [0081], [0128]; figures 5,26C,28	2
A	US 2003/100930 A1 (COHEN EHUD [IL] ET AL) 29 May 2003 (2003-05-29) paragraph [0189]; figure 1	2
Y	US 5 957 956 A (KROLL MARK W [US] ET AL) 28 September 1999 (1999-09-28) column 13, line 1	10
Y	US 2006/206162 A1 (WAHLSTRAND CARL D [US] ET AL) 14 September 2006 (2006-09-14) paragraphs [0094], [0096]	9

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2009/050356

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008157435 A	24-12-2008	US 2009131995 A1	21-05-2009
US 2004176673 A1	09-09-2004	NONE	
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US 2006206162 A1	14-09-2006	EP 1861162 A1	05-12-2007
		WO 2006098824 A1	21-09-2006

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(30) Priority Data:
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(71) Applicant: **NEURENT MEDICAL LIMITED** [IE/IE]; No. 1 Ocean Point, Main Street, Oranmor, Galway (IE).

(72) Inventor: **TOWNLEY, David**; Latoon North, Newmarket-on-fergus, County Clare (IE).

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(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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(54) Title: SYSTEMS AND METHODS FOR THERAPEUTIC NASAL TREATMENT

(57) Abstract: The invention generally relates to systems and methods for treating at least one of rhinitis, congestion, and/or rhinorrhea to thereby reduce or eliminate symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

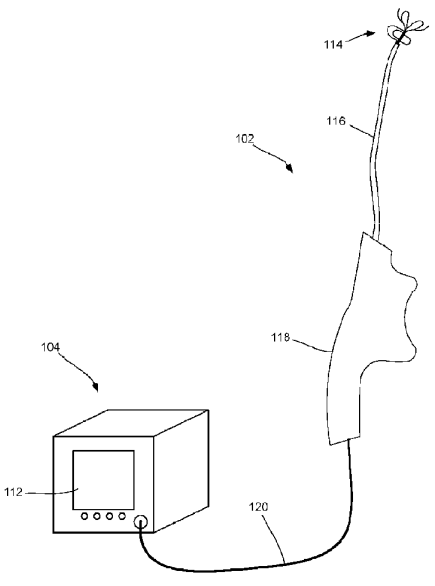


FIG. 2

WO 2021/205230 A1

SYSTEMS AND METHODS FOR THERAPEUTIC NASAL TREATMENT

Cross-reference to Related Applications

This application claims the benefit of, and priority to, U.S. Provisional Patent Application No. 63/007,575, filed April 9, 2020, the contents of which are incorporated by reference.

Field of the Invention

The invention generally relates to systems and methods for treating medical conditions, and, more particularly, systems and methods for treating at least one of rhinitis, congestion, and/or rhinorrhea to thereby reduce or eliminate symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

Background

Rhinitis is an inflammatory disease of the nose and is reported to affect up to 40% of the population. It is the fifth most common chronic disease in the United States. The most common and impactful symptoms of rhinitis are congestion and rhinorrhea. Allergic rhinitis accounts for up to 65% of all rhinitis patients. Allergic rhinitis is an immune response to an exposure to allergens, such as airborne plant pollens, pet dander or dust. Non-allergic rhinitis is the occurrence of common rhinitis symptoms of congestion and rhinorrhea. As non-allergic rhinitis is not an immune response, its symptoms are not normally seasonal and are often more persistent. The symptoms of rhinitis include a runny nose, coughing, sneezing, nasal and/or throat irritation and itching, and general congestion, all of which commonly leads to difficulty sleeping.

Allergen avoidance and pharmacotherapy are relatively effective in the majority of mild cases, but these medications need to be taken on a long-term basis, incurring costs and side effects and often have suboptimal efficacy. For example, pharmaceutical agents prescribed for rhinosinusitis have limited efficacy and undesirable side effects, such as sedation, irritation, impairment to taste, sore throat, dry nose, and other side effects.

There are two modern surgical options: the delivery of thermal energy to the inflamed soft tissue, resulting in scarring and temporary volumetric reduction of the tissue to improve nasal airflow; and microdebrider resection of the inflamed soft tissue, resulting in the removal of

tissue to improve nasal airflow. Both options address congestion as opposed to rhinorrhea and have risks ranging from bleeding and scarring to the use of general anesthetic.

Summary

The invention recognizes that a problem with current surgical procedures is that such procedures are not accurate and cause significant collateral damage in order to treat rhinitis and further fail to adequately treat the underlying symptoms.

The invention solves that problem by providing treatment devices having a combination of unique components, including an elongate body (which may be in the form of a shaft or sheath, or other elongate body), a retractable and expandable multi-segment end effector, and handle, that, as a whole, provide a high level of precise control and feedback to an operator during a procedure. In particular, the elongate body is configured to not only aid an operator in the positioning and delivery of the multi-segment end effector to a desired target site within the sino-nasal cavity, but further includes an electrode array provided along a length thereof that is configured to deliver energy to specific target sites within the nasal passage and nasal cavity, in conjunction with neuromodulation provided by the multi-segment end effector. The multi-segment end effector is configured to complement anatomy at multiple different locations within the nasal cavity. The handle is configured with multiple ergonomic and functional features that improve device use and feedback, such as independent control of deployment of the end effector and energy delivery and a shape associated with the architecture of the end effector in the deployed configuration. The handle may also include one or more markings that provide a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

In that manner, the present invention provides devices that are capable of highly conforming to anatomical variations within a nasal passage and nasal cavity while providing unprecedented control and guidance to an operator so that an operator can perform an accurate, minimally invasive, and localized application of energy to one or more target sites within the nasal passage and nasal cavity to cause multi-point interruption of neural signal without causing collateral damage or disruption to other neural structures.

Unlike other surgical treatments for rhinitis, the devices of the invention are minimally invasive. Accordingly, a procedure can be performed in an office environment under local

anesthetic. The multi-segment end-effector allows for targeting the autonomic supply to the nasal turbinates and will have a positive impact on both allergic and non-allergic rhinitis. Using this approach, it is expected that devices of the invention will be able to provide long-term symptom relief (e.g., years instead of months). Since the treatment is accurate with minimal collateral damage to the surrounding tissue, patients will begin to feel symptom relief immediately following the treatment. It is fully expected that patients will be removed from their pharmacotherapies following this therapy.

The systems and methods of the present invention include a handheld device comprising a retractable and expandable multi-segment end effector that, once delivered to the one more target sites within the nasal cavity, can expand to a specific shape and/or size corresponding to anatomical structures within the nasal cavity and associated with the target sites. In particular, the end effector includes at least a first flexible segment and a second flexible segment, each of which includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

The handheld device further includes an elongate body operably associated with the end effector and a handle operably associated with the elongate body. The elongate body may be in the form of a shaft or sheath (or other elongate body operably associated with or coupled to the end effector). The elongate body may include a pre-defined shape (i.e., bent or angled at a specific orientation) so as to assist the surgeon (or other medical professional) for placement of the end effector at the target sites. The elongate body further includes one or more electrodes provided on one or respective portions along a length thereof and can be used to deliver energy

to tissue adjacent to, or in contact with, such portions of the elongate body. For example, in some embodiments, the elongate body may reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes of the multi-segment end effector, the surgeon may also activate and deliver energy from electrodes associated with the elongate body to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

The handle includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. The handle further includes multiple user-operated mechanisms, including at least a

first mechanism for deployment of the end effector from the retracted configuration to the expanded deployed configuration and a second mechanism for controlling of energy output by the end effector. The user inputs for the first and second mechanisms are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome. Furthermore, the handle and/or the elongate body may include markings (e.g., text, symbols, color-coding insignia, etc.) that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. In particular, multiple markings may be provided on the handle and/or elongate body and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the elongate body, a surgeon can rely on the markings on the handle and/or elongate body as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

Accordingly, the handheld device of the present invention provides a user-friendly, non-invasive means of treating rhinosinusitis conditions, including precise and focused application of energy to the intended target sites for therapeutic modulation of the intended structures, including, but not limited to, engorged sub-mucosal tissue as well as neural structures without causing collateral and unintended damage or disruption to other structures. Thus, the efficacy of a vidian neurectomy procedure can be achieved with the systems and methods of the present invention without the drawbacks discussed above. Most notably, the handheld device provides a surgeon with a user-friendly, non-invasive, and precise means for treating rhinorrhea and other symptoms of rhinosinusitis, notably congestion, coughing, sneezing, nasal and throat irritation, to thereby improve sleep, by targeting only those specific structures associated with such conditions, notably tissue responsible for providing engorgement of certain structures (i.e., inferior turbinates) and postganglionic parasympathetic nerves innervating nasal mucosa, thereby reducing engorgement of inferior turbinate tissue to thereby increase volumetric flow through a nasal passage of the patient as well as disrupting the parasympathetic nerve supply and

interrupting parasympathetic tone. The device further allows for treatment of multiple areas within the nasal passage and/or nasal cavity that would normally require repositioning of an end effector due to their separated locations. In particular, inclusion of an elongate body with a dedicated set of electrodes, in addition to the multi-segment end effector with its own set of electrodes, allows for two separate target sites to receive treatment simultaneously, thereby reducing the need to reposition the end effector. Accordingly, such treatment is effective at treating rhinosinusitis conditions while greatly reducing the risk of causing lateral damage or disruption to other tissues, including other nerve fibers, thereby reducing the likelihood of unintended complications and side effects.

One aspect of the invention provides a device for treating a condition within a nasal cavity of a patient. The device includes an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon.

In some embodiments, the elongate body generally includes a shaft to which the end effector is coupled. For example, the shaft may include an outer sheath surrounding a hypotube or metallic member, such that at least one of the outer sheath, the hypotube, and the metallic member includes one or more of the first set of electrodes provided thereon. In other embodiments, the elongate body includes one or more of a plurality of support elements forming at least a portion of the end effector.

In some embodiments, each of the first set of electrodes is positioned on separate respective portion of the elongate body. In some embodiments, one or more of the separate respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

Each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of a patient. The energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or

result in local hypoxia or coagulation necrosis of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

In some embodiments, each of the one or more of the first set of electrodes is configured to be independently activated and controlled to thereby deliver energy independent of one another. Accordingly, in some embodiments, an operator (i.e., surgeon) may selectively activate one or more of the first set of electrodes as desired to treat specific sites of inferior turbinate tissue.

In some embodiments, the end effector is multi-segmented and includes a proximal segment that is spaced apart from a separate distal segment. The proximal segment may include a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate. The distal segment may include a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Each of the second set of electrodes may be configured to deliver energy to a second target site associated with a sphenopalatine foramen within the sino-nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina or microforamina of a palatine bone of the patient.

In some embodiments, each of the one or more of the second set of electrodes is configured to be independently activated and controlled to thereby deliver energy independent of one another. Accordingly, in some embodiments, an operator (i.e., surgeon) may selectively activate one or more of the second set of electrodes as desired to treat specific sites associated with the sphenopalatine foramen.

Another aspect of the invention provides a method for treating a condition within a sino-nasal cavity of a patient. The method includes providing a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon. The method further

includes advancing the elongate body and end effector through a nasal passage and into a nasal cavity of a patient until a length of the elongate body is positioned at a first target site and the end effector is positioned at a separate second target site. The method further includes delivering energy, via the first and second sets of electrodes, to tissue at the respective first and second target sites.

In some embodiments, the elongate body generally includes a shaft to which the end effector is coupled. For example, the shaft may include an outer sheath surrounding a hypotube or metallic member, such that at least one of the outer sheath, the hypotube, and the metallic member includes one or more of the first set of electrodes provided thereon. In other embodiments, the elongate body includes one or more of a plurality of support elements forming at least a portion of the end effector.

In some embodiments, each of the first set of electrodes is positioned on separate respective portion of the elongate body. In some embodiments, one or more of the separate respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

Each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of a patient. The energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or result in local hypoxia of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

In some embodiments, the end effector is multi-segmented and includes a proximal segment that is spaced apart from a separate distal segment. The proximal segment may include a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate. The distal segment may include a second set of

flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Each of the second set of electrodes may be configured to deliver energy to a second target site associated with a sphenopalatine foramen within the nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina or microforamina of a palatine bone of the patient.

Brief Description of the Drawings

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic neuromodulation system for treating a condition within a nasal cavity using a handheld device according to some embodiments of the present disclosure.

FIG. 2 is a diagrammatic illustration of the console coupled to the handheld neuromodulation device consistent with the present disclosure, further illustrating a multi-segment end effector of the handheld device for delivering energy, via proximal and distal segments, to tissue at the one or more target sites within the nasal cavity.

FIG. 3A is a cut-away side view illustrating the anatomy of a lateral nasal wall.

FIG. 3B is an enlarged side view of the nerves of the lateral nasal wall of FIG. 1A.

FIG. 3C is a front view of a left palatine bone illustrating geometry of microforamina in the left palatine bone.

FIG. 4 is a side view of one embodiment of a handheld device for providing therapeutic nasal neuromodulation consistent with the present disclosure.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment and second (distal) segment.

FIG. 5B is an exploded, perspective view of the multi-segment end effector.

FIG. 5C is an enlarged, top view of the multi-segment end effector.

FIG. 5D is an enlarged, side view of the multi-segment end effector.

FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment of the multi-segment end effector.

FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment of the multi-segment end effector.

FIG. 6 is a perspective view, partly in section, of a portion of a support element illustrating an exposed conductive wire serving as an energy delivery element or electrode element.

FIG. 7 is a cross-sectional view of a portion of the shaft of the handheld device taken along lines 7-7 of FIG. 4.

FIG. 7A is a side view of the shaft and multi-segment end effector extending from a distal end thereof, further illustrating a plurality of electrodes provided on separate respective portions of the shaft.

FIG. 7B is a sectional view of the shaft illustrating one embodiment in which a plurality of electrodes are embedded within the outer sheath of the shaft.

FIG. 7C is a sectional view of the shaft illustrating another embodiment in which a plurality of electrodes are provided on the hypotube and associated portions of the outer sheath are absent or removed to thereby expose the underlying electrodes on the hypotube.

FIG. 7D is a perspective view of a length of the shaft illustrating exposed portions of the outer sheath to reveal the underlying electrodes provided on the hypotube.

FIG. 7E is a sectional view of the shaft illustrating another embodiment in which a plurality of electrodes are provided on one or more support elements extending through the hypotube, portions of which form the end effector.

FIG. 7F is an enlarged, perspective view of the multi-segment end effector extending from the shaft and illustrating the plurality of electrodes provided on the support elements.

FIG. 7G is a cross-sectional view of the shaft illustrating exemplary portions of the shaft that are retractable and expandable.

FIG. 8 is a side view of the handle of the handheld device.

FIG. 9 is a side view of the handle illustrating internal components enclosed within.

FIG. 10 is a side view of the handle illustrating multiple markings on a portion of the handle for providing a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

FIG. 11 is a perspective view of the shaft illustrating multiple markings on a distal portion thereof for providing a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

FIG. 12 is a partial cut-away side views illustrating one approach for delivering a shaft and an associated end effector to respective target sites within a nasal region in accordance with embodiments of the present disclosure.

FIG. 13 is a flow diagram illustrating one embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 14 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 15 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 16 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

Detailed Description

There are various conditions related to the nasal cavity which may impact breathing and other functions of the nose. One of the more common conditions is rhinitis, which is defined as inflammation of the membranes lining the nose. The symptoms of rhinitis include nasal blockage, obstruction, congestion, nasal discharge (e.g., rhinorrhea and/or posterior nasal drip), facial pain, facial pressure, and/or reduction or complete loss of smell and/or taste. Sinusitis is another common condition, which involves an inflammation or swelling of the tissue lining the sinuses, and results in similar symptoms as rhinitis, and may further lead to infection if left untreated or if it persists for prolonged periods of time. As a result of such symptoms, many individuals have sleeping difficulties (i.e., difficulty falling asleep and/or remaining asleep). Rhinitis and sinusitis are frequently associated with one another, as sinusitis is often preceded by rhinitis. Accordingly, the term rhinosinusitis is often used to describe both conditions.

Depending on the duration and type of systems, rhinosinusitis can fall within different subtypes, including allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, recurrent rhinitis, chronic sinusitis, acute sinusitis, recurrent sinusitis, and medical resistant rhinitis and/or sinusitis, in addition to combinations of one or more of the preceding conditions. It should be noted that an acute rhinosinusitis condition is one in which symptoms last for less than twelve weeks, whereas a chronic rhinosinusitis condition refers to symptoms lasting longer than twelve weeks.

A recurrent rhinosinusitis condition refers to four or more episodes of an acute rhinosinusitis condition within a twelve-month period, with resolution of symptoms between each episode. There are numerous environmental and biological causes of rhinosinusitis. Non-allergic rhinosinusitis, for example, can be caused by environmental irritants, medications, foods, hormonal changes, and/or nasal septum deviation. Triggers of allergic rhinitis can include exposure to seasonal allergens, perennial allergens that occur any time of year, and/or occupational allergens. Accordingly, rhinosinusitis affects millions of people and is a leading cause for patients to seek medical care.

The invention recognizes that a problem with current surgical procedures is that such procedures are not accurate and cause significant collateral damage in order to treat rhinitis and further fail to adequately treat the underlying symptoms.

The invention solves that problem by providing treatment devices having a combination of unique components, including an elongate body (which may be in the form of a shaft or sheath, or other elongate body), a retractable and expandable multi-segment end effector, and handle, that, as a whole, provide a high level of precise control and feedback to an operator during a procedure. In particular, the elongate body is configured to not only aid an operator in the positioning and delivery of the multi-segment end effector to a desired target site within the sino-nasal cavity, but further includes an electrode array provided along a length thereof that is configured to deliver energy to specific target sites within the nasal passage and sino-nasal cavity, in conjunction with neuromodulation provided by the multi-segment end effector. The multi-segment end effector is configured to complement anatomy at multiple different locations within the sino-nasal cavity. The handle is configured with multiple ergonomic and functional features that improve device use and feedback, such as independent control of deployment of the end effector and energy delivery and a shape associated with the architecture of the end effector in the deployed configuration. The handle may also include one or more markings that provide a user with a spatial orientation of the end effector while the end effector is in a sino-nasal cavity.

In that manner, the present invention provides devices that are capable of highly conforming to anatomical variations within a nasal passage and sino-nasal cavity while providing unprecedented control and guidance to an operator so that an operator can perform an accurate, minimally invasive, and localized application of energy to one or more target sites within the nasal passage and nasal cavity to cause multi-point interruption of neural signal without causing

collateral damage or disruption to other neural structures.

Unlike other surgical treatments for rhinitis, the devices of the invention are minimally invasive. Accordingly, a procedure can be performed in an office environment under local anesthetic. The multi-segment end-effector allows for targeting the autonomic supply to the nasal turbinates and will have a positive impact on both allergic and non-allergic rhinitis. Using this approach, it is expected that devices of the invention will be able to provide long-term symptom relief (e.g., years instead of months). Since the treatment is accurate with minimal collateral damage to the surrounding tissue, patients will begin to feel symptom relief immediately following the treatment. It is fully expected that patients will be removed from their pharmacotherapies following this therapy.

The systems and methods of the present invention include a handheld device comprising a retractable and expandable multi-segment end effector that, once delivered to the one more target sites within the sino-nasal cavity, can expand to a specific shape and/or size corresponding to anatomical structures within the sino-nasal cavity and associated with the target sites. In particular, the end effector includes at least a first flexible segment and a second flexible segment, each of which includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments become accurately positioned within the sino-nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

The handheld device further includes an elongate body operably associated with the end effector and a handle operably associated with the elongate body. The elongate body may be in the form of a shaft or sheath (or other elongate body operably associated with or coupled to the end effector). The elongate body may include a pre-defined shape (i.e., bent or angled at a

specific orientation) so as to assist the surgeon (or other medical professional) for placement of the end effector at the target sites. The elongate body further includes one or more electrodes provided on one or respective portions along a length thereof and can be used to deliver energy to tissue adjacent to, or in contact with, such portions of the elongate body. For example, in some embodiments, the elongate body may reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes of the multi-segment end effector, the surgeon may also activate and deliver energy from electrodes associated with the elongate body to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

It should be noted that, although many of the embodiments are described with respect to

devices, systems, and methods for therapeutically modulating tissue (neural and/or non-neural tissue) in the nasal region for the treatment of rhinitis, congestion, and/or rhinorrhea, other applications and other embodiments in addition to those described herein are within the scope of the present disclosure. For example, at least some embodiments of the present disclosure may be useful for the treatment of other indications, such as the treatment of chronic sinusitis and epistaxis. In particular, the embodiments described herein may be configured to treat allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, chronic sinusitis, acute sinusitis, chronic rhinosinusitis, acute rhinosinusitis, and/or medical resistant rhinitis.

It should further be noted that the devices described herein, most notably the elongate body (which may be in the form of a shaft, outer sheath, hypotube, metallic member, or other elongate body that is operably associated with the end effector) may be included and incorporated in any of the treatment devices, systems, and methods illustrated and described in U.S. Publication Nos.: 2016/0331459; 2018/0133460; 2017/0231651; 2017/0252089; 2018/0177542; 2018/0177546; 2018/0185085; 2018/0228533; 2018/0317997; 2018/0344378; 2019/0076185; 2019/0175242; 2019/0201069; 2019/0231409; 2019/0282289; 2016/0354136; 2017/0231474; 2018/0078327; 2018/0103994; 2018/0125560; 2018/0153375; 2018/0317993; 2018/0344411; and 2019/0083157, as well as U.S. Patent Nos.: 8,936,594; 8,986,301; 9,072,597; 9,179,964; 9,179,967; 9,237,924; 9,415,194; 9,433,463; 9,452,010; 9,486,278; 9,526,571; 9,687,296; 9,788,886; 9,801,752; 9,888,957; 9,913,682; 9,943,361; 10,028,780; 10,265,115; 10,335,221; 10,376,300; 10,398,489; 10,456,185; 10,456,186; 10,485,603; 7,758,571; 9,687,288; 9,763,723; 9,763,743; 10,028,781; 10,159,538; 10,201,687; 10,307,200; and 10,448,985, the contents of each of which are incorporated by reference herein in their entireties.

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic neuromodulation system 100 for treating a condition within a nasal cavity using a handheld device 102 according to some embodiments of the present disclosure. The system 100 generally includes a neuromodulation device 102 and a neuromodulation console 104 to which the device 102 is to be connected. FIG. 2 is a diagrammatic illustration of the console 104 coupled to the handheld neuromodulation device 102. As illustrated, the neuromodulation device 102 is a handheld device, which includes a retractable and expandable multi-segment end effector 114, a shaft 116 operably associated with the end effector 114 and a handle 118 operably associated with the shaft 116. The end effector 114 is configured to be advanced into the nasal cavity of a patient 12 and positioned at a

location associated with one or more target sites to undergo therapeutic neuromodulation treatment. It should be noted that the terms "end effector" and "therapeutic assembly" may be used interchangeably throughout this disclosure.

For example, a surgeon or other medical professional performing a procedure can utilize the handle 118 to manipulate and advance the shaft 116 within the nasal cavity, wherein the shaft 116 is configured to locate at least a distal portion thereof intraluminally at a treatment or target site within a nasal region. The one or more target sites may generally be associated with postganglionic parasympathetic fibers that innervate the nasal mucosa. The target site may be a region, volume, or area in which the target nerves are located and may differ in size and shape depending upon the anatomy of the patient. Once positioned, the end effector 114 may be deployed and subsequently deliver energy to the one or more target sites to thereby therapeutically modulating nerves of interest, particularly nerves associated with a rhinosinusitis condition so as to treat such condition. For example, the end effector 114 may include at least one energy delivery element, such as an electrode, configured to therapeutically modulate the postganglionic parasympathetic nerves. For example, one or more electrodes may be provided by one or more portions of the end-effector 114, wherein the electrodes may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the end effector 114 may include other energy delivery elements configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power.

In some embodiments, the end effector 114 may include one or more sensors (not shown), such as one or more temperature sensors (e.g., thermocouples, thermistors, etc.), impedance sensors, and/or other sensors. The sensors and/or the electrodes may be connected to one or more wires extending through the shaft 116 and configured to transmit signals to and from the sensors and/or convey energy to the electrodes.

As shown, the device 102 is operatively coupled to the console 104 via a wired connection, such as cable 120. It should be noted, however, that the device 102 and console 104 may be operatively coupled to one another via a wireless connection. The console 104 is configured to provide various functions for the neuromodulation device 102, which may include,

but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the neuromodulation device 102. For example, when the neuromodulation device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 may include an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the neuromodulation device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the neuromodulation device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via evaluation/feedback algorithms 110. For example, the evaluation/feedback algorithms 110 can be configured to provide information associated with the temperature of the tissue at the treatment site, the location of nerves at the treatment site, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In

certain embodiments, the evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to monitor temperature at the treatment site during therapy and automatically shut off the energy delivery when the temperature reaches a predetermined maximum (e.g., when applying RF energy) or predetermined minimum (e.g., when applying cryotherapy). In other embodiments, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a graphical user interface (GUI) 112 provided via a display on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104, such as a tablet or monitor. The GUI 112 may generally provide operational instructions for the procedure, such as directing the operator to select which nasal cavity to treat, indicating when the device 102 is primed and ready to perform treatment, and further providing status of therapy during the procedure, including indicating when the treatment is complete.

For example, in some embodiments, the end effector 114and/or other portions of the system 100 can be configured to detect various parameters of the heterogeneous tissue at the target site to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate nerves and/or other structures, and allow for neural mapping. For example, the end effector 114 may be configured to detect impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers in the target region. As shown in FIG. 1, the console 104 may further include a monitoring system 108 configured to receive detected electrical and/or thermal measurements of tissue at the target site taken by the end effector 114, specifically sensed by appropriate sensors (e.g., temperature sensors and/or impedance sensors), and process this information to identify the presence of nerves, the location of nerves, and/or neural activity at the target site. The nerve monitoring system 108 can be operably coupled to the electrodes and/or other features of the end effector 102 via signal wires (e.g., copper wires) that extend through the cable 120 and through

the length of the shaft 116. In other embodiments, the end effector 114 can be communicatively coupled to the nerve monitoring system 108 using other suitable communication means.

The nerve monitoring system 108 can determine neural locations and activity before therapeutic neuromodulation to determine precise treatment regions corresponding to the positions of the desired nerves, during treatment to determine the effect of the therapeutic neuromodulation, and/or after treatment to evaluate whether the therapeutic neuromodulation treated the target nerves to a desired degree. This information can be used to make various determinations related to the nerves proximate to the target site, such as whether the target site is suitable for neuromodulation. In addition, the nerve monitoring system 108 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site. For example, the nerve monitoring system 108 can further determine electroneurogram (ENG) signals based on recordings of electrical activity of neurons taken by the end effector 114 before and after therapeutic neuromodulation. Statistically meaningful (e.g., measurable or noticeable) decreases in the ENG signal(s) taken after neuromodulation can serve as an indicator that the nerves were sufficiently ablated. Additional features and functions of the nerve monitoring system 108, as well as other functions of the various components of the console 104, including the evaluation/feedback algorithms 110 for providing real-time feedback capabilities for ensuring optimal therapy for a given treatment is administered, are described in at least U.S. Publication No. 2016/0331459 and U.S. Publication No. 2018/0133460, the contents of each of which are incorporated by reference herein in their entireties.

As will be described in greater detail herein, the neuromodulation device 102 provides access to target sites deep within the nasal region, such as at the immediate entrance of parasympathetic fibers into the nasal cavity to therapeutically modulate autonomic activity within the nasal cavity. In certain embodiments, for example, the neuromodulation device 102 can position the end effector 114 into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

FIG. 3A is a cut-away side view illustrating the anatomy of a lateral nasal wall and FIG. 3B is an enlarged side view of the nerves of the lateral nasal wall of FIG. 1A. The sphenopalatine foramen (SPF) is an opening or conduit defined by the palatine bone and the

sphenoid bone through which the sphenopalatine vessels and the posterior superior nasal nerves travel into the nasal cavity. More specifically, the orbital and sphenoidal processes of the perpendicular plate of the palatine bone define the sphenopalatine notch, which is converted into the SPF by the articulation with the surface of the body of the sphenoid bone.

The location of the SPF is highly variable within the posterior region of the lateral nasal cavity, which makes it difficult to visually locate the SPF. Typically, the SPF is located in the middle meatus (MM). However, anatomical variations also result in the SPF being located in the superior meatus (SM) or at the transition of the superior and middle meatuses. In certain individuals, for example, the inferior border of the SPF has been measured at about 19 mm above the horizontal plate of the palatine bone (i.e., the nasal sill), which is about 13 mm above the horizontal lamina of the inferior turbinate (IT) and the average distance from the nasal sill to the SPF is about 64.4 mm, resulting in an angle of approach from the nasal sill to the SPA of about 11.4°. However, studies to measure the precise location of the SPF are of limited practical application due to the wide variation of its location.

The anatomical variations of the SPF are expected to correspond to alterations of the autonomic and vascular pathways traversing into the nasal cavity. In general, it is thought that the posterior nasal nerves (also referred to as lateral posterior superior nasal nerves) branch from the pterygopalatine ganglion (PPG), which is also referred to as the sphenopalatine ganglion, through the SPF to enter the lateral nasal wall of the nasal cavity, and the sphenopalatine artery passes from the pterygopalatine fossa through the SPF on the lateral nasal wall. The sphenopalatine artery branches into two main portions: the posterior lateral nasal branch and the posterior septal branch. The main branch of the posterior lateral nasal artery travels inferiorly into the inferior turbinate IT (e.g., between about 1.0 mm and 1.5 mm from the posterior tip of the inferior turbinate IT), while another branch enters the middle turbinate MT and branches anteriorly and posteriorly.

Beyond the SPF, studies have shown that over 30% of human patients have one or more accessory foramen that also carries arteries and nerves into the nasal cavity. The accessory foramen are typically smaller than the SPF and positioned inferior to the SPF. For example, there can be one, two, three or more branches of the posterior nasal artery and posterior nasal nerves that extend through corresponding accessory foramen. The variability in location, size, and quantity associated with the accessory foramen and the associated branching arteries and

nerves that travel through the accessory foramen gives rise to a great deal of uncertainty regarding the positions of the vasculature and nerves of the sphenopalatine region. Furthermore, the natural anatomy extending from the SPF often includes deep inferior and/or superior grooves that carry neural and arterial pathways, which make it difficult to locate arterial and neural branches. For example the grooves can extend more than 5 mm long, more than 2 mm wide, and more than 1 mm deep, thereby creating a path significant enough to carry both arteries and nerves. The variations caused by the grooves and the accessory foramen in the sphenopalatine region make locating and accessing the arteries and nerves (positioned posterior to the arteries) extremely difficult for surgeons.

Recent microanatomic dissection of the pterygopalatine fossa (PPF) have further evidenced the highly variable anatomy of the region surrounding the SPF, showing that a multiplicity of efferent rami that project from the pterygopalatine ganglion (PPG) to innervate the orbit and nasal mucosa via numerous groups of small nerve fascicles, rather than an individual postganglionic autonomic nerves (e.g., the posterior nasal nerve). Studies have shown that at least 87% of humans have microforamina and micro rami in the palatine bone.

FIG. 3C, for example, is a front view of a left palatine bone illustrating geometry of microforamina and micro rami in a left palatine bone. In FIG. 3C, the solid regions represent nerves traversing directly through the palatine bone, and the open circles represent nerves that were associated with distinct microforamina. As such, FIG. 3C illustrates that a medial portion of the palatine bone can include at least 25 accessory posterolateral nerves.

The respiratory portion of the nasal cavity mucosa is composed of a type of ciliated pseudostratified columnar epithelium with a basement membrane. Nasal secretions (e.g., mucus) are secreted by goblet cells, submucosal glands, and transudate from plasma. Nasal seromucous glands and blood vessels are highly regulated by parasympathetic innervation deriving from the vidian and other nerves. Parasympathetic (cholinergic) stimulation through acetylcholine and vasoactive intestinal peptide generally results in mucus production. Accordingly, the parasympathetic innervation of the mucosa is primarily responsible submucosal gland activation/hyper activation, venous engorgement (e.g., congestion), and increased blood flow to the blood vessels lining the nose. Accordingly, severing or modulating the parasympathetic pathways that innervate the mucosa are expected to reduce or eliminate the hyper activation of

the submucosal glands and engorgement of vessels that cause symptoms associated with rhinosinusitis and other indications.

As previously described herein, postganglionic parasympathetic fibers that innervate the nasal mucosa (i.e., posterior superior nasal nerves) were thought to travel exclusively through the SPF as a sphenopalatine neurovascular bundle. The posterior nasal nerves are branches of the maxillary nerve that innervate the nasal cavity via a number of smaller medial and lateral branches extending through the mucosa of the superior and middle turbinates ST, MT (i.e., nasal conchae) and to the nasal septum. The nasopalatine nerve is generally the largest of the medial posterior superior nasal nerves, and it passes anteroinferiorly in a groove on the vomer to the floor of the nasal cavity. From here, the nasopalatine nerve passes through the incisive fossa of the hard palate and communicates with the greater palatine nerve to supply the mucosa of the hard palate. The posterior superior nasal nerves pass through the pterygopalatine ganglion PPG without synapsing and onto the maxillary nerve via its ganglionic branches.

Based on the understanding that the posterior nasal nerves exclusively traverse the SPF to innervate the nasal mucosa, surgeries have been performed to selectively sever the posterior nasal nerve as it exits the SPF. However, as discussed above, the sinonasal parasympathetic pathway actually comprises individual rami project from the pterygopalatine ganglion (PPG) to innervate the nasal mucosa via multiple small nerve fascicles (i.e., accessory posterolateral nerves), not a single branch extending through the SPF. These rami are transmitted through multiple fissures, accessory foramina, and microforamina throughout the palatine bone and may demonstrate anastomotic loops with both the SPF and other accessory nerves. Thus, if only the parasympathetic nerves traversing the SPF were severed, almost all patients (e.g., 90% of patients or more) would retain intact accessory secretomotor fibers to the posterolateral mucosa, which would result in the persistence of symptoms the neurectomy was meant to alieve.

Accordingly, embodiments of the present disclosure are configured to therapeutically modulate nerves at precise and focused treatment sites corresponding to the sites of rami extending through fissures, accessory foramina, and microforamina throughout the palatine bone (e.g., target region T shown in FIG. 3B). In certain embodiments, the targeted nerves are postganglionic parasympathetic nerves that go on to innervate the nasal mucosa. This selective neural treatment is also expected to decrease the rate of postoperative nasal crusting and dryness because it allows a clinician to titrate the degree of anterior denervation through judicious

sparing of the rami orbitonasal. Furthermore, embodiments of the present disclosure are also expected to maintain at least some sympathetic tone by preserving a portion of the sympathetic contributions from the deep petrosal nerve and internal maxillary periarterial plexus, leading to improved outcomes with respect to nasal obstruction. In addition, embodiments of the present disclosure are configured to target a multitude of parasympathetic neural entry locations (e.g., accessory foramen, fissures, and microforamina) to the nasal region to provide for a complete resection of all anastomotic loops, thereby reducing the rate of long-term re-innervation.

FIG. 4 is a side view of one embodiment of a handheld device 102 for providing therapeutic nasal neuromodulation consistent with the present disclosure. As illustrated, the device 102 includes a multi-segment end effector 114 transformable between a retracted configuration and an expanded deployed configuration, a shaft 116 operably associated with the end effector 114, and a handle 118 operably associated with the shaft 116. The multi-segment end effector 114 includes at least a first segment 122 and a second segment 124 spaced apart from one another. The first segment 122 is generally positioned closer to a distal end of the shaft 116, and is thus sometimes referred to herein as the proximal segment 122, while the second segment 124 is generally positioned further from the distal end of the shaft 116 and is thus sometimes referred to herein as the distal segment 124. Each of the first and second segments 122 and 124 is transformable between a retracted configuration, which includes a low-profile delivery state to facilitate intraluminal delivery of the end effector 114 to a treatment site within the nasal region, and a deployed configuration, which includes an expanded state, as shown in FIG. 4 and further illustrated in FIGS. 5A-5F. The handle 118 includes at least a first mechanism 126 for deployment of the multi-segment end effector 114, notably the first and second segments 122, 124, from the retracted configuration to the deployed configuration and a second mechanism 128, separate from the first mechanism 124, for control of energy output by either of the first and second segments 122, 124 of the end effector 114, specifically electrodes or other energy elements provided by first and/or second segments 122, 124. The handheld device 102 may further include an auxiliary line 121, which may provide a fluid connection between a fluid source, for example, and the shaft 116 such that fluid may be provided to a target site via the distal end of the shaft 116. In some embodiments, the auxiliary line 121 may provide a connection between a vacuum source and the shaft 116, such that the device 102 may include suction capabilities (via the distal end of the shaft 116).

FIGS. 5A, 5B, 5C, 5D, 5E, and 5F are enlarged views of the multi-segment end effector 114, illustrating various views of the first and second segments 122, 124 in greater detail. FIG. 5A is an enlarged, perspective view of the multi-segment end effector 114. FIG. 5B is an exploded, perspective view of the multi-segment end effector 114. FIGS. 5C and 5D are enlarged, top and side views, respectively, of the multi-segment end effector 114. FIG. 5E is an enlarged, front (proximal facing) view of the first segment 122 of the multi-segment end effector 114. FIG. 5F is an enlarged, front (proximal facing) view of the second segment 124 of the multi-segment end effector 114.

As illustrated, the first segment 122 includes at least a first set of flexible support elements, generally in the form of wires, arranged in a first configuration, and the second segment 124 includes a second set of flexible support elements, also in the form of wires, arranged in a second configuration. The first and second sets of flexible support elements include composite wires having conductive and elastic properties. For example, in some embodiments, the composite wires include a shape memory material, such as nitinol. The flexible support elements may further include a highly lubricious coating, which may allow for desirable electrical insulation properties as well as desirable low friction surface finish. Each of the first and second segments 122, 124 is transformable between a retracted configuration and an expanded deployed configuration such that the first and second sets of flexible support elements are configured to position one or more electrodes provided on the respective segments (see electrodes 136 in FIGS. 5E and 5F) into contact with one or more target sites when in the deployed configuration.

As shown, when in the expanded deployed configuration, the first set of support elements of the first segment 122 includes at least a first pair of struts 130a, 130b, each comprising a loop (or leaflet) shape and extending in an upward direction and a second pair of struts 132a, 132b, each comprising a loop (or leaflet) shape and extending in a downward direction, generally in an opposite direction relative to at least the first pair of struts 130a, 130b. It should be noted that the terms upward and downward are used to describe the orientation of the first and second segments 122, 124 relative to one another. More specifically, the first pair of struts 130a, 130b generally extend in an outward inclination in a first direction relative to a longitudinal axis of the multi-segment end effector 114 and are spaced apart from one another. Similarly, the second pair of struts 132a, 132b extend in an outward inclination in a second direction substantially

opposite the first direction relative to the longitudinal axis of the multi-segment end effector and spaced apart from one another.

The second set of support elements of the second segment 124, when in the expanded deployed configuration, includes a second set of struts 134(1), 134(2), 134(n) (approximately six struts), each comprising a loop shape extending outward to form an open-ended circumferential shape. As shown, the open-ended circumferential shape generally resembles a blooming flower, wherein each looped strut 134 may generally resemble a flower petal. It should be noted that the second set of struts 134 may include any number of individual struts and is not limited to six, as illustrated. For example, in some embodiments, the second segment 124 may include two, three, four, five, six, seven, eight, nine, ten, or more struts 134.

The first and second segments 122, 124, specifically struts 130, 132, and 134 include one or more energy delivery elements, such as a plurality of electrodes 136. It should be noted that any individual strut may include any number of electrodes 136 and is not limited to one electrode, as shown. In the expanded state, the struts 130, 132, and 134 can position any number of electrodes 136 against tissue at a target site within the nasal region (e.g., proximate to the palatine bone inferior to the SPF). The electrodes 136 can apply bipolar or multi-polar radiofrequency (RF) energy to the target site to therapeutically modulate postganglionic parasympathetic nerves that innervate the nasal mucosa proximate to the target site. In various embodiments, the electrodes 136 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

The first and second segments 122, 124 and the associated struts 130, 132, and 134 can have sufficient rigidity to support the electrodes 136 and position or press the electrodes 136 against tissue at the target site. In addition, each of the expanded first and second segments 122, 124 can press against surrounding anatomical structures proximate to the target site (e.g., the turbinates, the palatine bone, etc.) and the individual struts 130, 132, 134 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 114 In addition, the expansion and conformability of the struts 130, 132, 134 can facilitate placing the electrodes 136 in contact with the surrounding tissue at the target site. The electrodes 136 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene (PEDOT), titanium, titanium nitride, carbon, carbon

nanotubes, platinum grey, Drawn Filled Tubing (DFT) with a silver core, and/or other suitable materials for delivery RF energy to target tissue. In some embodiments, such as illustrated in FIG. 6, a strut may include an outer jacket surrounding a conductive wire, wherein portions of the outer jacket are selectively absent along a length of the strut, thereby exposing the underlying conductive wire so as to act as an energy delivering element (i.e., an electrode) and/or sensing element, as described in greater detail herein.

In certain embodiments, each electrode 136 can be operated independently of the other electrodes 136. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein. The selective independent control of the electrodes 136 allows the end effector 114 to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 136 can be activated to target neural fibers in a specific region while the other electrodes 136 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 124 that is adjacent to tissue at the target site, and the electrodes 136 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves on the lateral nasal wall within one nostril without applying energy to structures in other portions of the nasal cavity.

The electrodes 136 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1) via wires (not shown) that extend from the electrodes 136, through the shaft 116, and to the RF generator. When each of the electrodes 136 is independently controlled, each electrode 136 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 136 can be controlled together and, therefore, multiple electrodes 136 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 136. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 136, and do so while activating the electrodes 136 in a predetermined pattern selected based on the position of the end effector 114 relative to the treatment site and/or the identified locations of the target nerves. The RF generator is able to provide bipolar low power (10 watts with maximum

setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

Once deployed, the first and second segments 122, 124 contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments 122, 124 become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes 136, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments 122, 124 have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments 122, 124, and thus one or more electrodes associated therewith 136, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

For example, the first set of flexible support elements of the first segment 122 conforms to and complements a shape of a first anatomical structure at the first location when the first segment 122 is in the deployed configuration and the second set of flexible support elements of the second segment 124 conforms to and complements a shape of a second anatomical structure at the second location when the second segment is in the deployed configuration. The first and second anatomical structures may include, but are not limited to, inferior turbinate, middle turbinate, superior turbinate, inferior meatus, middle meatus, superior meatus, pterygopalatine region, pterygopalatine fossa, sphenopalatine foramen, accessory sphenopalatine foramen(ae), and sphenopalatine micro-foramen(ae).

In some embodiments, the first segment 122 of the multi-segment end effector 114 is configured in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to the middle turbinate and the second segment 124 of the multi-segment end effector is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the middle turbinate.

For example, the first set of flexible support elements of the first segment (i.e., struts 130 and 132) conforms to and complements a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 122 is in the deployed configuration and the second set of flexible support elements (i.e., struts 134) of the second segment 124 contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment

and posterior-inferior edge of middle turbinate when the second segment 124 is in the deployed configuration. Accordingly, when in the deployed configuration, the first and second segments 122, 124 are configured to position one or more associated electrodes 136 at one or more target sites relative to either of the middle turbinate and the plurality of tissue locations in the cavity behind the middle turbinate. In turn, electrodes 136 are configured to deliver RF energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

As illustrated in FIG. 5E, the first segment 122 comprises a bilateral geometry. In particular, the first segment 122 includes two identical sides, including a first side formed of struts 130a, 132a and a second side formed of struts 130b, 132b. This bilateral geometry allows at least one of the two sides to conform to and accommodate an anatomical structure within the nasal cavity when the first segment 122 is in an expanded state. For example, when in the expanded state, the plurality of struts 130a, 132a contact multiple locations along multiple portions of the anatomical structure and electrodes provided by the struts are configured to emit energy at a level sufficient to create multiple micro-lesions in tissue of the anatomical structure that interrupt neural signals to mucus producing and/or mucosal engorgement elements. In particular, struts 130a, 132a conform to and complement a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 122 is in the deployed configuration, thereby allowing for both sides of the anatomical structure to receive energy from the electrodes. By having this independence between first and second side (i.e., right and left side) configurations, the first segment 122 is a true bilateral device. By providing a bilateral geometry, the multi-segment end effector 114 does not require a repeat use configuration to treat the other side of the anatomical structure, as both sides of the structure are accounted at the same time due to the bilateral geometry. The resultant micro-lesion pattern can be repeatable and is predictable in both macro element (depth, volume, shape parameter, surface area) and can be controlled to establish low to high effects of each, as well as micro elements (the thresholding of effects within the range of the macro envelope can be controlled), as well be described in greater detail herein. The systems of the present invention are further able to establish gradients within allowing for control over neural effects without having widespread effect to other cellular bodies, as will be described in greater detail herein.

FIG. 7 is a cross-sectional view of a portion of the shaft 116 of the handheld device taken along lines 7-7 of FIG. 4. As illustrated, the shaft 116 may be constructed from multiple components so as to have the ability to constrain the end effector 114 in the retracted configuration (i.e., the low-profile delivery state) when the end effector 114 is retracted within the shaft 116, and to further provide an atraumatic, low profile and durable means to deliver the end effector 114 to the target site. The shaft 116 includes coaxial tubes which travel from the handle 118 to a distal end of the shaft 116. The shaft 116 assembly is low profile to ensure trans-nasal delivery of therapy. The shaft 116 includes an outer sheath 138, surrounding a hypotube 140, which is further assembled over electrode wires 129 which surround an inner lumen 142. The outer sheath 138 serves as the interface between the anatomy and the device 102. The outer sheath 138 may generally include a low friction PTFE liner to minimize friction between the outer sheath 138 and the hypotube 140 during deployment and retraction. In particular, the outer sheath 138 may generally include an encapsulated braid along a length of the shaft 116 to provide flexibility while retaining kink resistance and further retaining column and/or tensile strength. For example, the outer sheath 138 may include a soft Pebax material, which is atraumatic and enables smooth delivery through the nasal passage. The outer sheath 138 may further include orientation/landmark markings on an exterior surface thereof, generally at the distal end, wherein the markings may provide a visual indication to an operator of the architecture and/or spatial orientation of first and/or second segments 122, 124 of the end effector 114 to assist in positioning and deployment of the end effector 114.

The hypotube 140 is assembled over the electrode wires starting within the handle 118 and travelling to the proximal end of the end effector 114. The hypotube 140 generally acts to protect the wires during delivery and is malleable to enable flexibility without kinking to thereby improve trackability. The hypotube 140 provides stiffness and enables torqueability of the device 102 to ensure accurate placement of the end effector 114. The hypotube 140 also provides a low friction exterior surface which enables low forces when the outer sheath 138 moves relative to the hypotube 140 during deployment and retraction or constraint. The shaft 116 may be pre-shaped in such a manner so as to complement the nasal cavity. For example, the hypotube 140 may be annealed to create a bent shaft 116 with a pre-set curve. The hypotube 140 may include a stainless-steel tubing, for example, which interfaces with a liner in the outer sheath 138 for low friction movement.

The inner lumen 142 may generally provide a channel for fluid extraction during a treatment procedure. For example, the inner lumen 142 extends from the distal end of the shaft 116 through the hypotube 140 and to atmosphere via a fluid line (line 121 of FIG. 4). The inner lumen 142 materials are chosen to resist forces of external components acting thereon during a procedure.

FIG. 7A is a side view of one embodiment of an elongate body and a multi-segment end effector extending from a distal end thereof, further illustrating a plurality of electrodes provided on separate respective portions of the elongate body. In the illustrated example, the elongate body may generally be in the form of the shaft 116, including one or more specific components of the shaft 116, as previously described herein. For example, the elongate body in the present example may include the outer sheath 138, such that one or more electrodes 137 are provided and positioned on separate respective portions of the outer sheath 138. FIG. 7B is a sectional view of the shaft 116 illustrating one embodiment in which a plurality of electrodes are embedded within the outer sheath 138. As further illustrated in FIG. 7B, the electrodes 137 may be provided along an entirety of the circumference of the outer sheath 138 (i.e., along substantially all sides of the outer sheath 138).

FIG. 7C is a sectional view of the shaft 116 illustrating another embodiment in which a plurality of electrodes 137 are provided on the hypotube 140 and associated portions of the outer sheath 138 are absent or removed to thereby expose the underlying electrodes 137 on the hypotube 140. FIG. 7D is a perspective view of a length of the shaft 116 illustrating exposed portions of the outer sheath 138 to reveal the underlying electrodes 137 provided on the hypotube 140. More specifically, portions of the outer sheath 138 may be selectively absent along a length thereof, thereby exposing any underlying electrodes 137 provided on the enclosed portion of the hypotube 140. Accordingly, in such an embodiment, the elongate body is in the form of the hypotube 140.

FIG. 7E is a sectional view of the shaft 116 illustrating another embodiment in which a plurality of electrodes 137 are provided on one or more support elements 129 extending through the hypotube 140, portions of which form the end effector 114. FIG. 7F is an enlarged, perspective view of the multi-segment end effector 114 extending from the shaft 116, specifically the hypotube 140 and illustrating the plurality of electrodes 137 provided on the support elements 129. For example, during deployment of the end effector 114 from the

retracted to expanded configurations, proximal portions of the support elements 129 that form the proximal and distal segments 122 and 124 may be further exposed to thereby further expose the electrodes 137 provided thereon. Accordingly, in such an embodiment, the elongate body is in the form of the assembly of support elements 129.

In some embodiments, respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration. For example, FIG. 7G is a cross-sectional view of the shaft 116, specifically the outer sheath 138, illustrating exemplary portions of the sheath 138 that may be retractable and expandable. When in the expanded configuration, each separate respective portion of the outer sheath 138 may be configured to position a separate associated one of the electrodes 137 into contact with a target tissue.

Similar to electrodes 136, the electrodes 137 may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the electrodes 137 may be configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power. Yet still, in other embodiments, the electrodes can apply bipolar or multi-polar radiofrequency (RF) energy to a target site to therapeutically modulate tissue at the target site, which may include ablation of the tissue. For example, in various embodiments, the electrodes 136 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

In certain embodiments, each electrode 137 can be operated independently of the other electrodes 137. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein. The selective independent control of the electrodes 137 allows respective portions of the shaft to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 137 can be activated to target tissue in a specific portion of the inferior turbinate while the other electrodes 137 remain inactive.

The electrodes 137 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1) via wires (not shown) that extend from the electrodes 137, through the shaft 116, and to the RF generator. When each of the electrodes 137 is independently controlled, each electrode

137 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 137 can be controlled together and, therefore, multiple electrodes 137 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 137. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 137, and do so while activating the electrodes 137 in a predetermined pattern selected based on the position of the shaft 116 relative to the treatment site and/or the identified locations of the target tissue. The RF generator is able to provide bipolar low power (10 watts with maximum setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

The electrodes 137 may be used to deliver energy to tissue adjacent to, or in contact with, such the respective portions of the shaft 116. For example, in some embodiments, the shaft 116 may generally reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector 114 in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes 136 of the multi-segment end effector 114, the surgeon may also activate and deliver energy from electrodes 137 associated with a given component of the shaft 116 (i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient and improve a patient's ability to breathe. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or result in local hypoxia of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

Accordingly, in a given procedure, the surgeon may utilize the multi-segment end effector 114 to deliver energy (via electrodes 136) at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a

palatine bone of the patient and further utilize a component of the shaft 116 or other elongate body operably associated with the end effector 114 (i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to deliver energy (via electrodes 137) at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient. Such a combination of energy delivery to two specific targeted sites improves the manner in which at least one of rhinitis, congestion, and rhinorrhea are treated, thereby increasing the potential for reducing or completely eliminating symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

FIG. 8 is a side view of the handle 118. FIG. 9 is a side view of the handle 118 illustrating internal components enclosed within. The handle 118 generally includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. For example, the handle 118 may include specific contours, including recesses 144, 146, and 148 which are designed to naturally receive one or more of an operator's fingers in either of an overhand grip or underhand grip style and provide a comfortable feel for the operator. For example, in an underhand grip, recess 144 may naturally receive an operator's index finger, recess 146 may naturally receive an operator's middle finger, and recess 148 may naturally receive an operator's ring and little (pinkie or pinky) fingers which wrap around the proximal protrusion 150 and the operator's thumb naturally rests on a top portion of the handle 118 in a location adjacent to the first mechanism 126. In an overhand grip, the operator's index finger may naturally rest on the top portion of the handle 118, adjacent to the first mechanism 126, while recess 144 may naturally receive the operator's middle finger, recess 146 may naturally receive a portion of the operator's middle and/or ring fingers, and recess 148 may naturally receive and rest within the space (sometimes referred to as the purlicue) between the operator's thumb and index finger.

As previously described, the handle includes multiple user-operated mechanisms, including at least a first mechanism 126 for deployment of the end effector 114 from the retracted configuration to the expanded deployed configuration and a second mechanism 128 for controlling of energy output by the end effector, notably energy delivery from one or more electrodes 136. As shown, the user inputs for the first and second mechanisms 126, 128 are

positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. For example, user input for the first mechanism 126 is positioned on a top portion of the handle 118 adjacent the grip portion and user input for the second mechanism 128 is positioned on side portions of the handle 118 adjacent the grip portion. As such, in an underhand grip style, the operator's thumb rests on the top portion of the handle adjacent to the first mechanism 126 and at least their middle finger is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. In an overhand grip system, the operator's index finger rests on the top portion of the handle adjacent to the first mechanism 126 and at least their thumb is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

Referring to FIG. 9, the various components provided within the handle 118 are illustrated. As shown, the first mechanism 126 may generally include a rack and pinion assembly providing movement of the end effector 114 between the retracted and deployed configurations in response to input from a user-operated controller. The rack and pinion assembly generally includes a set of gears 152 for receiving input from the user-operated controller and converting the input to linear motion of a rack member 154 operably associated with at least one of the shaft 116 and the end effector 114. The rack and pinion assembly comprises a gearing ratio sufficient to balance a stroke length and retraction and deployment forces, thereby improving control over the deployment of the end effector. As shown, the rack member 154 may be coupled to a portion of the shaft 116, for example, such that movement of the rack member 154 in a direction towards a proximal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector 114 remains stationary, thereby exposing the end effector 114 and allowing the end effector 114 to transition from the constrained, retracted configuration to the expanded, deployed configuration. Similarly, upon movement of the rack member 154 in a direction towards a distal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector 114 remains stationary, thereby enclosing the end effector 114 within the shaft 116. It should be noted that, in other embodiments, the rack member 154 may be directly coupled to a portion of the end effector 114

such that movement of the rack member 154 results in corresponding movement of the end effector 114 while the shaft 116 remains stationary, thereby transitioning the end effector 114 between the retracted and deployed configurations.

The user-operated controller associated with the first mechanism 126 may include a slider mechanism operably associated with the rack and pinion rail assembly. Movement of the slider mechanism in a rearward direction towards a proximal end of the handle results in transitioning of the end effector 114 to the deployed configuration and movement of the slider mechanism in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration. In other embodiment, the user-operated controller associated with the first mechanism 126 may include a scroll wheel mechanism operably associated with the rack and pinion rail assembly. Rotation of the wheel in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and rotation of the wheel in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration.

The user-operated controller associated with the first mechanism 126 may generally provide a high degree of precision and control over the deployment (and retraction) of the first and second segments 122, 124. For example, in some instances, the operator may wish to only deploy the second segment 124 during the procedure, while the first segment 122 remains in the retracted configuration. The user-operated controller allows for an operator to provide a sufficient degree of input (i.e., slide the slider mechanism or scroll the scroll wheel to a specific position) which results in only the second segment 124 transitioning from the retracted configuration to the deployed configuration (while the first segment 122 remains enclosed within the shaft 116 and in the retracted configuration). For example, in some embodiments, the end effector 114 may further include a detent feature, such as a catch or similar element, positioned between the first and second segments 122, 124 and configured to provide a surgeon with feedback, such as haptic or tactile feedback, during deployment of the end effector segments, alerting the surgeon when at least the second segment 124 is fully deployed. In particular, as the surgeon slides the slider mechanism or scrolls the scroll wheel during deployment of the second segment 124, the detect feature (provided between the first and second segments 122, 124) may then reach a portion of the shaft 116 and cause an increase in resistance on the slider mechanism or scroll wheel, thereby indicating to the surgeon that the second segment 124 has been deployed

and the first segment 122 remains in the retracted configuration. Accordingly, the surgeon can position and orient the second segment 124 as they desire without concern over the first segment 122 as it remains in the retracted configuration. In turn, one the second segment 124 is positioned at the desired target site, the surgeon may then deploy the first segment 122 to perform the procedure. Yet still, in some instances, only the second segment 124 may be used to perform a procedure (i.e., deliver energy to one or more target sites in contact with the second segment 124) and, as such, the first segment 122 may never be deployed.

The second mechanism 128 may generally include a user-operated controller configured to be actuated between at least an active position and an inactive position to thereby control delivery of energy from the end effector 114, notable delivery of energy from the electrodes 136. The user-operated controller may be multi-modal in that the user-operated controller may be actuated between multiple positions providing different functions/modes. For example, upon a single user input (i.e., single press of button associated within controller), the second mechanism may provide a baseline apposition / sensing check function prior to modulation. Upon pressing and holding the controller button for a pre-defined period of time, the energy output from the end effector may be activated. Further, upon double-tapping the controller button, energy output is deactivated.

Furthermore, the handle and/or the shaft may include markings that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. FIG. 10 is a side view of the handle 118 illustrating multiple markings on a distal end of the handle 118 and FIG. 11 is a perspective view of a portion of the shaft 116 illustrating multiple markings on a distal end thereof. In particular, multiple markings may be provided on the handle and/or shaft and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. The markings may include, for example, text, symbols, color-coding insignia, or the like. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the shaft, a surgeon can rely on the markings on the handle and/or shaft as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

For example, the handle and/or shaft may include markings associated with each of the first pair of struts 130a, 130b and each of the second pair of struts 132a, 132b, so as to provide an operator with a visual indication as to the resulting spatial orientation and architecture of at least the first segment 122 when initially navigating the nasal cavity and delivering the distal end of the shaft 116 to a target site, prior to deployment of the end effector 114. In other words, the markings provide an operator with an indication of the orientation of at least the first segment 122 of the end effector 114 prior to deploying the end effector 114, thereby ensuring accurate positioning at the desired location.

FIG. 12 is a partial cut-away side view illustrating one approach for delivering an end effector 114 a target site within a nasal region in accordance with embodiments of the present disclosure. As shown, the distal portion of the shaft 116 extends into the nasal passage (NP), through the inferior meatus (IM) between the inferior turbinate (IT) and the nasal sill (NS), and around the posterior portion of the inferior turbinate (IT) where the end effector 114 is deployed at a treatment site. The treatment site can be located proximate to the access point or points of postganglionic parasympathetic nerves (e.g., branches of the posterior nasal nerve and/or other parasympathetic neural fibers that innervate the nasal mucosa) into the nasal cavity. In other embodiments, the target site can be elsewhere within the nasal cavity depending on the location of the target nerves.

In various embodiments, the distal portion of the shaft 116 may be guided into position at the target site via a guidewire (not shown) using an over-the-wire (OTW) or a rapid exchange (RX) technique. For example, the end effector 114 can include a channel for engaging the guidewire. Intraluminal delivery of the end effector 114 can include inserting the guide wire into an orifice in communication with the nasal cavity (e.g., the nasal passage or mouth), and moving the shaft 116 and/or the end effector 114 along the guide wire until the end effector 114 reaches a target site (e.g., inferior to the SPF).

Yet still, in further embodiments, the neuromodulation device 102 can be configured for delivery via a guide catheter or introducer sheath (not shown) with or without using a guide wire. The introducer sheath can first be inserted intraluminally to the target site in the nasal region, and the distal portion of the shaft 116 can then be inserted through the introducer sheath. At the target site, the end effector 114 can be deployed through a distal end opening of the introducer sheath or a side port of the introducer sheath. In certain embodiments, the introducer sheath can

include a straight portion and a pre-shaped portion with a fixed curve (e.g., a 5 mm curve, a 4 mm curve, a 3 mm curve, etc.) that can be deployed intraluminally to access the target site. In this embodiment, the introducer sheath may have a side port proximal to or along the pre-shaped curved portion through which the end effector 114 can be deployed. In other embodiments, the introducer sheath may be made from a rigid material, such as a metal material coated with an insulative or dielectric material. In this embodiment, the introducer sheath may be substantially straight and used to deliver the end effector 114 to the target site via a substantially straight pathway, such as through the middle meatus (MM) (FIG. 3A).

Image guidance may be used to aid the surgeon's positioning and manipulation of the distal portion of the shaft 116, as well as the deployment and manipulation of the end effector 114, specifically the first and second segments 122 thereof. For example, an endoscope 100 and/or other visualization device can be positioned to visualize the target site, the positioning of the end effector 114 at the target site, and/or the end effector 114 during therapeutic neuromodulation. The endoscope 100 may be delivered proximate to the target site by extending through the nasal passage NP and through the middle meatus MM between the inferior and middle turbinates IT and MT. From the visualization location within the middle meatus MM, the endoscope 100 can be used to visualize the treatment site, surrounding regions of the nasal anatomy, and the end effector 114.

In some embodiments, the distal portion of the shaft 116 may be delivered via a working channel extending through an endoscope, and therefore the endoscope can provide direct in-line visualization of the target site and the end effector 114. In other embodiments, an endoscope is incorporated with the end effector 114 and/or the distal portion of the shaft 116 to provide in-line visualization of the end effector 114 and/or the surrounding nasal anatomy. In other embodiments, image guidance can be provided with various other guidance modalities, such as image filtering in the infrared (IR) spectrum to visualize the vasculature and/or other anatomical structures, computed tomography (CT), fluoroscopy, ultrasound, optical coherence tomography (OCT), and/or combinations thereof. Yet still, in some embodiments, image guidance components may be integrated with the neuromodulation device 102 to provide image guidance during positioning of the end effector 114.

Once positioned at the target site, the therapeutic modulation may be applied via the one or more electrodes 136 and/or other features of the end effector 114 to precise, localized regions

of tissue to induce one or more desired therapeutic neuromodulating effects to disrupt parasympathetic motor sensory function. The end effector 114 can selectively target postganglionic parasympathetic fibers that innervate the nasal mucosa at a target or treatment site proximate to or at their entrance into the nasal region. For example, the end effector 114 can be positioned to apply therapeutic neuromodulation at least proximate to the SPF (FIG. 3A) to therapeutically modulate nerves entering the nasal region via the SPF. The end effector 114 can also be positioned to inferior to the SPF to apply therapeutic neuromodulation energy across accessory foramen and microforamina (e.g., in the palatine bone) through which smaller medial and lateral branches of the posterior superior lateral nasal nerve enter the nasal region. The purposeful application of the energy at the target site may achieve therapeutic neuromodulation along all or at least a portion of posterior nasal neural fibers entering the nasal region. The therapeutic neuromodulating effects are generally a function of, at least in part, power, time, and contact between the energy delivery elements and the adjacent tissue. For example, in certain embodiments therapeutic neuromodulation of autonomic neural fibers are produced by applying RF energy at a power of about 2-20 W (e.g., 5 W, 7 W, 10 W, etc.) for a time period of about 1-20 sections (e.g., 5-10 seconds, 8-10 seconds, 10-12 seconds, etc.).

The therapeutic neuromodulating effects may include partial or complete denervation via thermal ablation and/or non-ablative thermal alteration or damage (e.g., via sustained heating and/or resistive heating). Desired thermal heating effects may include raising the temperature of target neural fibers above a desired threshold to achieve non-ablative thermal alteration, or above a higher temperature to achieve ablative thermal alteration. For example, the target temperature may be above body temperature (e.g., approximately 37° C.) but less than about 90° C. (e.g., 70-75° C.) for non-ablative thermal alteration, or the target temperature may be about 100° C. or higher (e.g., 110° C., 120° C., etc.) for the ablative thermal alteration. Desired non-thermal neuromodulation effects may include altering the electrical signals transmitted in a nerve.

Sufficiently modulating at least a portion of the parasympathetic nerves is expected to slow or potentially block conduction of autonomic neural signals to the nasal mucosa to produce a prolonged or permanent reduction in nasal parasympathetic activity. This is expected to reduce or eliminate activation or hyperactivation of the submucosal glands and venous engorgement and, thereby, reduce or eliminate the symptoms of rhinosinusitis. Further, because the device 102 applies therapeutic neuromodulation to the multitude of branches of the posterior nasal

nerves rather than a single large branch of the posterior nasal nerve branch entering the nasal cavity at the SPF, the device 102 provides a more complete disruption of the parasympathetic neural pathway that affects the nasal mucosa and results in rhinosinusitis. Accordingly, the device 102 is expected to have enhanced therapeutic effects for the treatment of rhinosinusitis and reduced re-innervation of the treated mucosa.

In other embodiments, the device 102 can be configured to therapeutically modulate nerves and/or other structures to treat different indications. For example, the device 102 can be used to therapeutically modulate nerves that innervate the para-nasal sinuses to treat chronic sinusitis. In further embodiments, the system 100 and the device 102 disclosed herein can be configured therapeutically modulate the vasculature within the nasal anatomy to treat other indications, such as epistaxis (i.e., excessive bleeding from the nose). For example, the system 100 and the device 102 devices described herein can be used to apply therapeutically effective energy to arteries (e.g., the sphenopalatine artery and its branches) as they enter the nasal cavity (e.g., via the SPF, accessory foramen, etc.) to partially or completely coagulate or ligate the arteries. In other embodiments, the system 100 and the device 102 can be configured to partially or completely coagulate or ligate veins and/or other vessels. For such embodiments in which the end effector 114 ligates or coagulates the vasculature, the system 100 and device 102 would be modified to deliver energy at significantly higher power (e.g., about 100 W) and/or longer times (e.g., 1 minute or longer) than would be required for therapeutic neuromodulation.

As further illustrated in FIG. 12, the shaft 116 may reside with a portion of the nasal cavity proximate to the IT upon advancing and deploying the multi-segment end effector 114 in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes 136 of the multi-segment end effector 114, the surgeon may also activate and deliver energy from electrodes 137 associated with the shaft 116 ((i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to tissue associated with the IT. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the IT to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

FIG. 13 is a flow diagram illustrating one embodiment of a method 400 for treating a condition within a nasal cavity of a patient. The method 400 includes advancing a multi-segment end effector within the nasal cavity of the patient (operation 410) wherein the multi-segment end

effector includes a first segment spaced apart from a second segment. The multi-segment end effector is retractable and expandable such that, once delivered to the one more target sites within the nasal cavity, the first and second segments can expand to a specific shape and/or size corresponding to anatomical structures within the nasal cavity and associated with the target sites. The method 400 further includes deploying the first and second segments at respective first and second locations within the nasal cavity (operation 420). In particular, each of the first and second flexible segments includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Accordingly, once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. The method 400 further includes delivering energy, via the first and second segments, to tissue at one or more target sites with respect to the first and second locations (operation 430). In particular, the first and second segments become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. The first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

FIG. 14 is a flow diagram illustrating another embodiment of a method 500 for treating a condition within a nasal cavity of a patient. The method 500 includes providing a treatment device comprising an end effector transformable between a retracted configuration and an expanded deployed configuration, a shaft operably associated with the end effector, and a handle operably associated with the shaft (operation 510). The method 500 further includes advancing the end effector to one or more target sites within the nasal cavity of the patient (operation 520). The shaft may include a pre-defined shape (i.e., bent or angled at a specific orientation) so as to assist the operation for placement of the end effector at the target sites. The handle includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure.

The handle and/or the shaft may include markings (e.g., text, symbols, color-coding insignia, etc.) that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. In particular, multiple markings may be provided on the handle and/or shaft and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the shaft, a surgeon can rely on the markings on the handle and/or shaft as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

The method 500 further includes deploying the end effector at the one or more target sites (operation 530) and delivering energy from the end effector to tissue at the one or more target sites (operation 540). The handle includes multiple user-operated mechanisms, including at least a first mechanism for deployment of the end effector from the retracted configuration to the expanded deployed configuration and a second mechanism for controlling of energy output by the end effector. The user inputs for the first and second mechanisms are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

FIG. 15 is a flow diagram illustrating another embodiment of a method 600 for treating a condition within a nasal cavity of a patient. The method 600 includes providing a treatment device comprising a multi-segment end effector, including a proximal segment that is spaced apart from a distal segment, and a visual marker (operation 610). As previously described herein, the visual marker may be provided by a shaft, for example, operably associated with the multi-segment end effector. The visual marker may be in the form of text, symbols, color-coding insignia, or the like, that generally provides a user (i.e., a surgeon or other medical professional) with a visual indication of a spatial orientation of one or more portions of the proximal segment while the multi-segment end effector is in a nasal cavity.

The method 600 further includes advancing, under image guidance, the proximal segment and the distal segment through a nasal cavity of a patient and past a middle turbinate (operation

620) and deploying the distal segment from a retracted configuration to an expanded configuration (operation 630). The image guidance may be in the form of an endoscope and/or other visualization device that can be positioned to so as to provide visualization to the user of one or more locations within the nasal cavity and to further provide visualization of the multi-segment end effector and other portions of the treatment device (i.e., at least a distal portion of the shaft with a visual marker) during advancement into the nasal cavity to assist the user in placement of the multi-segment end effector.

Upon deploying the distal segment to an expanded configuration, the method 600 further includes aligning, under the image guidance and with reference to the visual marker, the proximal segment with respect to the middle turbinate (operation 640). The visual marker may be provided on the shaft, for example, and provide a visual indication of the spatial orientation of one or more portions of the proximal segment when in the deployed configuration. For example, the deployed proximal segment may include a geometry to complement a shape of the middle turbinate. More specifically, the proximal segment may include a set of flexible support elements that conform to and complement a shape of the middle turbinate when the proximal segment is in the deployed expanded configuration. The visual marker, provided by the shaft, provides a visual indication of the spatial orientation of one or more portions of the proximal segment, including, for example, a spatial orientation of the set of flexible support elements when in a deployed expanded configuration. Accordingly, aligning the proximal segment with respect to the middle turbinate includes the user positioning, under the image guidance, the shaft and associated visual marker relative to the middle turbinate.

Thus, during initial placement of at least the proximal segment when it is in a retracted configuration, a surgeon can rely on the markings on the shaft as a visual indication of the spatial orientation (e.g., linear, axial, and/or depth position) of one or more portions of the proximal segment prior to its deployment, thereby ensuring that, once deployed, the proximal segment is positioned in the intended location within the nasal cavity.

The method 600 further includes deploying the proximal segment around the middle turbinate and advancing the deployed proximal segment toward the middle turbinate to establish contact and secure the proximal segment to the middle turbinate (operation 650). Again, the set of flexible support elements of the proximal segment are able to conform to and complement a shape of the middle turbinate when the proximal segment is in the deployed expanded

configuration, thereby ensuring that the deployed proximal segment is secured to the middle turbinate.

It should be noted that the treatment device further includes a handle operably associated with the multi-segment end effector and the shaft. The handle generally includes a controller mechanism for providing independent, controlled deployment of each of the proximal and distal segments from a retracted configuration to an expanded configuration within the nasal cavity. In particular, in some embodiments, the controller mechanism includes a rack and pinion assembly providing movement of the at least one of the proximal and distal segments between the retracted configuration and expanded configuration in response to user input from an associated user-operated controller. The rack and pinion assembly may include, for example, a set of gears for receiving user input from the user-operated controller and converting the user input to linear motion of a rack member operably associated with the multi-segment end effector.

The controller mechanism may further include a detent feature positioned relative to the proximal and distal segments and configured to provide active feedback to a user indicative of deployment of at least one of the proximal and distal segments. The active feedback may be in the form haptic feedback provided by the controller mechanism. For example, the haptic feedback may include an increase or decrease in resistance associated with user input with the controller mechanism for corresponding movement of the at least one of the proximal and distal segments between retracted and expanded configurations, and/or configurations therebetween (i.e., a plurality of configurations between a fully retracted configuration and a fully expanded configuration). For example, upon deploying the distal segment, the controller mechanism, as a result of interaction with the detent, may provide haptic feedback, in the form of a vibration or other motion (e.g., click(s) or change in resistance), to the user via the user-operated controller. The haptic feedback may indicate to the user that the distal segment is fully deployed and any further input with the user-operated controller will result in deployment of the proximal segment. The controller mechanism may further provide specific haptic feedback during deployment of a given segment, such as deployment of the proximal segment. For example, the haptic feedback may be in the form of an increase or decrease in resistance upon the user-operated controller, for example, which corresponds to the degree to which the proximal segment is deployed.

In some embodiments, the controller mechanism may further include a friction-based feature configured to provide stable movement of at least one of the proximal and distal

segments between the retracted and expanded configurations and further provide active feedback to a user indicative of deployment of at least one of the proximal and distal segments. The friction-based feature may include, for example, a lock mechanism configured to provide constant friction between one or more portions of the rack and pinion assembly sufficient to maintain a position of at least one of the proximal and distal segments during deployment thereof.

For example, the constant friction may be sufficient to hold either of the proximal or distal segments in a certain position as the segment transitions between retracted and expanded configurations regardless of whether the user maintains contact with the user-operated controller. In other words, a user does not need to maintain contact with the user-operated controller in order to ensure that the proximal or distal segment holds a certain position during deployment thereof. Rather, a user can simply interact with the user-operated controller to transition one of the proximal and distal segments to a desired configuration and the constant friction provided by the locking mechanism is sufficient to maintain the configuration of proximal or distal segment in the event that the user goes hands free (i.e., removes any contact with the user-operated controller). The constant friction is of a level sufficient to prevent undesired movement of the proximal or distal segments (i.e., unintended collapsing or expanding), while still allowing for a user to overcome such friction to move the proximal or distal segment to a desired configuration upon user input with the user-operated controller.

In some embodiments, the user-operated controller includes a slider mechanism operably associated with the rack and pinion rail assembly, wherein movement of the slider mechanism in a first direction results in transitioning of at least one of the proximal and distal segments to an expanded configuration and movement of the slider mechanism in a second opposite direction results in transitioning of at least one of the proximal and distal segments to the retracted configuration. In other embodiments, the user-operated controller includes a scroll wheel mechanism operably associated with the rack and pinion rail assembly, wherein rotation of the wheel in a first direction results in transitioning of at least one of the proximal and distal segments to an expanded configuration and rotation of the wheel in a second opposite direction results in transitioning of at least one of the proximal and distal segments to the retracted configuration. As such, during deployment of the proximal segment, the slider mechanism or

scroll wheel may provide increased resistance to a user as the user transitions the proximal segment from a fully retracted configuration to a fully deployed configuration.

Accordingly, during deployment of either of the distal and proximal segments, the controller mechanism provides active feedback to the user, wherein such active feedback can be indicative of which segment is being actively controlled and/or the extent of deployment of either of the distal or proximal segments, thereby improving user control over the deployment of either of the distal and proximal segments.

Upon securing the proximal segment to the middle turbinate, the method 600 further includes delivering energy, via the proximal segment, to the middle turbinate to treat a condition (operation 660). The condition may include, but is not limited to, allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, chronic sinusitis, acute sinusitis, chronic rhinosinusitis, acute rhinosinusitis, and medical resistant rhinitis, and a combination thereof. In some embodiments, delivering energy from the proximal segment includes delivering radiofrequency (RF) energy, via one or more electrodes provided by the proximal segment, to tissue of the middle turbinate at one or more target sites, wherein the one or more target sites are associated with parasympathetic nerve supply. In some embodiments, RF energy is delivered, via the one or more electrodes provided by the proximal segment, at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

FIG. 16 is a flow diagram illustrating another embodiment of a method 700 for treating a condition within a nasal cavity of a patient. The method 700 includes providing a treatment device comprising an elongate body including one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and including one or more of a second set of electrodes provided thereon (operation 710).

The method 700 further includes advancing the shaft and end effector through a nasal passage and into a nasal cavity of a patient (operation 720) at which point a length of the elongate body is positioned at a first target site and the end effector is positioned at a second target site separate from the first target site (operation 730). For example, in some embodiments, the procedure may involve extending the elongate body into the nasal passage (NP), through the inferior meatus (IM) between the inferior turbinate (IT) and the nasal sill (NS). In other

embodiments, the procedure may involve extending the elongate body into the nasal passage (NP), through the middle meatus (MM) between the inferior turbinate (IT) and the middle turbinate (MT). In each instance, a proximal segment (of the end effector) is arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate and a separate distal segment (of the end effector) is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Additionally, the elongate body resides in a location adjacent to the inferior turbinate (IT).

The method 700 further includes delivering energy from the first and second sets of electrodes (associated with elongate body and end effector, respectively) to tissue at the first and second target sites, respectively (operation 740). In particular, a given procedure, the surgeon may utilize the multi-segment end effector to deliver energy (via electrodes) at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the patient and further utilize the elongate body to deliver energy (via electrodes) at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient. Such a combination of energy delivery to two specific targeted sites improves the manner in which at least one of rhinitis, congestion, and rhinorrhea are treated, thereby increasing the potential for reducing or completely eliminating symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end

effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

Neuromodulation Monitoring, Feedback, and Mapping Capabilities

As previously described, the system 100 includes a console 104 to which the device 102 is to be connected. The console 104 is configured to provide various functions for the neuromodulation device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the neuromodulation device 102. The console 104 can further be configured to generate a selected form and/or magnitude of energy for delivery to tissue or nerves at the target site via the end effector 114, and therefore the console 104 may have different configurations depending on the treatment modality of the device 102. For example, when device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 includes an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy. When the device 102 is configured for cryotherapeutic treatment, the console 104 can include a refrigerant reservoir (not shown), and can be configured to supply the device 102 with refrigerant. Similarly, when the device 102 is configured for chemical-based treatment (e.g., drug infusion), the console 104 can include a chemical reservoir (not shown) and can be configured to supply the device 102 with one or more chemicals.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the neuromodulation device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the

neuromodulation device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, perform nerve mapping, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via mapping/evaluation/feedback algorithms 110. For example, the mapping/evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the location of other anatomical structures (e.g., vessels) at the treatment site, the temperature at the treatment site during monitoring and modulation, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the mapping/evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107 and the end effector 114, can be configured to monitor neural activity and/or temperature at the treatment site during therapy and automatically shut off the energy delivery when the neural activity and/or temperature reaches a predetermined threshold (e.g., a threshold reduction in neural activity, a threshold maximum temperature when applying RF energy, or a threshold minimum temperature when applying cryotherapy). In other embodiments, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum

time, a predetermined maximum impedance or resistance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a display 112 (e.g., a monitor, touchscreen, user interface, etc.) on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104.

In various embodiments, the end effector 114 and/or other portions of the system 100 can be configured to detect various bioelectric-parameters of the tissue at the target site, and this information can be used by the mapping/evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate neural structures, differentiate between different types of neural structures, map the anatomical and/or neural structure at the target site, and/or identify neuromodulation patterns of the end effector 114 with respect to the patient's anatomy. For example, the end effector 114 can be used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in the target region. In certain embodiments, the end effector 114, together with the mapping/evaluation/feedback algorithms 110, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. The mapping/evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes 136).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-50Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures, including the firing of neural structures, differences between neural structures and other anatomical structures (e.g., blood vessels), and event different types of neural structures. This information can be analyzed by the mapping/evaluation/feedback algorithms and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural structures and other anatomy at the

treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode 136 can be operated independently of the other electrodes 136. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes 136 allows the end effector 114 to detect information and deliver RF energy to highly customized regions. For example, a select portion of the electrodes 136 can be activated to target specific neural fibers in a specific region while the other electrodes 136 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 124 that is adjacent to tissue at the target site, and the electrodes 136 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. In addition, the electrodes 136 can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

The electrodes 136 can be electrically coupled to the energy generator 106 via wires (not shown) that extend from the electrodes 136, through the shaft 116, and to the energy generator 106. When each of the electrodes 136 is independently controlled, each electrode 136 couples to a corresponding wire that extends through the shaft 116. This allows each electrode 136 to be independently activated for stimulation or neuromodulation to provide precise ablation patterns and/or individually detected via the console 104 to provide information specific to each electrode 136 for neural or anatomical detection and mapping. In other embodiments, multiple electrodes 136 can be controlled together and, therefore, multiple electrodes 136 can be electrically coupled to the same wire extending through the shaft 116. The energy generator 16 and/or components (e.g., a control module) operably coupled thereto can include custom algorithms to control the activation of the electrodes 136. For example, the RF generator can deliver RF power at about 200-100 W to the electrodes 136, and do so while activating the electrodes 136 in a predetermined pattern selected based on the position of the end effector 114 relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the energy generator 106 delivers power at lower levels (e.g., less than 1 W, 1-5 W, 5-15 W, 15-50

W, 50-150 W, etc.) for stimulation and/or higher power levels. For example, the energy generator 106 can be configured to delivery stimulating energy pulses of 1-3 W via the electrodes 136 to stimulate specific targets in the tissue.

As previously described, the end effector 114 can further include one or more temperature sensors disposed on the flexible first and second segments 122, 124 and/or other portions of the end effector 114 and electrically coupled to the console 104 via wires (not shown) that extend through the shaft 116. In various embodiments, the temperature sensors can be positioned proximate to the electrodes 136 to detect the temperature at the interface between tissue at the target site and the electrodes 136. In other embodiments, the temperature sensors can penetrate the tissue at the target site (e.g., a penetrating thermocouple) to detect the temperature at a depth within the tissue. The temperature measurements can provide the operator or the system with feedback regarding the effect of the therapeutic neuromodulation on the tissue. For example, in certain embodiments the operator may wish to prevent or reduce damage to the tissue at the treatment site (e.g., the nasal mucosa), and therefore the temperature sensors can be used to determine if the tissue temperature reaches a predetermined threshold for irreversible tissue damage. Once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and avoid significant tissue sloughing during wound healing. In certain embodiments, the energy delivery can automatically terminate based on the mapping/evaluation/feedback algorithm 110 stored on the console 104 operably coupled to the temperature sensors.

In certain embodiments, the system 100 can determine the locations and/or morphology of neural structures and/or other anatomical structures before therapy such that the therapeutic neuromodulation can be applied to precise regions including target neural structures, while avoiding negative effects on non-target structures, such as blood vessels. As described in further detail below, the system 100 can detect various bioelectrical parameters in an interest zone (e.g., within in the nasal cavity) to determine the location and morphology of various neural structures (e.g., different types of neural structures, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony regions, etc.). In some embodiments, the system 100 is configured to measure bioelectric potential. To do so, one or more of the electrodes 136 is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies) are applied to the

tissue by one or more electrodes 136 at or near the treatment site, and the voltage and/or current differences at various different frequencies between various pairs of electrodes 136 of the end effector 114 may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural structures, and/or other types of tissue) in the region of interest. For example, current (i.e., direct or alternating current) can be applied to a pair of electrodes 136 adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes 136 are measured. It will be appreciated that the current injection electrodes 136 and measurement electrodes 136 need not be adjacent, and that modifying the spacing between the two current injection electrodes 136 can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes 136 provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes 136 that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric potential measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector 114), and this information can be used to map the neural and anatomical structures by the use of frequency differentiation reconstruction. Applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters. At high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of the neural structures do not impede current flow, and the current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes of the cells or cell spacing. The stimulation frequencies can be in the megahertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone

of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

Further, the inherent morphology and composition of the anatomical structures in the nasal region react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural structures, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy. In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes 136 at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes 136 and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes 136 are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural structures that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural structures that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate the postganglionic parasympathetic neural fibers that innervate the mucosa at the numerous neural entrance points into the nasal cavity. Further, because there are not any clear anatomical markers denoting the location of the SPF, accessory foramen, and microforamina, the neural mapping allows the operator to identify and therapeutically modulate nerves that would otherwise be unidentifiable without intricate dissection of the mucosa. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the mapping/evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

In various embodiments, the system 100 can also be configured to map the expected therapeutic modulation patterns of the electrodes 136 at specific temperatures and, in certain embodiments, take into account tissue properties based on the anatomical mapping of the target site. For example, the system 100 can be configured to map the ablation pattern of a specific electrode ablation pattern at the 45° C. isotherm, the 55° C. isotherm, the 65° C. isotherm, and/or other temperature/ranges (e.g., temperatures ranging from 45° C. to 70° C. or higher) depending on the target site and/or structure.

The system 100 may provide, via the display 112, three-dimensional views of such projected ablation patterns of the electrodes 136 of the end effector 114. The ablation pattern mapping may define a region of influence that each electrode 136 has on the surrounding tissue. The region of influence may correspond to the region of tissue that would be exposed to therapeutically modulating energy based on a defined electrode activation pattern (i.e., one, two, three, four, or more electrodes on any given strut of the first and second segments 122, 124). In other words, the ablation pattern mapping can be used to illustrate the ablation pattern of any number of electrodes 136, any geometry of the electrode layout, and/or any ablation activation protocol (e.g., pulsed activation, multi-polar/sequential activation, etc.).

In some embodiments, the ablation pattern may be configured such that each electrode 136 has a region of influence surrounding only the individual electrode 136 (i.e., a "dot" pattern). In other embodiments, the ablation pattern may be such that two or more electrodes 136 may link together to form a sub-grouped regions of influence that define peanut-like or linear shapes between two or more electrodes 136. In further embodiments, the ablation pattern can result in a more expansive or contiguous pattern in which the region of influence extends along multiple electrodes 136 (e.g., along each strut). In still further embodiments, the ablation pattern may result in different regions of influence depending upon the electrode activation pattern, phase angle, target temperature, pulse duration, device structure, and/or other treatment parameters. The three-dimensional views of the ablation patterns can be output to the display 112 and/or other user interfaces to allow the clinician to visualize the changing regions of influence based on different durations of energy application, different electrode activation sequences (e.g., multiplexing), different pulse sequences, different temperature isotherms, and/or other treatment parameters. This information can be used to determine the appropriate ablation algorithm for a patient's specific anatomy. In other embodiments, the three-dimensional visualization of the

regions of influence can be used to illustrate the regions from which the electrodes 136 detect data when measuring bioelectrical properties for anatomical mapping. In this embodiment, the three dimensional visualization can be used to determine which electrode activation pattern should be used to determine the desired properties (e.g., impedance, resistance, etc.) in the desired area. In certain embodiments, it may be better to use dot assessments, whereas in other embodiments it may be more appropriate to detect information from linear or larger contiguous regions.

In some embodiments, the mapped ablation pattern is superimposed on the anatomical mapping to identify what structures (e.g., neural structures, vessels, etc.) will be therapeutically modulated or otherwise affected by the therapy. An image may be provided to the surgeon which includes a digital illustration of a predicted or planned neuromodulation zone in relation to previously identified anatomical structures in a zone of interest. For example, the illustration may show numerous neural structures and, based on the predicted neuromodulation zone, identifies which neural structures are expected to be therapeutically modulated. The expected therapeutically modulated neural structures may be shaded to differentiate them from the non-affected neural structures. In other embodiments, the expected therapeutically modulated neural structures can be differentiated from the non-affected neural structures using different colors and/or other indicators. In further embodiments, the predicted neuromodulation zone and surrounding anatomy (based on anatomical mapping) can be shown in a three dimensional view (and/or include different visualization features (e.g., color-coding to identify certain anatomical structures, bioelectric properties of the target tissue, etc.). The combined predicted ablation pattern and anatomical mapping can be output to the display 112 and/or other user interfaces to allow the clinician to select the appropriate ablation algorithm for a patient's specific anatomy.

The imaging provided by the system 100 allows the clinician to visualize the ablation pattern before therapy and adjust the ablation pattern to target specific anatomical structures while avoiding others to prevent collateral effects. For example, the clinician can select a treatment pattern to avoid blood vessels, thereby reducing exposure of the vessel to the therapeutic neuromodulation energy. This reduces the risk of damaging or rupturing vessels and, therefore, prevents immediate or latent bleeding. Further, the selective energy application provided by the neural mapping reduces collateral effects of the therapeutic neuromodulation,

such as tissue sloughing off during wound healing (e.g., 1-3 weeks post ablation), thereby reducing the aspiration risk associated with the neuromodulation procedure.

The system 100 can be further configured to apply neuromodulation energy (via the electrodes 136) at specific frequencies attuned to the target neural structure and, therefore, specifically target desired neural structures over non-target structures. For example, the specific neuromodulation frequencies can correspond to the frequencies identified as corresponding to the target structure during neural mapping. As described above, the inherent morphology and composition of the anatomical structures react differently to different frequencies. Thus, frequency-tuned neuromodulation energy tailored to a target structure does not have the same modulating effects on non-target structures. More specifically, applying the neuromodulation energy at the target-specific frequency causes ionic agitation in the target neural structure, leading to differentials in osmotic potentials of the targeted neural structures and dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure). This causes degeneration, possibly resulting in vacuolar degeneration and, eventually, necrosis at the target neural structure, but is not expected to functionally affect at least some non-target structures (e.g., blood vessels). Accordingly, the system 100 can use the neural-structure specific frequencies to both (1) identify the locations of target neural structures to plan electrode ablation configurations (e.g., electrode geometry and/or activation pattern) that specifically focus the neuromodulation on the target neural structure; and (2) apply the neuromodulation energy at the characteristic neural frequencies to selectively ablate the neural structures responsive to the characteristic neural frequencies. For example, the end effector 114 of the system 100 may selectively stimulate and/or modulate parasympathetic fibers, sympathetic fibers, sensory fibers, alpha/beta/delta fibers, C-fibers, anoxic terminals of one or more of the foregoing, insulated over non-insulated fibers (regions with fibers), and/or other neural structures. In some embodiments, the system 100 may also selectively target specific cells or cellular regions during anatomical mapping and/or therapeutic modulation, such as smooth muscle cells, sub-mucosal glands, goblet cells, stratified cellular regions within the nasal mucosa. Therefore, the system 100 provides highly selective neuromodulation therapy specific to targeted neural structures, and reduces the collateral effects of neuromodulation therapy to non-target structures (e.g., blood vessels).

The present disclosure provides a method of anatomical mapping and therapeutic neuromodulation. The method includes expanding an end effector (i.e., end effector 114) at a zone of interest ("interest zone"), such as in a portion of the nasal cavity. For example, the end effector 114 can be expanded such that at least some of the electrodes 136 are placed in contact with mucosal tissue at the interest zone. The expanded device can then take bioelectric measurements via the electrodes 136 and/or other sensors to ensure that the desired electrodes are in proper contact with the tissue at the interest zone. In some embodiments, for example, the system 100 detects the impedance and/or resistance across pairs of the electrodes 136 to confirm that the desired electrodes have appropriate surface contact with the tissue and that all of the electrodes are 136 functioning properly.

The method continues by optionally applying an electrical stimulus to the tissue, and detecting bioelectric properties of the tissue to establish baseline norms of the tissue. For example, the method can include measuring resistance, complex impedance, current, voltage, nerve firing rate, neuromagnetic field, muscular activation, and/or other parameters that are indicative of the location and/or function of neural structures and/or other anatomical structures (e.g., glandular structures, blood vessels, etc.). In some embodiments, the electrodes 136 send one or more stimulation signals (e.g., pulsed signals or constant signals) to the interest zone to stimulate neural activity and initiate action potentials. The stimulation signal can have a frequency attuned to a specific target structure (e.g., a specific neural structure, a glandular structure, a vessel) that allows for identification of the location of the specific target structure. The specific frequency of the stimulation signal is a function of the host permeability and, therefore, applying the unique frequency alters the tissue attenuation and the depth into the tissue the RF energy will penetrate. For example, lower frequencies typically penetrate deeper into the tissue than higher frequencies.

Pairs of the non-stimulating electrodes 136 of the end effector 114 can then detect one or more bioelectric properties of the tissue that occur in response to the stimulus, such as impedance or resistance. For example, an array of electrodes (e.g., the electrodes 136) can be selectively paired together in a desired pattern (e.g., multiplexing the electrodes 136) to detect the bioelectric properties at desired depths and/or across desired regions to provide a high level of spatial awareness at the interest zone. In certain embodiments, the electrodes 136 can be paired together in a time-sequenced manner according to an algorithm (e.g., provided by the

mapping/evaluation/feedback algorithms 110). In various embodiments, stimuli can be injected into the tissue at two or more different frequencies, and the resultant bioelectric responses (e.g., action potentials) in response to each of the injected frequencies can be detected via various pairs of the electrodes 136. For example, an anatomical or neural mapping algorithm can cause the end effector 114 to deliver pulsed RF energy at specific frequencies between different pairs of the electrodes 136 and the resultant bioelectric response can be recorded in a time sequenced rotation until the desired interest zone is adequately mapped (i.e., "multiplexing"). For example, the end effector 114 can deliver stimulation energy at a first frequency via adjacent pairs of the electrodes 136 for a predetermined time period (e.g., 1-50 milliseconds), and the resultant bioelectric activity (e.g., resistance) can be detected via one or more other pairs of electrodes 136 (e.g., spaced apart from each other to reach varying depths within the tissue). The end effector 114 can then apply stimulation energy at a second frequency different from the first frequency, and the resultant bioelectric activity can be detected via the other electrodes. This can continue when the interest zone has been adequately mapped at the desired frequencies. As described in further detail below, in some embodiments the baseline tissue bioelectric properties (e.g., nerve firing rate) are detected using static detection methods (without the injection of a stimulation signal).

After detecting the baseline bioelectric properties, the information can be used to map anatomical structures and/or functions at the interest zone. For example, the bioelectric properties detected by the electrodes 136 can be amazed via the mapping/evaluation/feedback algorithms 110, and an anatomical map can be output to a user via the display 112. In some embodiments, complex impedance, dielectric, or resistance measurements can be used to map parasympathetic nerves and, optionally, identify neural structures in a diseased state of hyperactivity. The bioelectric properties can also be used to map other non-target structures and the general anatomy, such as blood vessels, bone, and/or glandular structures. The anatomical locations can be provided to a user (e.g., on the display 112) as a two-dimensional map (e.g., illustrating relative intensities, illustrating specific sites of potential target structures) and/or as a three-dimensional image. This information can be used to differentiate structures on a submicron, cellular level and identify very specific target structures (e.g., hyperactive parasympathetic nerves). The method can also predict the ablation patterns of the end effector 114 based on different electrode neuromodulation protocol and, optionally, superimpose the

predicted neuromodulation patterns onto the mapped anatomy to indicate to the user which anatomical structures will be affected by a specific neuromodulation protocol. For example, when the predicted neuromodulation pattern is displayed in relation to the mapped anatomy, a clinician can determine whether target structures will be appropriately ablated and whether non-target structures (e.g., blood vessels) will be undesirably exposed to the therapeutic neuromodulation energy. Thus, the method can be used for planning neuromodulation therapy to locate very specific target structures, avoid non-target structures, and select electrode neuromodulation protocols.

Once the target structure is located and a desired electrode neuromodulation protocol has been selected, the method continues by applying therapeutic neuromodulation to the target structure. The neuromodulation energy can be applied to the tissue in a highly targeted manner that forms micro-lesions to selectively modulate the target structure, while avoiding non-targeted blood vessels and allowing the surrounding tissue structure to remain healthy for effective wound healing. In some embodiments, the neuromodulation energy can be applied in a pulsed manner, allowing the tissue to cool between modulation pulses to ensure appropriate modulation without undesirably affecting non-target tissue. In some embodiments, the neuromodulation algorithm can deliver pulsed RF energy between different pairs of the electrodes 136 in a time sequenced rotation until neuromodulation is predicted to be complete (i.e., "multiplexing"). For example, the end effector 114 can deliver neuromodulation energy (e.g., having a power of 5-10 W (e.g., 7 W, 8 W, 9 W) and a current of about 50-100 mA) via adjacent pairs of the electrodes 136 until at least one of the following conditions is met: (a) load resistance reaches a predefined maximum resistance (e.g., 350Ω); (b) a thermocouple temperature associated with the electrode pair reaches a predefined maximum temperature (e.g., 80° C.); or (c) a predetermined time period has elapsed (e.g., 10 seconds). After the predetermined conditions are met, the end effector 114 can move to the next pair of electrodes in the sequence, and the neuromodulation algorithm can terminate when all of the load resistances of the individual pairs of electrodes is at or above a predetermined threshold (e.g., 100Ω). In various embodiments, the RF energy can be applied at a predetermined frequency (e.g., 450-500 kHz) and is expected to initiate ionic agitation of the specific target structure, while avoiding functional disruption of non-target structures.

During and/or after neuromodulation therapy, the method continues by detecting and, optionally, mapping the post-therapy bioelectric properties of the target site. This can be performed in a similar manner as described above. The post-therapy evaluation can indicate if the target structures (e.g., hyperactive parasympathetic nerves) were adequately modulated or ablated. If the target structures are not adequately modulated (i.e., if neural activity is still detected in the target structure and/or the neural activity has not decreased), the method can continue by again applying therapeutic neuromodulation to the target. If the target structures were adequately ablated, the neuromodulation procedure can be completed.

Detection of Anatomical Structures and Function

Various embodiments of the present technology can include features that measure bio-electric, dielectric, and/or other properties of tissue at target sites to determine the presence, location, and/or activity of neural structures and other anatomical structures and, optionally, map the locations of the detected neural structures and/or other anatomical structures. For example, the present technology can be used to detect glandular structures and, optionally, their mucoserous functions and/or other functions. The present technology can also be configured to detect vascular structures (e.g., arteries) and, optionally, their arterial functions, volumetric pressures, and/or other functions. The mapping features discussed below can be incorporated into any the system 100 and/or any other devices disclosed herein to provide an accurate depiction of nerves at the target site.

Neural and/or anatomical detection can occur (a) before the application of a therapeutic neuromodulation energy to determine the presence or location of neural structures and other anatomical structures (e.g., blood vessels, glands, etc.) at the target site and/or record baseline levels of neural activity; (b) during therapeutic neuromodulation to determine the real-time effect of the energy application on the neural fibers at the treatment site; and/or (c) after therapeutic neuromodulation to confirm the efficacy of the treatment on the targeted structures (e.g., nerves glands, etc.). This allows for the identification of very specific anatomical structures (even to the micro-scale or cellular level) and, therefore, provides for highly targeted neuromodulation. This enhances the efficacy and efficiency of the neuromodulation therapy. In addition, the anatomical mapping reduces the collateral effects of neuromodulation therapy to non-target sites.

Accordingly, the targeted neuromodulation inhibits damage or rupture of blood vessels (i.e., inhibits undesired bleeding) and collateral damage to tissue that may be of concern during wound healing (e.g., when damage tissue sloughs off of the wall of the nasal wall).

In certain embodiments, the systems disclosed herein can use bioelectric measurements, such as impedance, resistance, voltage, current density, and/or other parameters (e.g., temperature) to determine the anatomy, in particular the neural, glandular, and vascular anatomy, at the target site. The bioelectric properties can be detected after the transmission of a stimulus (e.g., an electrical stimulus, such as RF energy delivered via the electrodes 136; i.e., "dynamic" detection) and/or without the transmission of a stimulus (i.e., "static" detection).

Dynamic measurements include various embodiments to excite and/or detect primary or secondary effects of neural activation and/or propagation. Such dynamic embodiments involve the heightened states of neural activation and propagation and use this dynamic measurement for nerve location and functional identification relative to the neighboring tissue types. For example, a method of dynamic detection can include: (1) delivering stimulation energy to a treatment site via a treatment device (e.g., the end effector 114) to excite parasympathetic nerves at the treatment site; (2) measuring one or more physiological parameters (e.g., resistance, impedance, etc.) at the treatment site via a measuring/sensing array of the treatment device (e.g., the electrodes 136); (4) based on the measurements, identifying the relative presence and position of parasympathetic nerves at the treatment site; and (5) delivering ablation energy to the identified parasympathetic nerves to block the detected para-sympathetic nerves.

Static measurements include various embodiments associated with specific native properties of the stratified or cellular composition at or near the treatment site. The static embodiments are directed to inherent biologic and electrical properties of tissue types at or near the treatment site, the stratified or cellular compositions at or near the treatment site, and contrasting both foregoing measurements with tissue types adjacent the treatment site (and that are not targeted for neuromodulation). This information can be used to localize specific targets (e.g., parasympathetic fibers) and non-targets (e.g., vessels, sensory nerves, etc.). For example, a method of static detection can include: (1) before ablation, utilizing a measuring/sensing array of a treatment device (e.g., the electrodes 136) to determine one or more baseline physiological parameters; (2) geometrically identifying inherent tissue properties within a region of interest based on the measured physiological parameters (e.g., resistance, impedance, etc.); (3) delivering

ablation energy to one or more nerves within the region of via treatment device interest; (4) during the delivery of the ablation energy, determining one or more mid-procedure physiological parameters via the measuring/sensing array; and (5) after the delivery of ablation energy, determining one or more post-procedure physiological parameters via the measurement/sensing array to determine the effectiveness of the delivery of the ablation energy on blocking the nerves that received the ablation energy.

After the initial static and/or dynamic detection of bioelectric properties, the location of anatomical features can be used to determine where the treatment site(s) should be with respect to various anatomical structures for therapeutically effective neuromodulation of the targeted parasympathetic nasal nerves. The bioelectric and other physiological properties described herein can be detected via electrodes (e.g., the electrodes 136 of the end effector 114), and the electrode pairings on a device (e.g., end effector 114) can be selected to obtain the bioelectric data at specific zones or regions and at specific depths of the targeted regions. The specific properties detected at or surrounding target neuromodulation sites and associated methods for obtaining these properties are described below. These specific detection and mapping methods discussed below are described with reference to the system 100 , although the methods can be implemented on other suitable systems and devices that provide for anatomical identification, anatomical mapping and/or neuromodulation therapy.

Neural Identification and Mapping

In many neuromodulation procedures, it is beneficial to identify the portions of the nerves that fall within a zone and/or region of influence (referred to as the "interest zone") of the energy delivered by a neuromodulation device 102, as well as the relative three-dimensional position of the neural structures relative to the neuromodulation device 102. Characterizing the portions of the neural structures within the interest zone and/or determining the relative positions of the neural structures within the interest zone enables the clinician to (1) selectively activate target neural structures over non-target structures (e.g., blood vessels), and (2) sub-select specific targeted neural structures (e.g., parasympathetic nerves) over non-target neural structures (e.g., sensory nerves, subgroups of neural structures, neural structures having certain compositions or morphologies). The target structures (e.g., parasympathetic nerves) and non-target structures

(e.g., blood vessels, sensory nerves, etc.) can be identified based on the inherent signatures of specific structures, which are defined by the unique morphological compositions of the structures and the bioelectrical properties associated with these morphological compositions. For example, unique, discrete frequencies can be associated with morphological compositions and, therefore, be used to identify certain structures. The target and non-target structures can also be identified based on relative bioelectrical activation of the structures to sub-select specific neuronal structures. Further, target and non-target structures can be identified by the differing detected responses of the structures to a tailored injected stimuli. For example, the systems described herein can detect the magnitude of response of structures and the difference in the responses of anatomical structures with respect to differing stimuli (e.g., stimuli injected at different frequencies).

At least for purposes of this disclosure, a nerve can include the following portions that are defined based on their respective orientations relative to the interest zone: terminating neural structures (e.g., terminating axonal structures), branching neural structures (e.g., branching axonal structures), and travelling neural structures (e.g., travelling axonal structures). For example, terminating neural structures enter the zone but do not exit. As such, terminating neural structures are terminal points for neuronal signaling and activation. Branching neural structures are nerves that enter the interest zone and increase number of nerves exiting the interest zone. Branching neural structures are typically associated with a reduction in relative geometry of nerve bundle. Travelling neural structures are nerves that enter the interest zone and exit the zone with no substantially no change in geometry or numerical value.

The system 100 can be used to detect voltage, current, complex impedance, resistance, permittivity, and/or conductivity, which are tied to the compound action potentials of nerves, to determine and/or map the relative positions and proportionalities of nerves in the interest zone. Neuronal cross-sectional area ("CSA") is expected to be due to the increase in axonic structures. Each axon is a standard size. Larger nerves (in cross-sectional dimension) have a larger number of axons than nerves having smaller cross-sectional dimensions. The compound action responses from the larger nerves, in both static and dynamic assessments, are greater than smaller nerves. This is at least in part because the compound action potential is the cumulative action response from each of the axons. When using static analysis, for example, the system 100 can directly measure and map impedance or resistance of nerves and, based on the determined

impedance or resistance, determine the location of nerves and/or relative size of the nerves. In dynamic analysis, the system 100 can be used to apply a stimulus to the interest zone and detect the dynamic response of the neural structures to the stimulus. Using this information, the system 100 can determine and/or map impedance or resistance in the interest zone to provide information related to the neural positions or relative nerve sizes. Neural impedance mapping can be illustrated by showing the varying complex impedance levels at a specific location at differing cross-sectional depths. In other embodiments, neural impedance or resistance can be mapped in a three-dimensional display.

Identifying the portions and/or relative positions of the nerves within the interest zone can inform and/or guide selection of one or more treatment parameters (e.g., electrode ablation patterns, electrode activation plans, etc.) of the system 100 for improving treatment efficiency and efficacy. For example, during neural monitoring and mapping, the system 100 can identify the directionality of the nerves based at least in part on the length of the neural structure extending along the interest zone, relative sizing of the neural structures, and/or the direction of the action potentials. This information can then be used by the system 100 or the clinician to automatically or manually adjust treatment parameters (e.g., selective electrode activation, bipolar and/or multipolar activation, and/or electrode positioning) to target specific nerves or regions of nerves. For example, the system 100 can selectively activate specific electrodes 136, electrode combinations (e.g., asymmetric or symmetric), and/or adjust the bi-polar or multi-polar electrode configuration. In some embodiments, the system 100 can adjust or select the waveform, phase angle, and/or other energy delivery parameters based on the nerve portion/position mapping and/or the nerve proportionality mapping. In some embodiments, structure and/or properties of the electrodes 136 themselves (e.g., material, surface roughening, coatings, cross-sectional area, perimeter, penetrating, penetration depth, surface-mounted, etc.) may be selected based on the nerve portion and proportionality mapping.

In various embodiments, treatment parameters and/or energy delivery parameters can be adjusted to target on-axis or near axis travelling neural structures and/or avoid the activation of traveling neural structures that are at least generally perpendicular to the end effector 114. Greater portions of the on-axis or near axis travelling neural structures are exposed and susceptible to the neuromodulation energy provided by the end effector 114 than a perpendicular travelling neural structure, which may only be exposed to therapeutic energy at a discrete cross-

section. Therefore, the end effector 114 is more likely to have a greater effect on the on-axis or near axis travelling neural structures. The identification of the neural structure positions (e.g., via complex impedance or resistance mapping) can also allow targeted energy delivery to travelling neural structures rather than branching neural structures (typically downstream of the travelling neural structures) because the travelling neural structures are closer to the nerve origin and, therefore, more of the nerve is affected by therapeutic neuromodulation, thereby resulting in a more efficient treatment and/or a higher efficacy of treatment. Similarly, the identification of neural structure positions can be used to target travelling and branching neural structures over terminal neural structures. In some embodiments, the treatment parameters can be adjusted based on the detected neural positions to provide a selective regional effect. For example, a clinician can target downstream portions of the neural structures if only wanting to influence partial effects on very specific anatomical structures or positions.

In various embodiments, neural locations and/or relative positions of nerves can be determined by detecting the nerve-firing voltage and/or current over time. An array of the electrodes 136 can be positioned in contact with tissue at the interest zone, and the electrodes 136 can measure the voltage and/or current associated with nerve-firing. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves in a hyper state (i.e., excessive parasympathetic tone). Rhinitis is at least in part the result of over-firing nerves because this hyper state drives the hyper-mucosal production and hyper-mucosal secretion. Therefore, detection of nerve firing rate via voltage and current measurements can be used to locate the portions of the interest region that include hyper-parasympathetic neural function (i.e., nerves in the diseased state). This allows the clinician to locate specific nerves (i.e., nerves with excessive parasympathetic tone) before neuromodulation therapy, rather than simply targeting all parasympathetic nerves (including non-diseased state parasympathetic nerves) to ensure that the correct tissue is treated during neuromodulation therapy. Further, nerve firing rate can be detected during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy. For example, recording decreases or elimination of nerve firing rate after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In various embodiments, the system 100 can detect neural activity using dynamic activation by injecting a stimulus signal (i.e., a signal that temporarily activates nerves) via one

or more of the electrodes 136 to induce an action potential, and other pairs of electrodes 136 can detect bioelectric properties of the neural response. Detecting neural structures using dynamic activation involves detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The ability to numerically measure, profile, map, and/or image fast neuronal depolarization for generating an accurate index of activity is a factor in measuring the rate of discharge in neurons and their processes. The action potential causes a rapid increase in the voltage across nerve fiber and the electrical impulse then spreads along the fiber. As an action potential occurs, the conductance of a neural cell membrane changes, becoming about 40 times larger than it is when the cell is at rest. During the action potential or neuronal depolarization, the membrane resistance diminishes by about 80 times, thereby allowing an applied current to enter the intracellular space as well. Over a population of neurons, this leads to a net decrease in the resistance during coherent neuronal activity, such as chronic para-sympathetic responses, as the intracellular space will provide additional conductive ions. The magnitude of such fast changes has been estimated to have local resistivity changes with recording near DC is 2.8-3.7% for peripheral nerve bundles (e.g., including the nerves in the nasal cavity).

Detecting neural structures using dynamic activation includes detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The basis of each this discharge is the action potential, during which there is a depolarization of the neuronal membrane of up to 110 mV or more, lasting approximately 2 milliseconds, and due to the transfer of micromolar quantities of ions (e.g., sodium and potassium) across the cellular membrane. The complex impedance or resistance change due to the neuronal membrane falls from 1000 to 25 Ωcm. The introduction of a stimulus and subsequent measurement of the neural response can attenuate noise and improve signal to noise ratios to precisely focus on the response region to improve neural detection, measurement, and mapping.

In some embodiments, the difference in measurements of physiological parameters (e.g., complex impedance, resistance, voltage) over time, which can reduce errors, can be used to create a neural profiles, spectrums, or maps. For example, the sensitivity of the system 100 can be improved because this process provides repeated averaging to a stimulus. As a result, the mapping function outputs can be a unit-less ratio between the reference and test collated data at a

single frequency and/or multiple frequencies and/or multiple amplitudes. Additional considerations may include multiple frequency evaluation methods that consequently expand the parameter assessments, such as resistivity, admittivity, center frequency, or ratio of extra- to intracellular resistivity.

In some embodiments, the system 100 may also be configured to indirectly measure the electrical activity of neural structures to quantify the metabolic recovery processes that accompany action potential activity and act to restore ionic gradients to normal. These are related to an accumulation of ions in the extracellular space. The indirect measurement of electrical activity can be approximately a thousand times larger (in the order of millimolar), and thus are easier to measure and can enhance the accuracy of the measured electrical properties used to generate the neural maps.

The system 100 can perform dynamic neural detection by detecting nerve-firing voltage and/or current and, optionally, nerve firing rate over time, in response to an external stimulation of the nerves. For example, an array of the electrodes 136 can be positioned in contact with tissue at the interest zone, one or more of the electrodes 136 can be activated to inject a signal into the tissue that stimulates the nerves, and other electrodes 136 of the electrode array can measure the neural voltage and/or current due to nerve firing in response to the stimulus. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves and, in certain embodiments, identify parasympathetic nerves in a hyper state (e.g., indicative of Rhinitis or other diseased state). The dynamic detection of neural activity (voltage, current, firing rate, etc.) can be performed before neuromodulation therapy to detect target nerve locations to select the target site and treatment parameters to ensure that the correct tissue is treated during neuromodulation therapy. Further, dynamic detection of neural activity can be performed during or after neuromodulation therapy to allow the clinician to monitor changes in neural activity to validate treatment efficacy. For example, recording decreases or elimination of neural activity after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In some embodiments, a stimulating signal can be delivered to the vicinity of the targeted nerve via one or more penetrating electrodes (e.g., microneedles that penetrate tissue) associated with the end effector 114 and/or a separate device. The stimulating signal generates an action potential, which causes smooth muscle cells or other cells to contract. The location and strength

of this contraction can be detected via the penetrating electrode(s) and, thereby, indicate to the clinician the distance to the nerve and/or the location of the nerve relative to the stimulating needle electrode. In some embodiments, the stimulating electrical signal may have a voltage of typically 1-2 mA or greater and a pulse width of typically 100-200 microseconds or greater. Shorter pulses of stimulation result in better discrimination of the detected contraction, but may require more current. The greater the distance between the electrode and the targeted nerve, the more energy is required to stimulate. The stimulation and detection of contraction strength and/or location enables identification of how close or far the electrodes are from the nerve, and therefore can be used to localize the nerve spatially. In some embodiments, varying pulse widths may be used to measure the distance to the nerve. As the needle becomes closer to the nerve, the pulse duration required to elicit a response becomes less and less.

To localize nerves via muscle contraction detection, the system 100 can vary pulse-width or amplitude to vary the energy (Energy=pulse-width*amplitude) of the stimulus delivered to the tissue via the penetrating electrode(s). By varying the stimulus energy and monitoring muscle contraction via the penetrating electrodes and/or other type of sensor, the system 100 can estimate the distance to the nerve. If a large amount of energy is required to stimulate the nerve/contract the muscle, the stimulating/penetrating electrode is far from the nerve. As the stimulating/penetrating electrode, moves closer to the nerve, the amount of energy required to induce muscle contraction will drop. For example, an array of penetrating electrodes can be positioned in the tissue at the interest zone and one or more of the electrodes can be activated to apply stimulus at different energy levels until they induce muscle contraction. Using an iterative process, localize the nerve (e.g., via the mapping/evaluation/feedback algorithm 110).

In some embodiments, the system 100 can measure the muscular activation from the nerve stimulus (e.g., via the electrodes 136) to determine neural positioning for neural mapping, without the use of penetrating electrodes. In this embodiment, the treatment device targets the smooth muscle cells' varicosities surrounding the submucosal glands and the vascular supply, and then the compound muscle action potential. This can be used to summate voltage response from the individual muscle fiber action potentials. The shortest latency is the time from stimulus artifact to onset of the response. The corresponding amplitude is measured from baseline to negative peak and measured in millivolts (mV). Nerve latencies (mean±SD) in adults typically range about 2-6 milliseconds, and more typically from about 3.4±0.8 to about 4.0±0.5

milliseconds. A comparative assessment may then be made which compares the outputs at each time interval (especially pre- and post-energy delivery) in addition to a group evaluation using the alternative nasal cavity. This is expected to provide an accurate assessment of the absolute value of the performance of the neural functioning because muscular action/activation may be used to infer neural action/activation and muscle action/activation is a secondary effect or by-product whilst the neural function is the absolute performance measure.

In some embodiments, the system 100 can record a neuromagnetic field outside of the nerves to determine the internal current of the nerves without physical disruption of the nerve membrane. Without being bound by theory, the contribution to the magnetic field from the current inside the membrane is two orders of magnitude larger than that from the external current, and that the contribution from current within the membrane is substantially negligible. Electrical stimulation of the nerve in tandem with measurements of the magnetic compound action fields ("CAFs") can yield sequential positions of the current dipoles such that the location of the conduction change can be estimated (e.g., via the least-squares method). Visual representation (e.g., via the display 112) using magnetic contour maps can show normal or non-normal neural characteristics (e.g., normal can be equated with a characteristic quadrupolar pattern propagating along the nerve), and therefore indicate which nerves are in a diseases, hyperactive state and suitable targets for neuromodulation.

During magnetic field detection, an array of the electrodes 136 can be positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes 136 can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire), and therefore changing magnetic fields are indicative of the nerve nerve-firing rate. The changing magnetic field caused by neural firing can induce a current detected by nearby sensor wire (e.g., the sensor 314) and/or wires associated with the nearby electrodes 136. By measuring this current, the magnetic field strength can be determined. The magnetic fields can optionally be mapped (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. Further, the magnetic field information can be used during or after neuromodulation

therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In other embodiments, the neuromagnetic field is measured with a Hall Probe or other suitable device, which can be integrated into the end effector 114 and/or part of a separate device delivered to the interest zone. Alternatively, rather than measuring the voltage in the second wire, the changing magnetic field can be measured in the original wire (i.e. the nerve) using a Hall probe. A current going through the Hall probe will be deflected in the semi-conductor. This will cause a voltage difference between the top and bottom portions, which can be measured. In some aspects of this embodiments, three orthogonal planes are utilized.

In some embodiments, the system 100 can be used to induce electromotive force ("EMF") in a wire (i.e., a frequency-selective circuit, such as a tunable/LC circuit) that is tunable to resonant frequency of a nerve. In this embodiment, the nerve can be considered to be a current carrying wire, and the firing action potential is a changing voltage. This causes a changing current which, in turn, causes a changing magnetic flux (i.e., the magnetic field that is perpendicular to the wire). Under Faraday's Law of Induction/Faraday's Principle, the changing magnetic flux induces EMF (including a changing voltage) in a nearby sensor wire (e.g., integrated into the end effector 114, the sensor 314, and/or other structure), and the changing voltage can be measured via the system 100.

In further embodiments, the sensor wire (e.g., the sensor 314) is an inductor and, therefore, provides an increase of the magnetic linkage between the nerve (i.e., first wire) and the sensor wire (i.e., second wire), with more turns for increasing effect. (e.g., V2,rms=V1,rms (N2/N1)). Due to the changing magnetic field, a voltage is induced in the sensor wire, and this voltage can be measured and used to estimate current changes in the nerve. Certain materials can be selected to enhance the efficiency of the EMF detection. For example, the sensor wire can include a soft iron core or other high permeability material for the inductor.

During induced EMF detection, the end effector 114 and/or other device including a sensor wire is positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes 136 can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire) that induces a current in the sensor wire (e.g., the sensor 314). This information can be used to determine neural location

and/or map the nerves (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. EMF information can also be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In some embodiments, the system 100 can detect magnetic fields and/or EMF generated at a selected frequency that corresponds to a particular type of nerve. The frequency and, by extension, the associated nerve type of the detected signal can be selected based on an external resonant circuit. Resonance occurs on the external circuit when it is matched to the frequency of the magnetic field of the particular nerve type and that nerve is firing. In manner, the system 100 can be used to locate a particular sub-group/type of nerves.

In some embodiments, the system 100 can include a variable capacitor frequency-selective circuit to identify the location and/or map specific nerves (e.g., parasympathetic nerve, sensory nerve, nerve fiber type, nerve subgroup, etc.). The variable capacitor frequency-selective circuit can be defined by the sensor 314 and/or other feature of the end effector 114. Nerves have different resonant frequencies based on their function and structure. Accordingly, the system 100 can include a tunable LC circuit with a variable capacitor (C) and/or variable inductor (L) that can be selectively tuned to the resonant frequency of desired nerve types. This allows for the detection of neural activity only associated with the selected nerve type and its associated resonant frequency. Tuning can be achieved by moving the core in and out of the inductor. For example, tunable LC circuits can tune the inductor by: (i) changing the number of coils around the core; (ii) changing the cross-sectional area of the coils around the core; (iii) changing the length of the coil; and/or (iv) changing the permeability of the core material (e.g., changing from air to a core material). Systems including such a tunable LC circuit provide a high degree of dissemination and differentiation not only as to the activation of a nerve signal, but also with respect to the nerve type that is activated and the frequency at which the nerve is firing.

Anatomical Mapping

In various embodiments, the system 100 is further configured to provide minimally-invasive anatomical mapping that uses focused energy current/voltage stimuli from a spatially localized source (e.g., the electrodes 136) to cause a change in the conductivity of the of the tissue at the interest zone and detect resultant biopotential and/or bioelectrical measurements (e.g., via the electrodes 136). The current density in the tissue changes in response to changes of voltage applied by the electrodes 136, which creates a change in the electric current that can be measured with the end effector 114 and/or other portions of the system 100. The results of the bioelectrical and/or biopotential measurements can be used to predict or estimate relative absorption profilometry to predict or estimate the tissue structures in the interest zone. More specifically, each cellular construct has unique conductivity and absorption profiles that can be indicative of a type of tissue or structure, such as bone, soft tissue, vessels, nerves, types of nerves, and/or certain neural structures. For example, different frequencies decay differently through different types of tissue. Accordingly, by detecting the absorption current in a region, the system 100 can determine the underlying structure and, in some instances, to a sub-microscale, cellular level that allows for highly specialized target localization and mapping. This highly specific target identification and mapping enhances the efficacy and efficiency of neuromodulation therapy, while also enhancing the safety profile of the system 100 to reduce collateral effects on non-target structures.

To detect electrical and dielectric tissue properties (e.g., resistance, complex impedance, conductivity, and/or, permittivity as a function of frequency), the electrodes 136 and/or another electrode array is placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli (current/voltage) to the tissue. The electrical properties of the tissue between the source and the receiver electrodes 136 are measured, as well as the current and/or voltage at the individual receiver electrodes 136. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest and, in certain embodiments, the location of firing nerves. For example, the anatomical mapping can be provided as a color-coded or gray-scale three-dimensional or two-dimensional map showing differing intensities of certain bioelectric properties (e.g., resistance, impedance, etc.), or the information can be processed to map the actual anatomical structures for the clinician. This information can also be used during neuromodulation therapy to monitor treatment progression with respect to the anatomy, and after

neuromodulation therapy to validate successful treatment. In addition, the anatomical mapping provided by the bioelectrical and/or biopotential measurements can be used to track the changes to non-target tissue (e.g., vessels) due to neuromodulation therapy to avoid negative collateral effects. For example, a clinician can identify when the therapy begins to ligate a vessel and/or damage tissue, and modify the therapy to avoid bleeding, detrimental tissue ablation, and/or other negative collateral effects.

Furthermore, the threshold frequency of electric current used to identify specific targets can subsequently be used when applying therapeutic neuromodulation energy. For example, the neuromodulation energy can be applied at the specific threshold frequencies of electric current that are target neuronal-specific and differentiated from other non-targets (e.g., blood vessels, non-target nerves, etc.). Applying ablation energy at the target-specific frequency results in an electric field that creates ionic agitation in the target neural structure, which leads to differentials in osmotic potentials of the targeted neural structures. These osmotic potential differentials cause dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure) that lead to vacuolar degeneration of the targeted neural structures and, eventually, necrosis. Using the highly targeted threshold neuromodulation energy to initiate the degeneration allows the system 100 to delivery therapeutic neuromodulation to the specific target, while surrounding blood vessels and other non-target structures are functionally maintained.

In some embodiments, the system 100 can further be configured to detect bioelectrical properties of tissue by non-invasively recording resistance changes during neuronal depolarization to map neural activity with electrical impedance, resistance, bio-impedance, conductivity, permittivity, and/or other bioelectrical measurements. Without being bound by theory, when a nerve depolarizes, the cell membrane resistance decreases (e.g., by approximately 80×) so that current will pass through open ion channels and into the intracellular space. Otherwise the current remains in the extracellular space. For non-invasive resistance measurements, tissue can be stimulated by applying a current of less than 100 Hz, such as applying a constant current square wave at 1 Hz with an amplitude less than 25% (e.g., 10%) of the threshold for stimulating neuronal activity, and thereby preventing or reducing the likelihood that the current does not cross into the intracellular space or stimulating at 2 Hz. In either case,

the resistance and/or complex impedance is recorded by recording the voltage changes. A complex impedance or resistance map or profile of the area can then be generated.

For impedance/conductivity/permittivity detection, the electrodes 136 and/or another electrode array are placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli to the tissue, and the current and/or voltage at the individual receiver electrodes 136 is measured. The stimuli can be applied at different frequencies to isolate different types of nerves. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest. The neural mapping can also be used during neuromodulation therapy to select specific nerves for therapy, monitor treatment progression with respect to the nerves and other anatomy, and validate successful treatment.

In some embodiments of the neural and/or anatomical detection methods described above, the procedure can include comparing the mid-procedure physiological parameter(s) to the baseline physiological parameter(s) and/or other, previously-acquired mid-procedure physiological parameter(s) (within the same energy delivery phase). Such a comparison can be used to analyze state changes in the treated tissue. The mid-procedure physiological parameter(s) may also be compared to one or more predetermined thresholds, for example, to indicate when to stop delivering treatment energy. In some embodiments of the present technology, the measured baseline, mid-, and post-procedure parameters include a complex impedance. In some embodiments of the present technology, the post-procedure physiological parameters are measured after a pre-determined time period to allow the dissipation of the electric field effects (ionic agitation and/or thermal thresholds), thus facilitating accurate assessment of the treatment.

In some embodiments, the anatomical mapping methods described above can be used to differentiate the depth of soft tissues within the nasal mucosa. The depth of mucosa on the turbinates is great whilst the depth off the turbinate is shallow and, therefore, identifying the tissue depth in the present technology also identifies positions within the nasal mucosa and where precisely to target. Further, by providing the micro-scale spatial impedance mapping of epithelial tissues as described above, the inherent unique signatures of stratified layers or cellular bodies can be used as identifying the region of interest. For example, different regions have

larger or small populations of specific structures, such as submucosal glands, so target regions can be identified via the identification of these structures.

In some embodiments, the system 100 includes additional features that can be used to detect anatomical structures and map anatomical features. For example, the system 100 can include an ultrasound probe for identification of neural structures and/or other anatomical structures. Higher frequency ultrasound provides higher resolution, but less depth of penetration. Accordingly, the frequency can be varied to achieve the appropriate depth and resolution for neural/anatomical localization. Functional identification may rely on the spatial pulse length ("SPL") (wavelength multiplied by number of cycles in a pulse). Axial resolution (SPL/2) may also be determined to locate nerves.

In some embodiments, the system 100 can further be configured to emit stimuli with selective parameters that suppress rather than fully stimulate neural activity. for example, in embodiments where the strength-duration relationship for extracellular neural stimulation is selected and controlled, a state exists where the extracellular current can hyperpolarize cells, resulting in suppression rather than stimulation spiking behavior (i.e., a full action potential is not achieved). Both models of ion channels, HH and RGC, suggest that it is possible to hyperpolarize cells with appropriately designed burst extracellular stimuli, rather than extending the stimuli. This phenomenon could be used to suppress rather than stimulate neural activity during any of the embodiments of neural detection and/or modulation described herein.

In various embodiments, the system 100 could apply the anatomical mapping techniques disclosed herein to locate or detect the targeted vasculature and surrounding anatomy before, during, and/or after treatment.

Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment. Thus, appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments.

The terms and expressions which have been employed herein are used as terms of description and not of limitation, and there is no intention, in the use of such terms and expressions, of excluding any equivalents of the features shown and described (or portions

thereof), and it is recognized that various modifications are possible within the scope of the claims. Accordingly, the claims are intended to cover all such equivalents.

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes.

Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein. The subject matter herein contains important information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

Claims

What is claimed is:

1. A device for treating a condition within a sino-nasal cavity of a patient, the device comprising:

an elongate body comprising one or more of a first set of electrodes provided along a length thereof; and

a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon.

2. The device of claim 1, wherein the elongate body comprises a shaft to which the end effector is coupled.

3. The device of claim 2, wherein the shaft comprises an outer sheath surrounding a hypotube or metallic member, wherein at least one of the outer sheath and hypotube and metallic member includes the one or more of the first set of electrodes provided thereon.

4. The device of claim 1, wherein the elongate body comprises one or more of a plurality of support elements forming at least a portion of the end effector.

5. The device of claim 1, wherein each of the first set of electrodes is positioned on separate respective portion of the elongate body.

6. The device of claim 5, wherein one or more of the separate respective portions of the elongate body are transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

7. The device of claim 1, wherein each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of

a patient at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient.

8. The device of claim 1, wherein the end effector comprises a proximal segment that is spaced apart from a separate distal segment.

9. The device of claim 8, wherein:

the proximal segment comprises a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate; and

the distal segment comprises a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate.

10. The device of claim 9, wherein each of the second set of electrodes is configured to deliver energy to a second target site associated with a sphenopalatine foramen within the nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the patient.

11. A method for treating a condition within a nasal cavity of a patient, the method comprising:

providing a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon,

advancing the elongate body and end effector through a nasal passage and into a sino-nasal cavity of a patient until a length of the elongate body is positioned at a first target site and the end effector is positioned at a separate second target site; and

delivering energy, via the first and second sets of electrodes, to tissue at the respective first and second target sites.

12. The method of claim 11, wherein the elongate body comprises a shaft to which the end effector is coupled.

13. The method of claim 12, wherein the shaft comprises an outer sheath surrounding a hypotube or metallic member, wherein at least one of the outer sheath and hypotube and metallic member includes the one or more of the first set of electrodes provided thereon.

14. The method of claim 11, wherein the elongate body comprises one or more of a plurality of support elements forming at least a portion of the end effector.

15. The method of claim 11, wherein each of the first set of electrodes is positioned on separate respective portion of the elongate body.

16. The method of claim 15, wherein one or more of the separate respective portions of the elongate body are transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

16. The method of claim 11, wherein the first target site associated with an inferior or middle turbinate of the patient and the second target site associated with a sphenopalatine foramen within the nasal cavity of the patient.

17. The method of claim 16, wherein delivering energy via the first set of electrodes comprises delivering energy at level sufficient to disrupt multiple neural signals to and/or result in local hypoxia or coagulation necrosis of mucus producing and/or mucosal engorgement elements associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient.

18. The method of claim 16, wherein the end effector comprises a proximal segment that is spaced apart from a separate distal segment.

19. The method of claim 18, wherein:

the proximal segment comprises a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate; and

the distal segment comprises a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate.

20. The method of claim 19, wherein delivering energy via the second set of electrodes comprises delivering energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient.

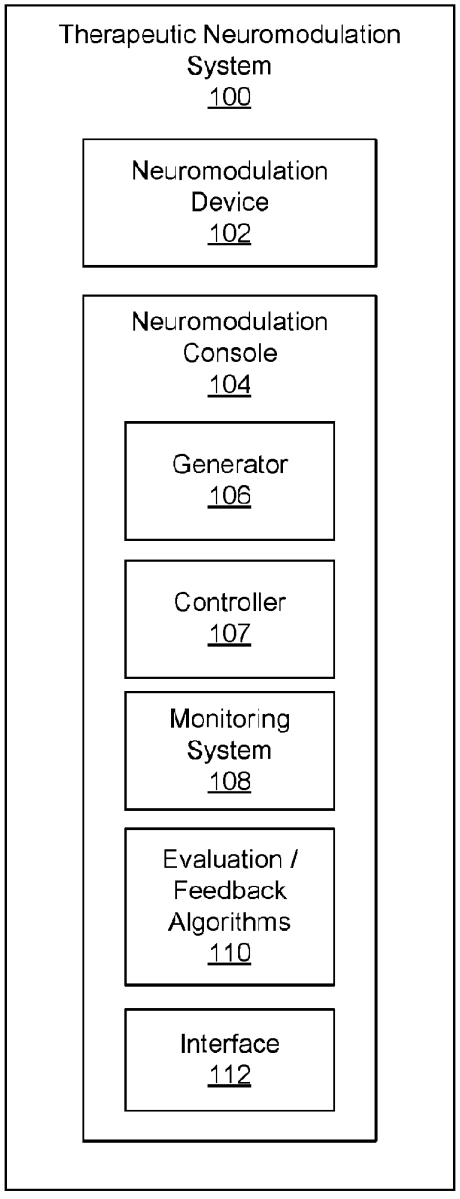

Therapeutic Neuromodulation System
100
Neuromodulation Device
102
Neuromodulation Console
104
Generator
106
Controller
107
Monitoring System
108
Evaluation / Feedback Algorithms
110
Interface
112

FIG. 1A

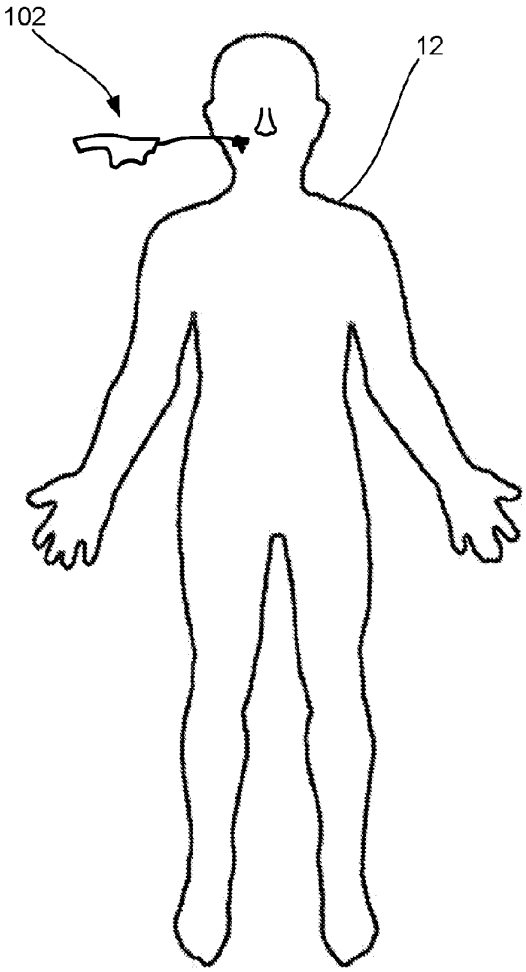

102
12

FIG. 1B

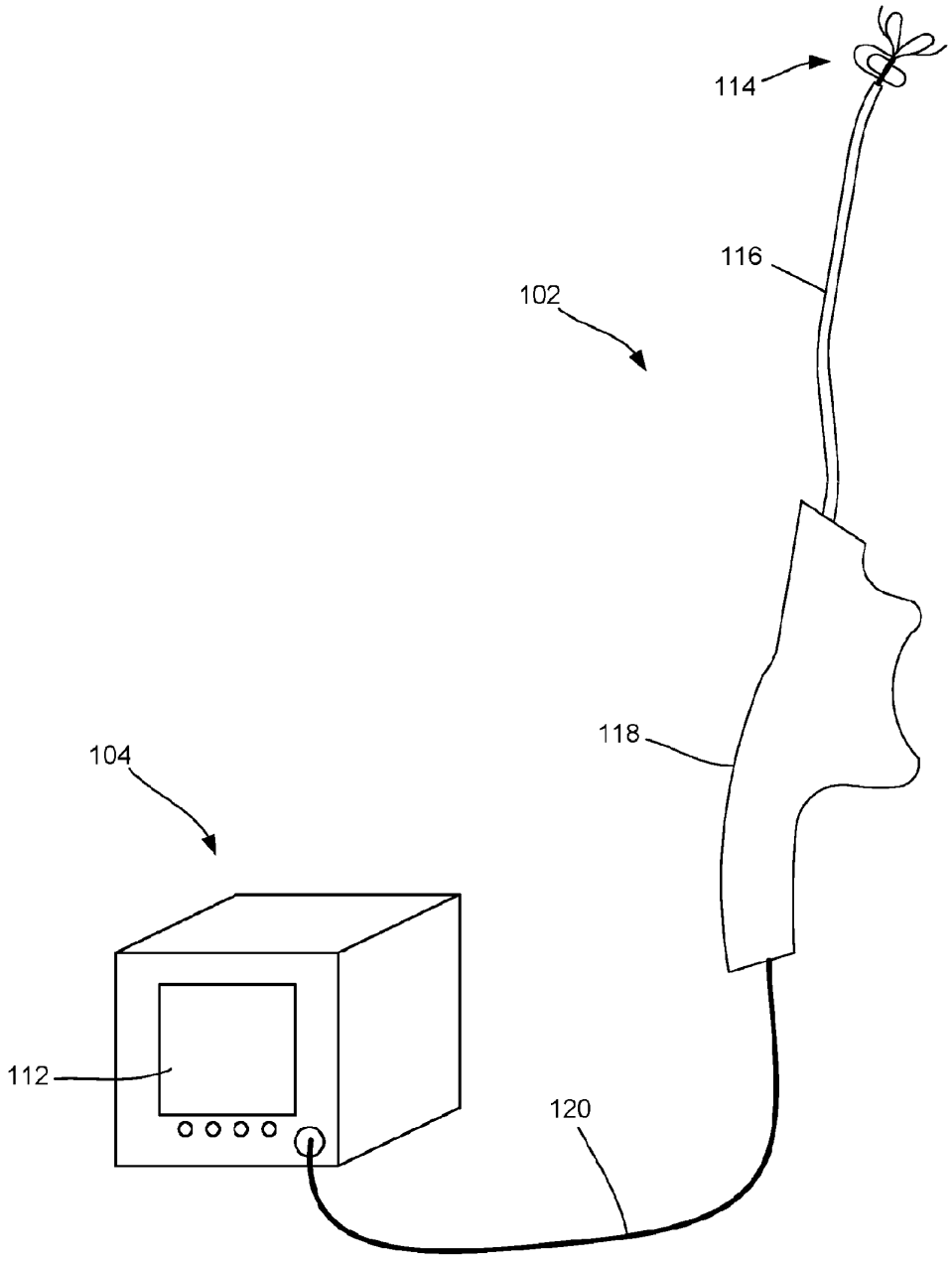


FIG. 2

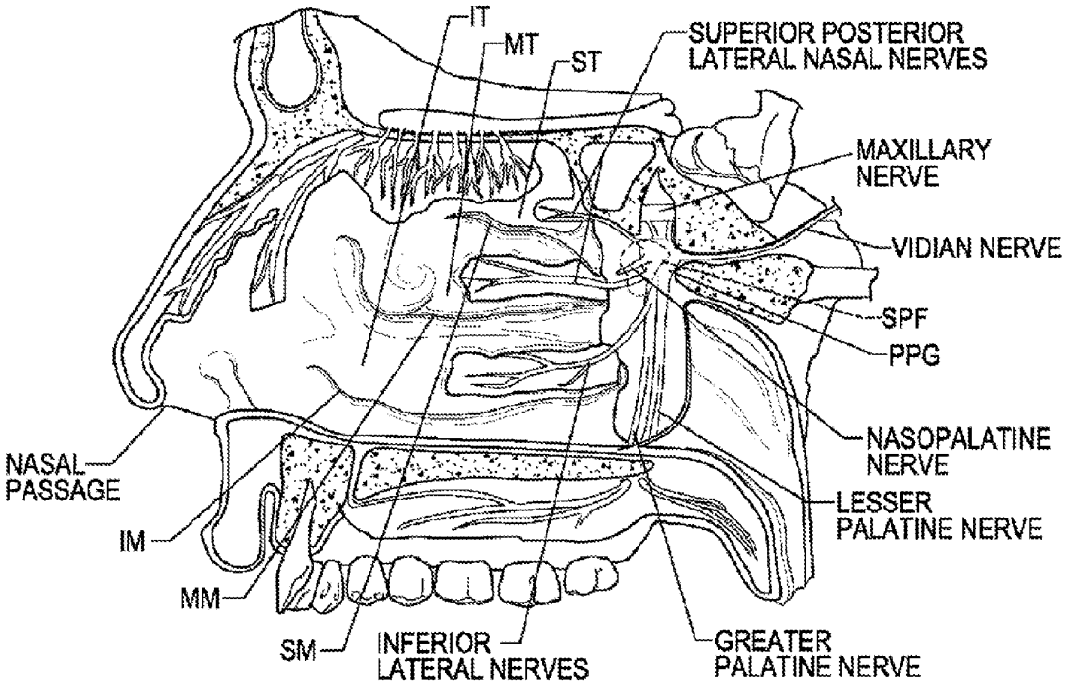

IT
MT
ST
SUPERIOR POSTERIOR LATERAL NASAL NERVES
MAXILLARY NERVE
VIDIAN NERVE
SPF
PPG
NASOPALATINE NERVE
LESSER PALATINE NERVE
NASAL PASSAGE
IM
MM
SM
INFERIOR LATERAL NERVES
GREATER PALATINE NERVE

FIG. 3A

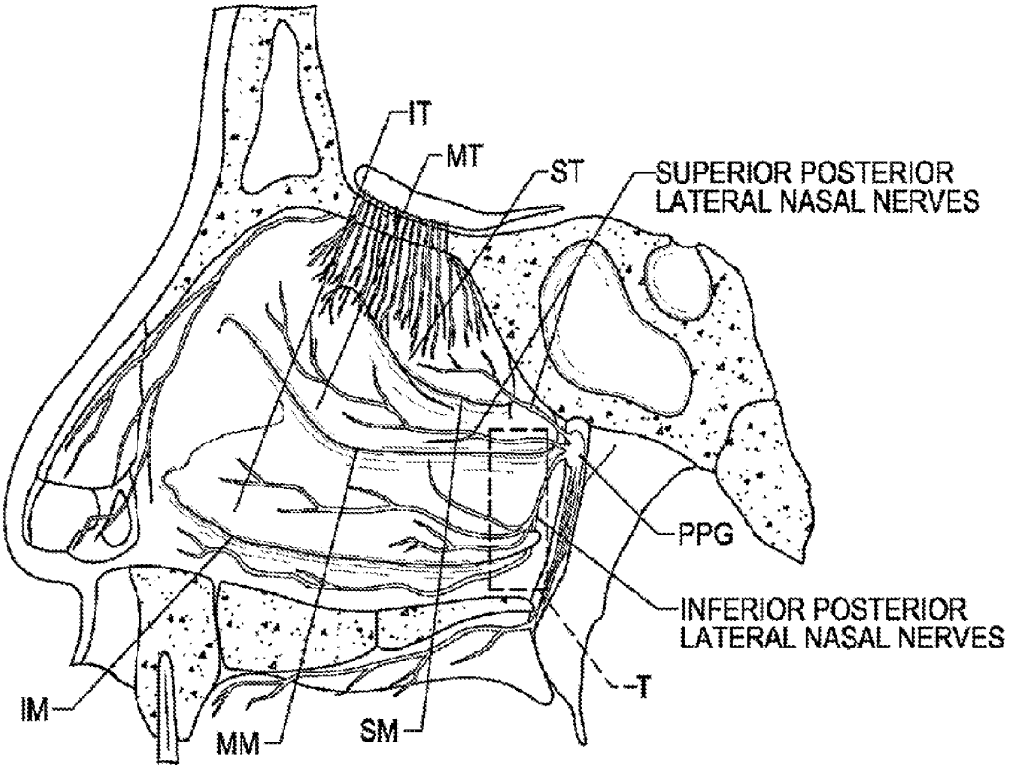

IT
MT
ST
SUPERIOR POSTERIOR
LATERAL NASAL NERVES
PPG
INFERIOR POSTERIOR
LATERAL NASAL NERVES
T
IM
MM
SM

FIG. 3B

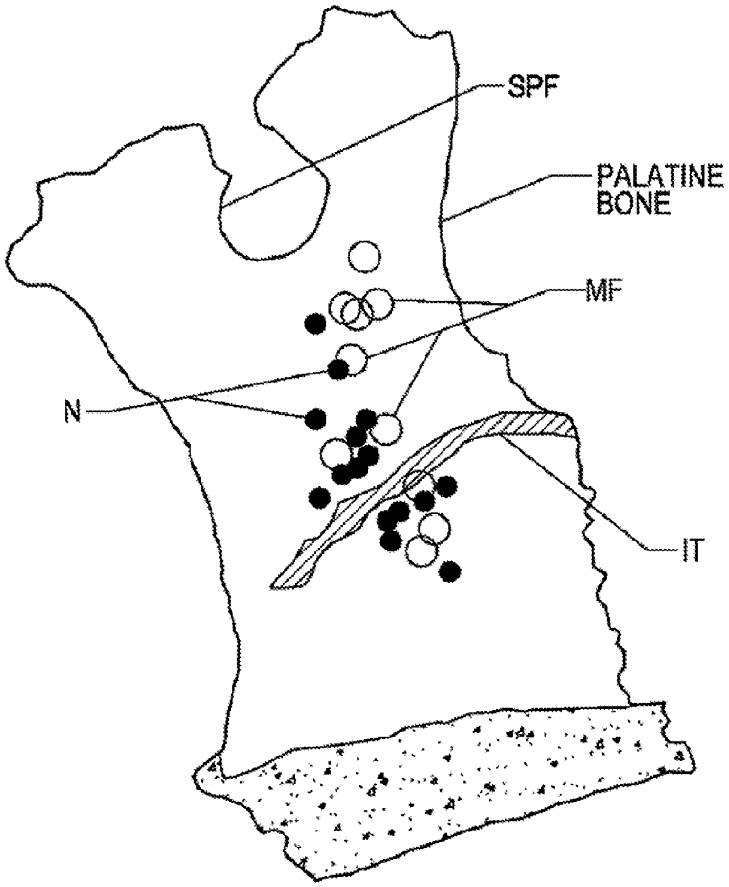


FIG. 3C

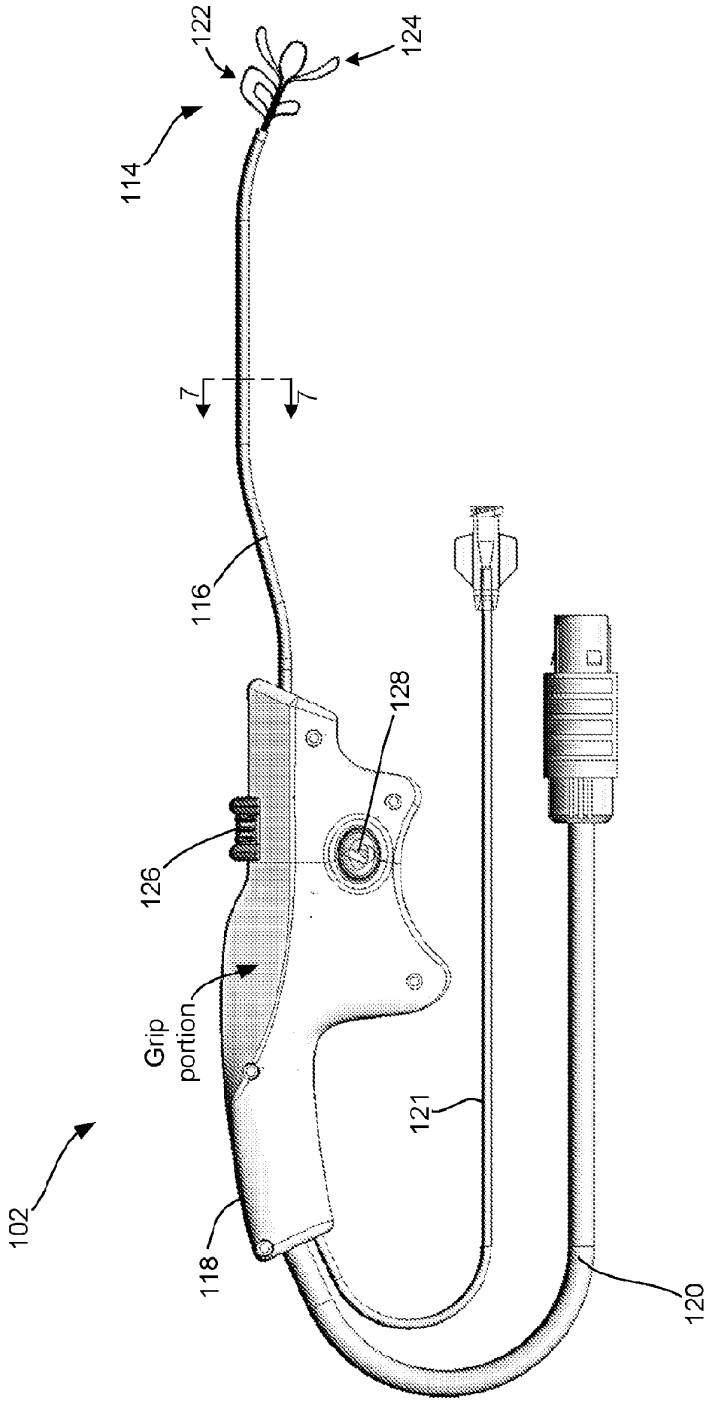


FIG. 4

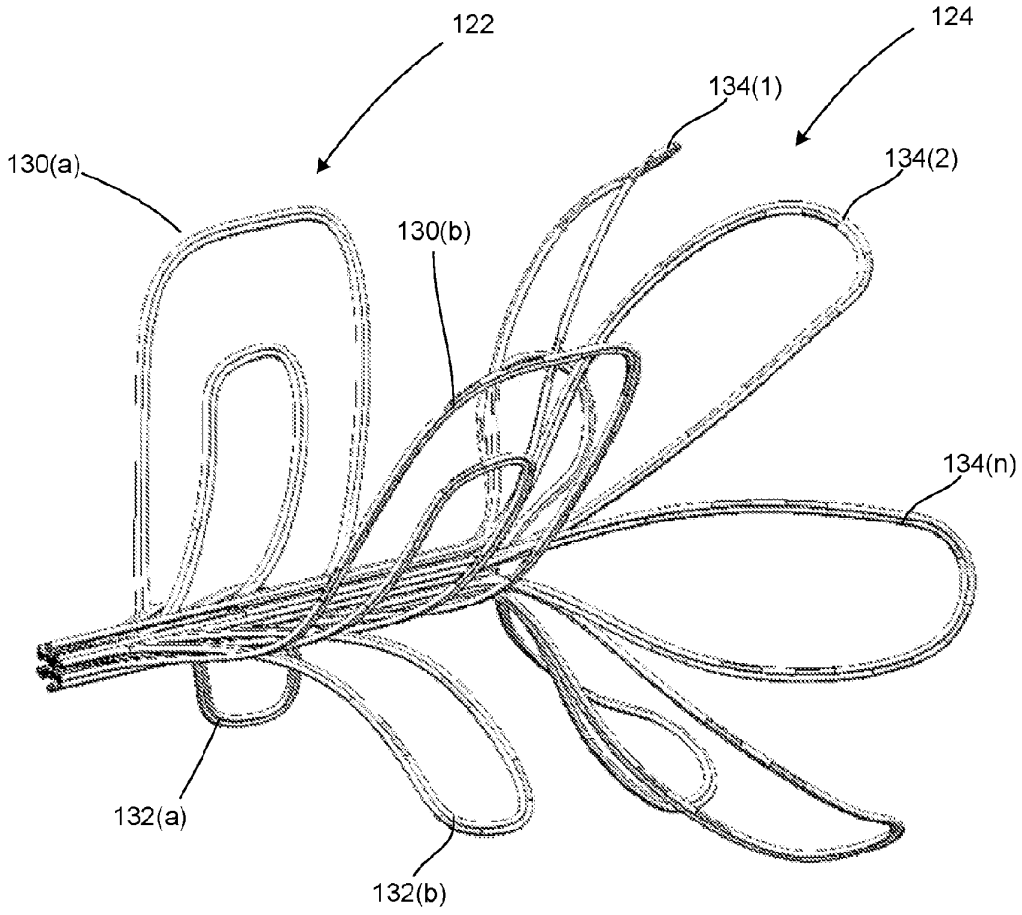


FIG. 5A

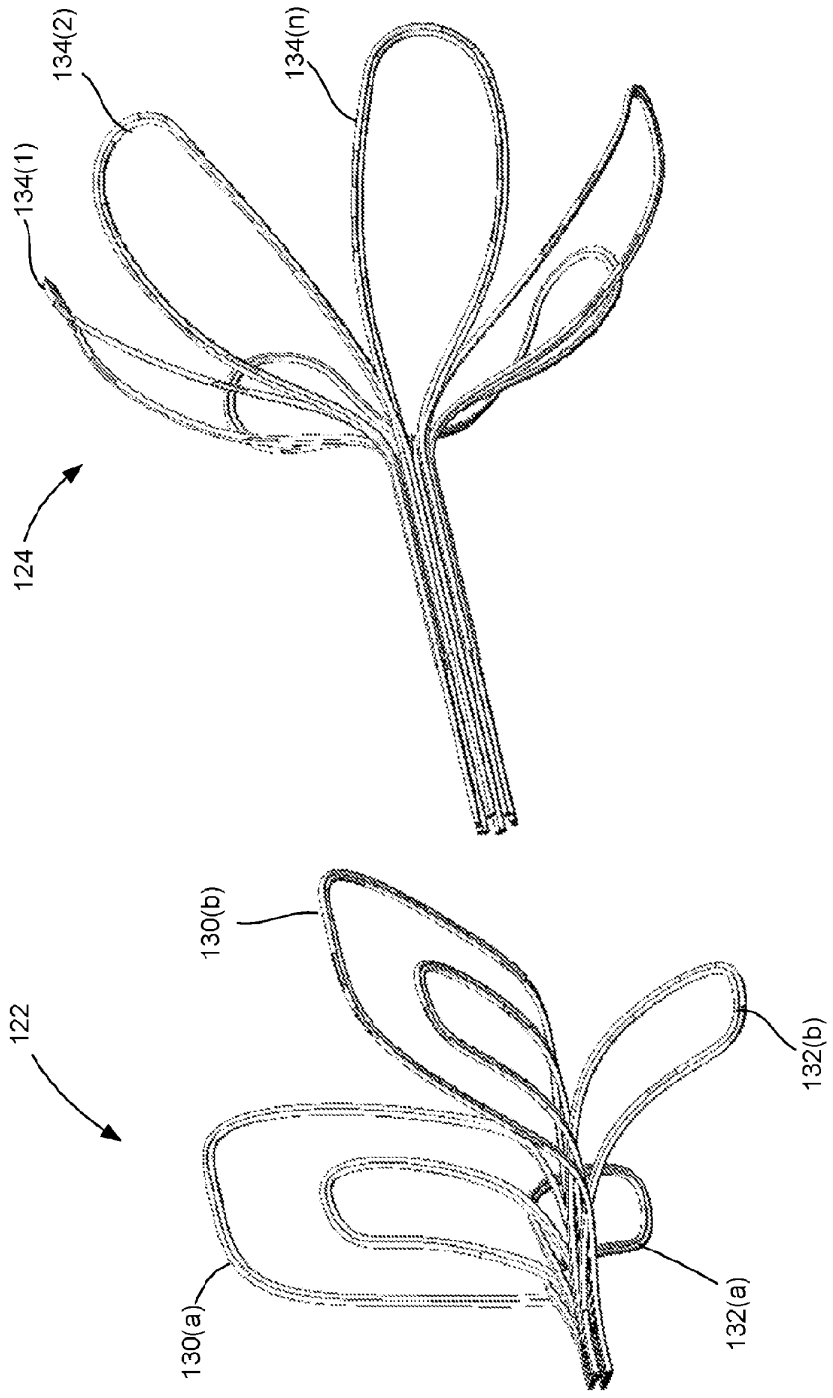


FIG. 5B

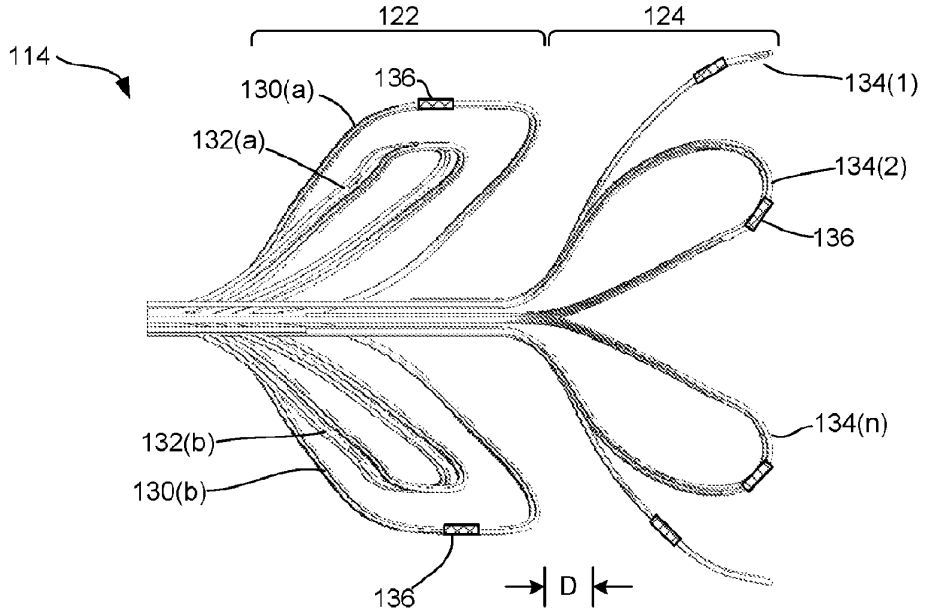

122
124
114
130(a)
136
134(1)
132(a)
134(2)
136
132(b)
134(n)
130(b)
136
D

FIG. 5C

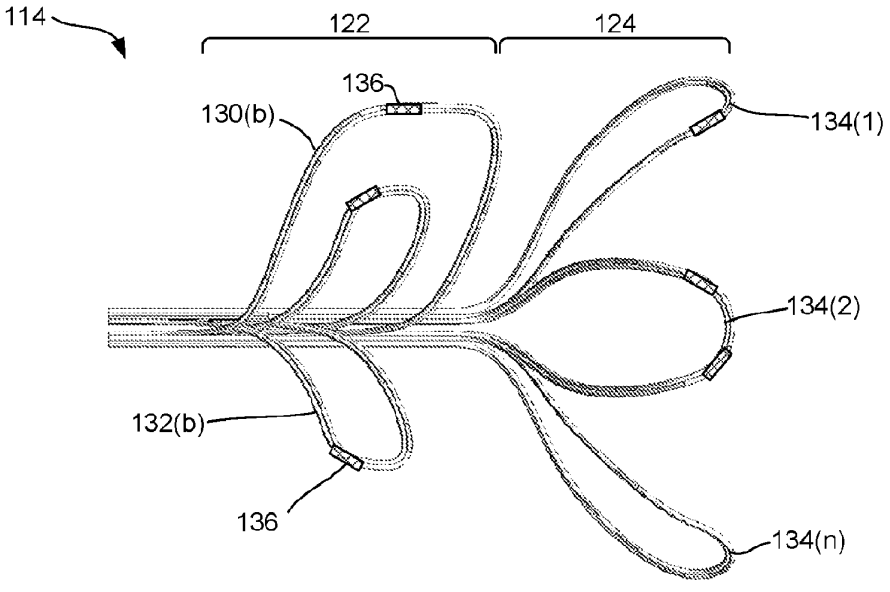

114
122
124
136
130(b)
134(1)
134(2)
132(b)
136
134(n)

FIG. 5D

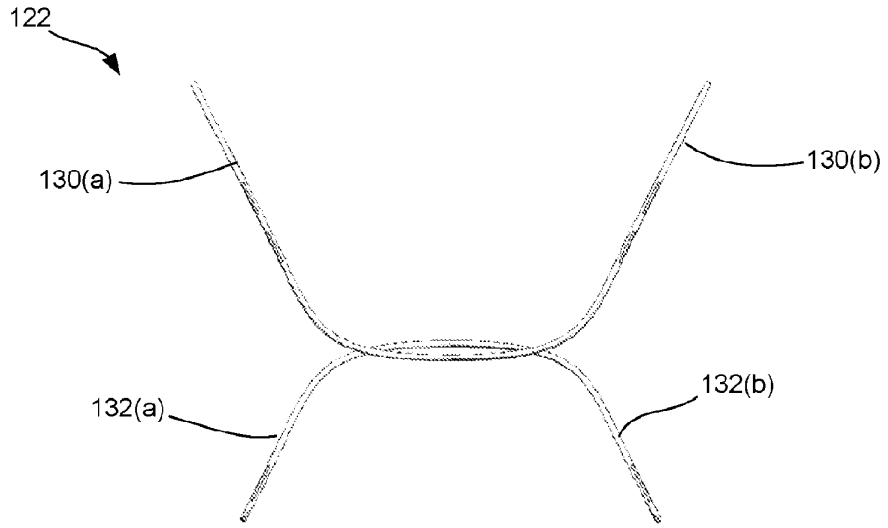


FIG. 5E

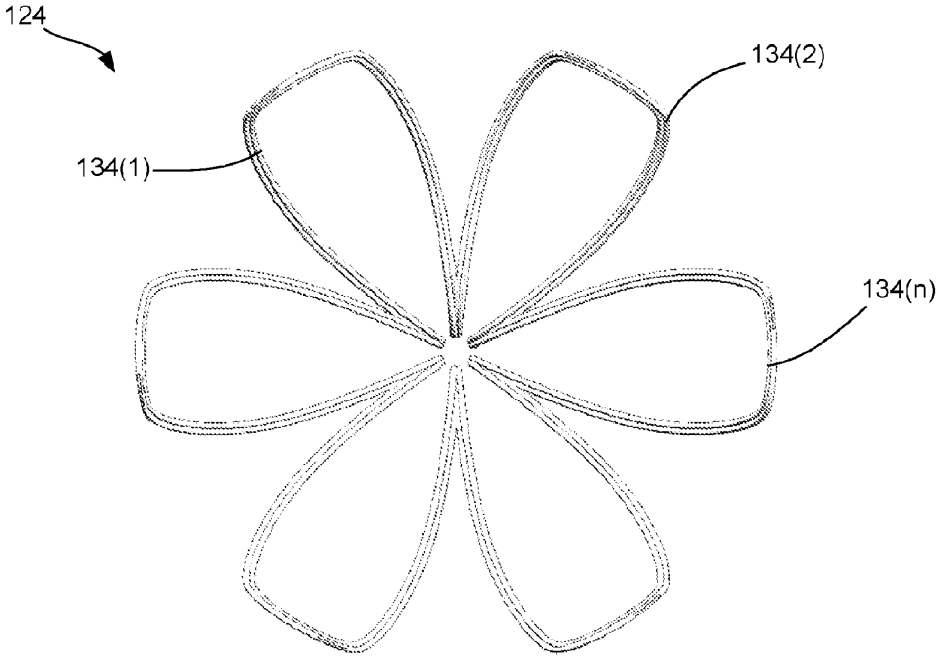


FIG. 5F

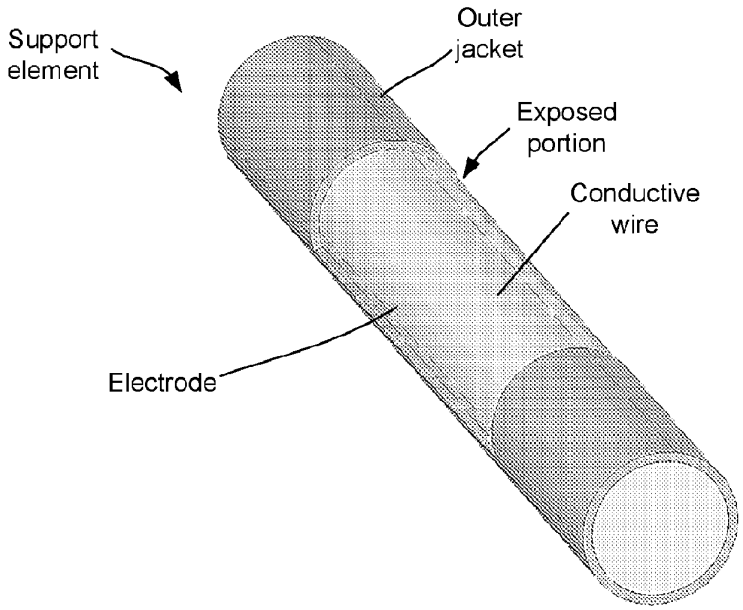

Support element
Outer jacket
Exposed portion
Conductive wire
Electrode

FIG. 6

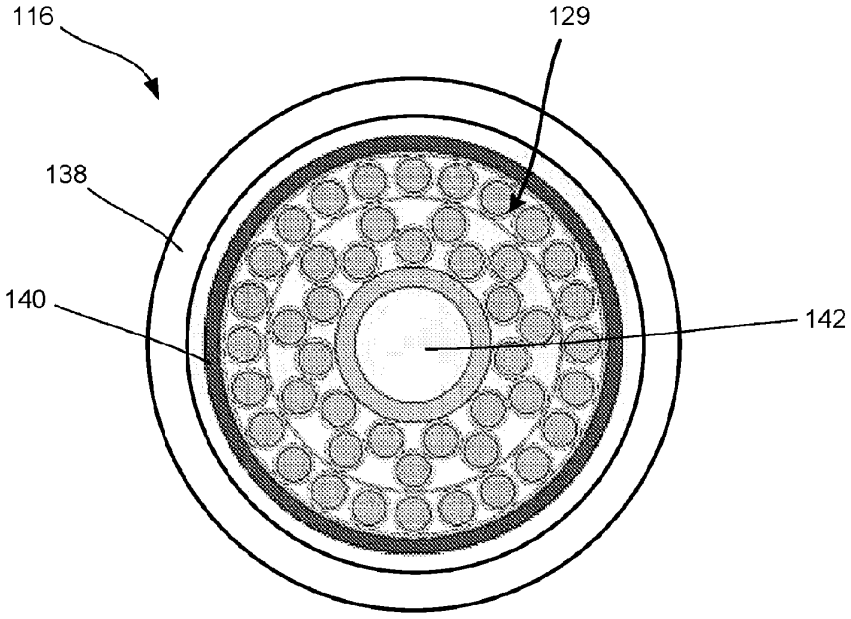

116
129
138
140
142

FIG. 7

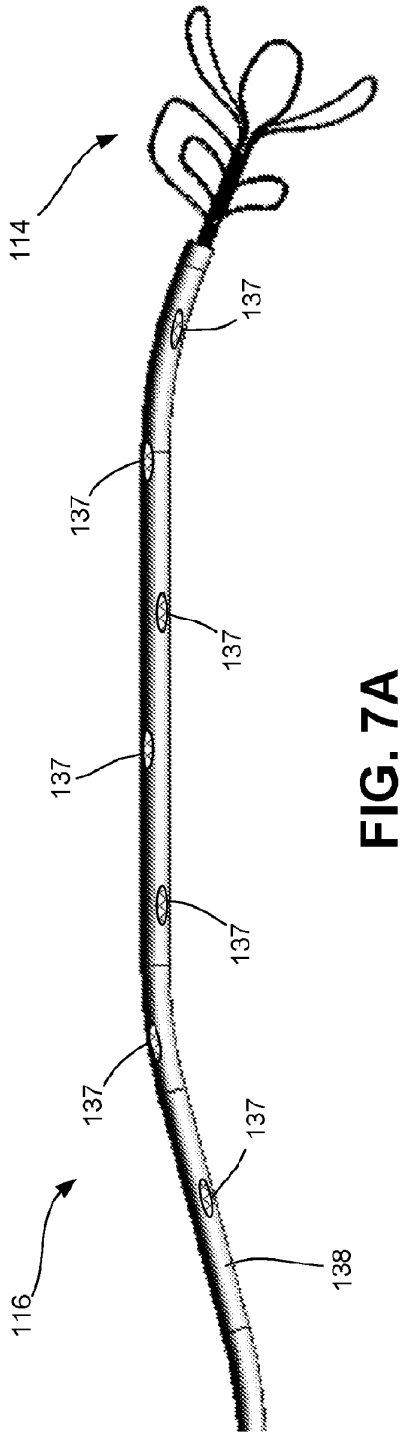


FIG. 7A

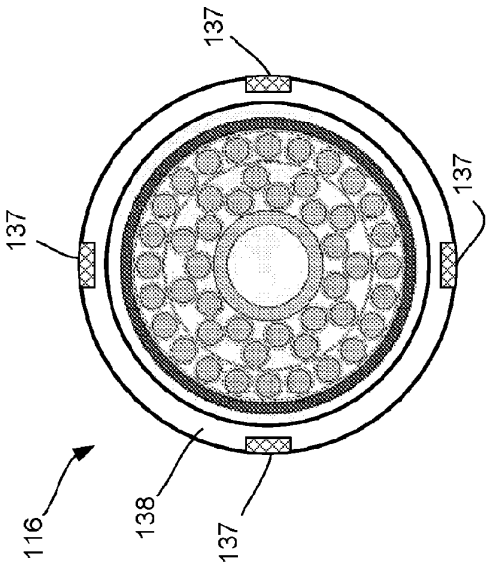


FIG. 7B

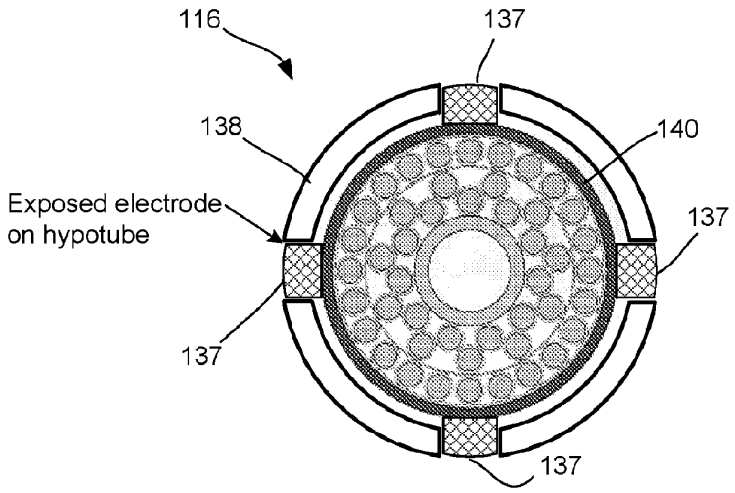

116
137
138
140
Exposed electrode on hypotube
137
137
137

FIG. 7C

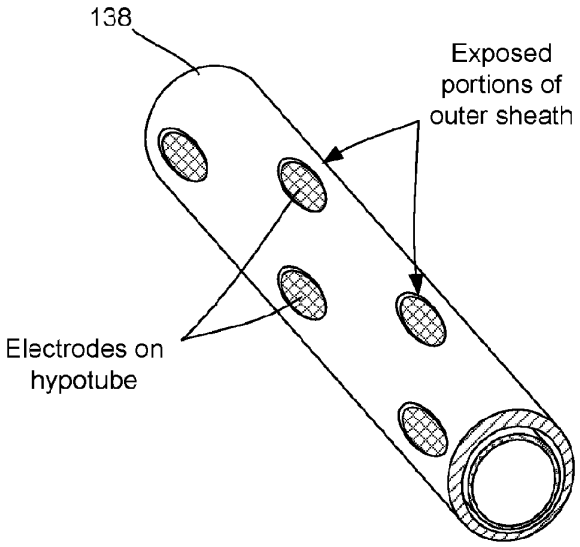

138
Exposed portions of outer sheath
Electrodes on hypotube

FIG. 7D

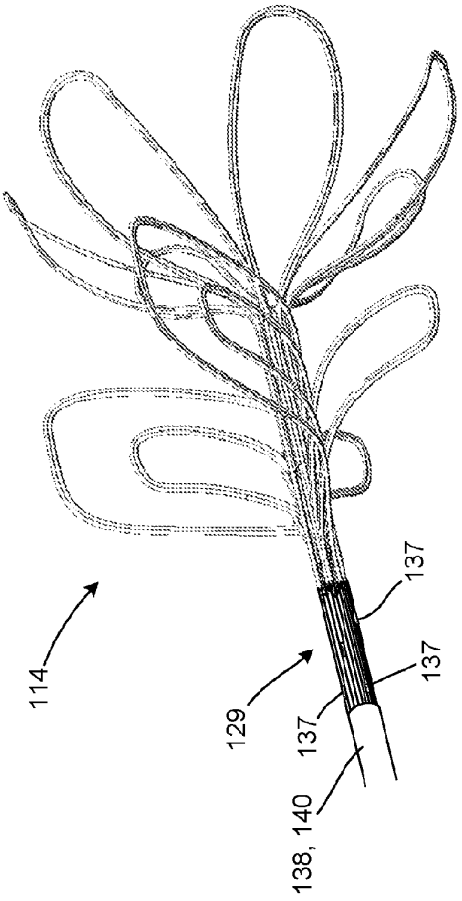


FIG. 7F

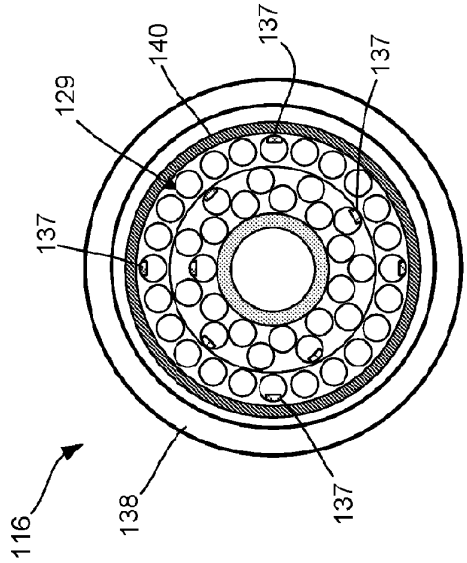


FIG. 7E

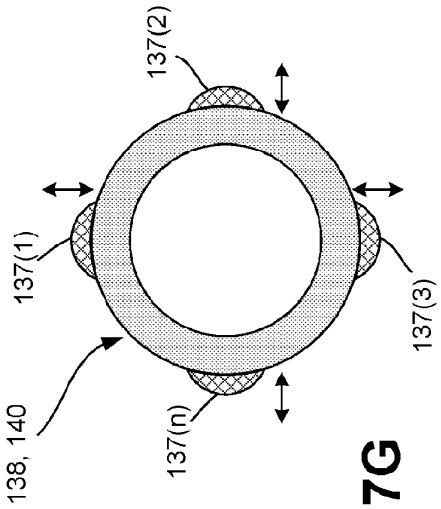


FIG. 7G

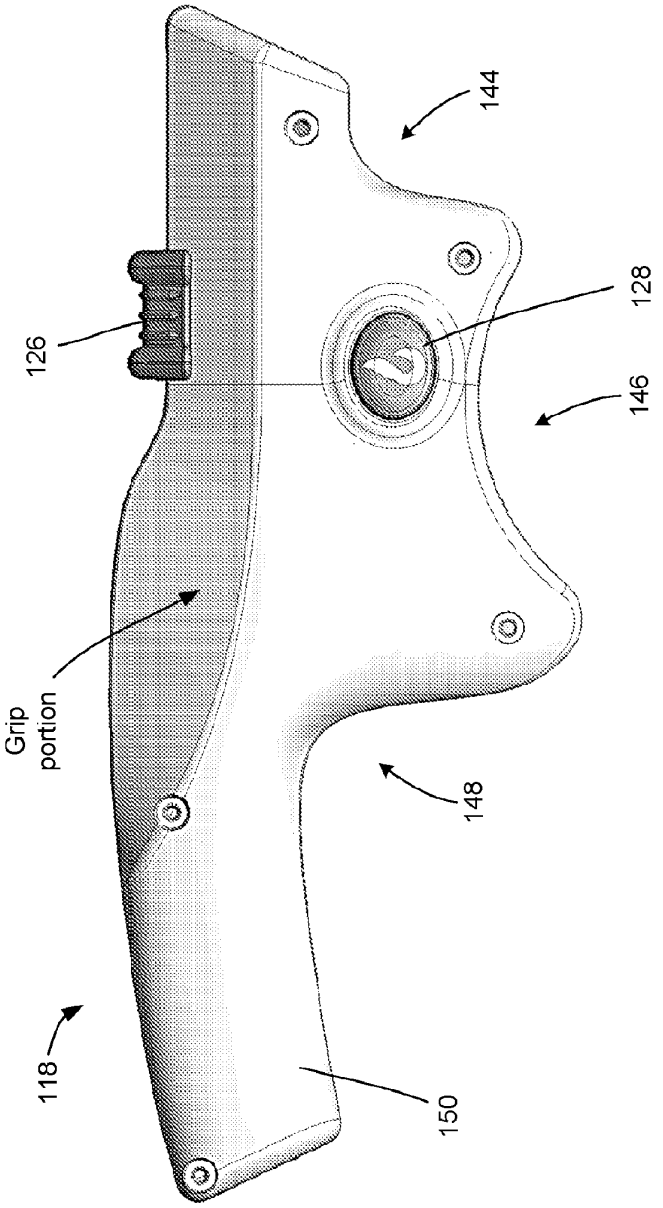


FIG. 8

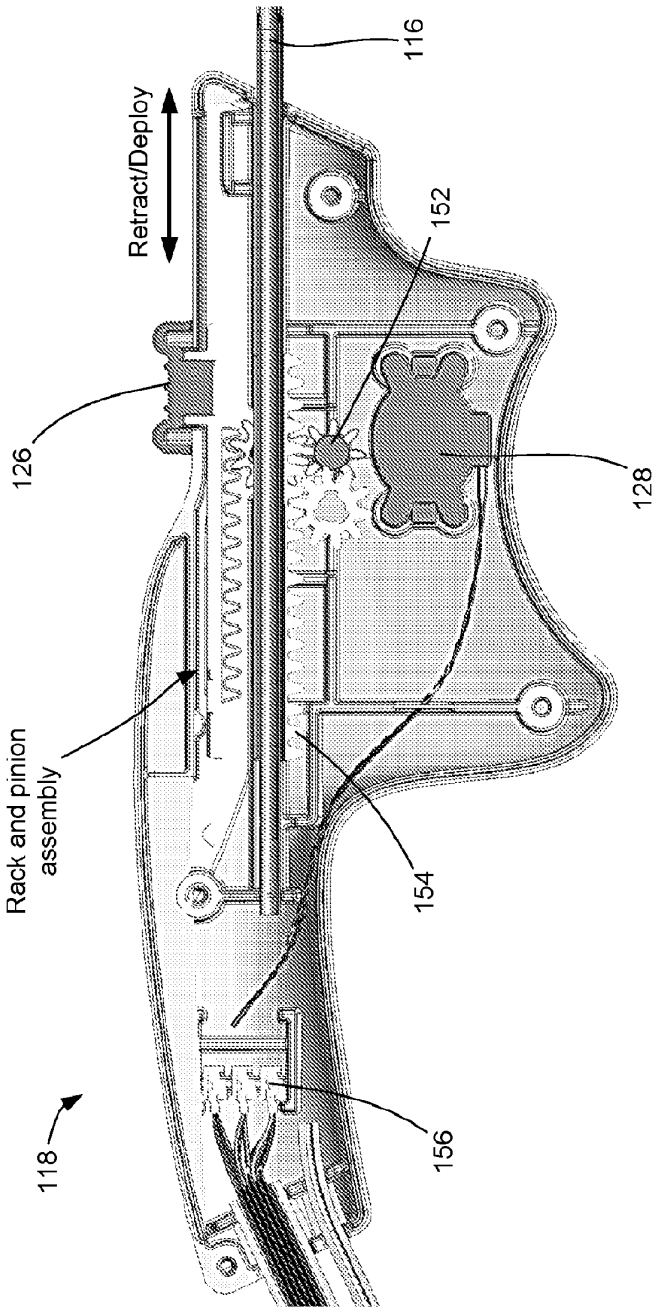

116
Retract/Deploy
152
126
128
Rack and pinion assembly
154
156
118

FIG. 9

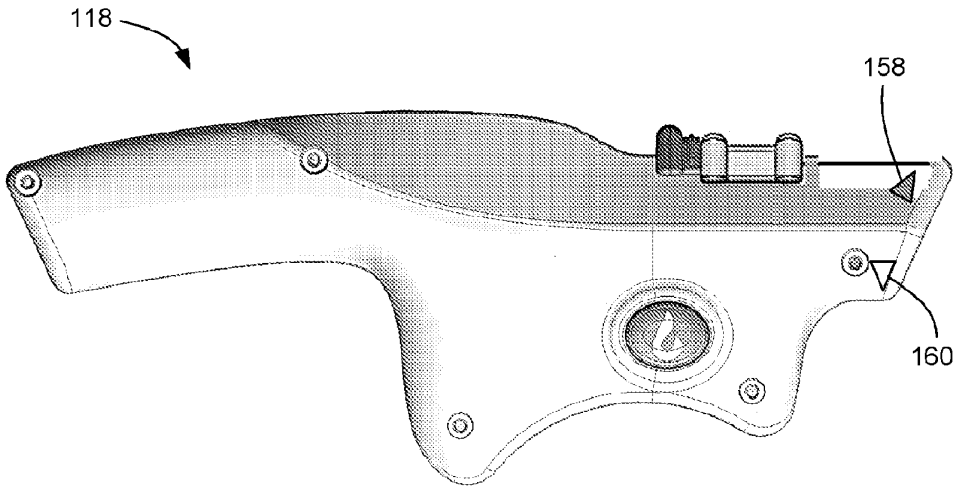


FIG. 10

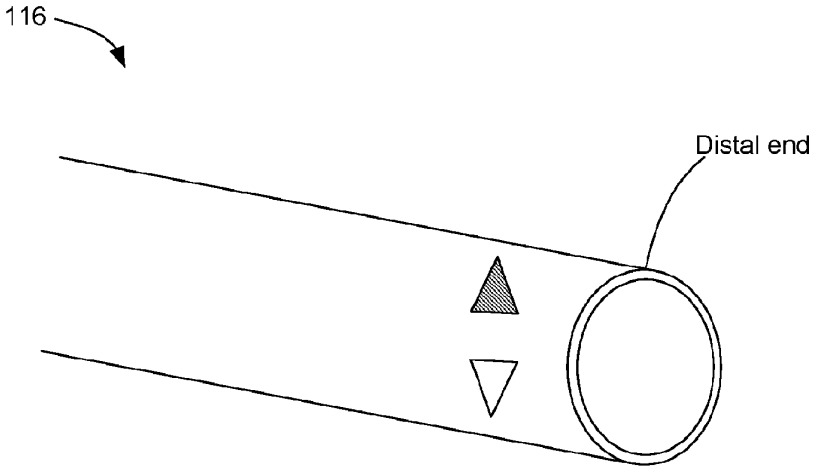


FIG. 11

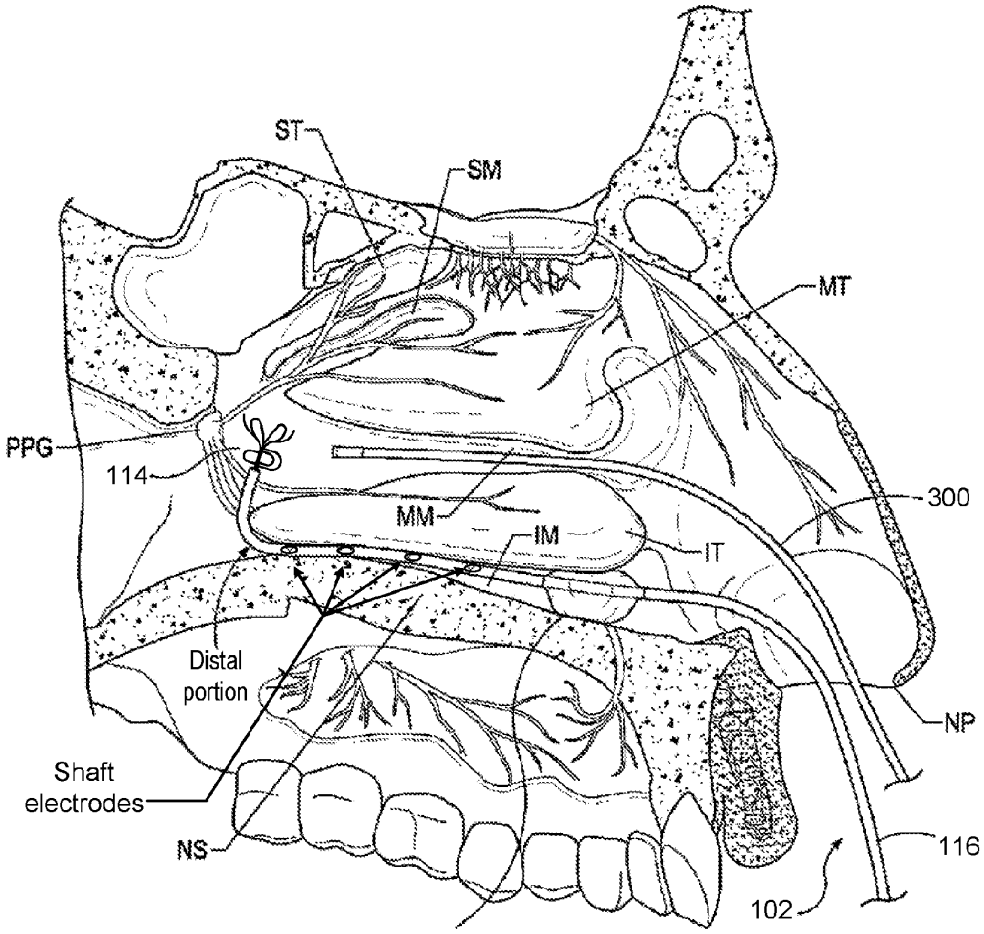

ST
SM
MT
PPG
114
300
MM
IM
IT
Distal
portion
NP
Shaft
electrodes
NS
116
102

FIG. 12

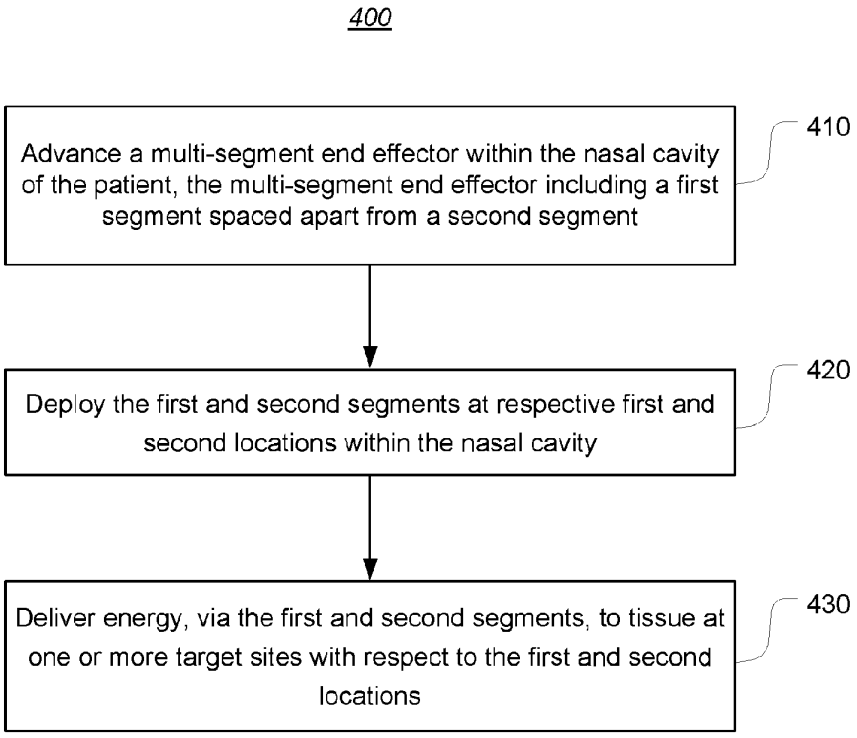

400
Advance a multi-segment end effector within the nasal cavity of the patient, the multi-segment end effector including a first segment spaced apart from a second segment
410
Deploy the first and second segments at respective first and second locations within the nasal cavity
420
Deliver energy, via the first and second segments, to tissue at one or more target sites with respect to the first and second locations
430

FIG. 13

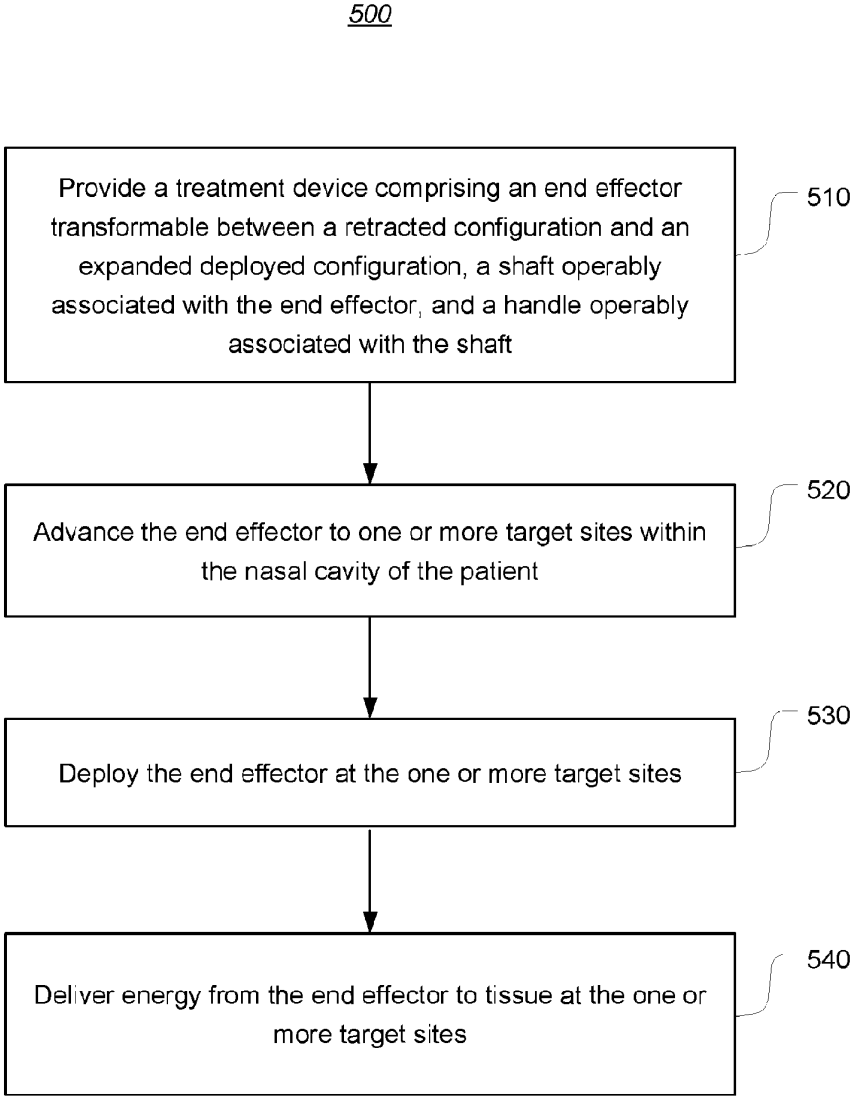

500
Provide a treatment device comprising an end effector transformable between a retracted configuration and an expanded deployed configuration, a shaft operably associated with the end effector, and a handle operably associated with the shaft
510
Advance the end effector to one or more target sites within the nasal cavity of the patient
520
Deploy the end effector at the one or more target sites
530
Deliver energy from the end effector to tissue at the one or more target sites
540

FIG. 14

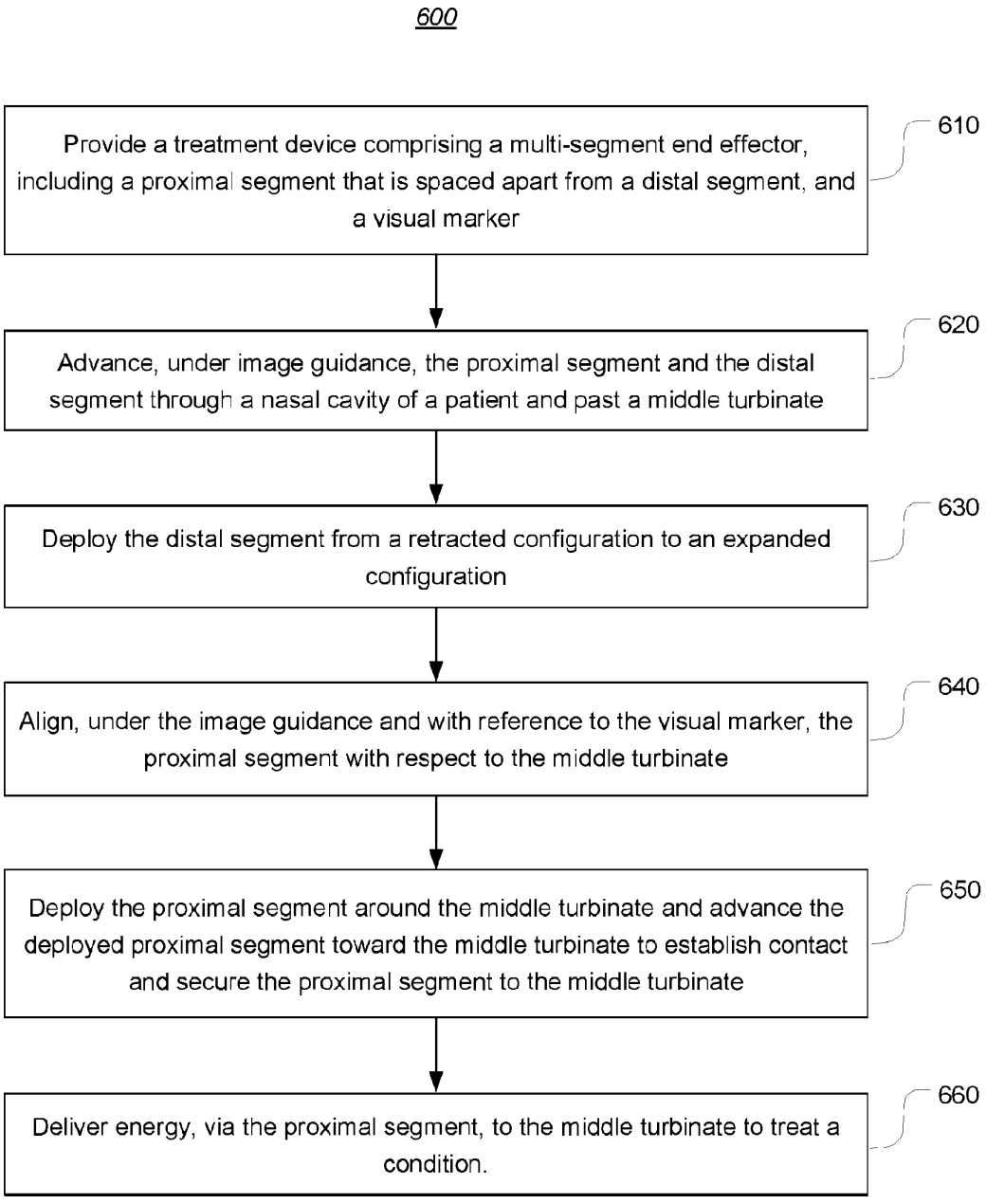

600
Provide a treatment device comprising a multi-segment end effector, including a proximal segment that is spaced apart from a distal segment, and a visual marker
610
Advance, under image guidance, the proximal segment and the distal segment through a nasal cavity of a patient and past a middle turbinate
620
Deploy the distal segment from a retracted configuration to an expanded configuration
630
Align, under the image guidance and with reference to the visual marker, the proximal segment with respect to the middle turbinate
640
Deploy the proximal segment around the middle turbinate and advance the deployed proximal segment toward the middle turbinate to establish contact and secure the proximal segment to the middle turbinate
650
Deliver energy, via the proximal segment, to the middle turbinate to treat a condition.
660

FIG. 15

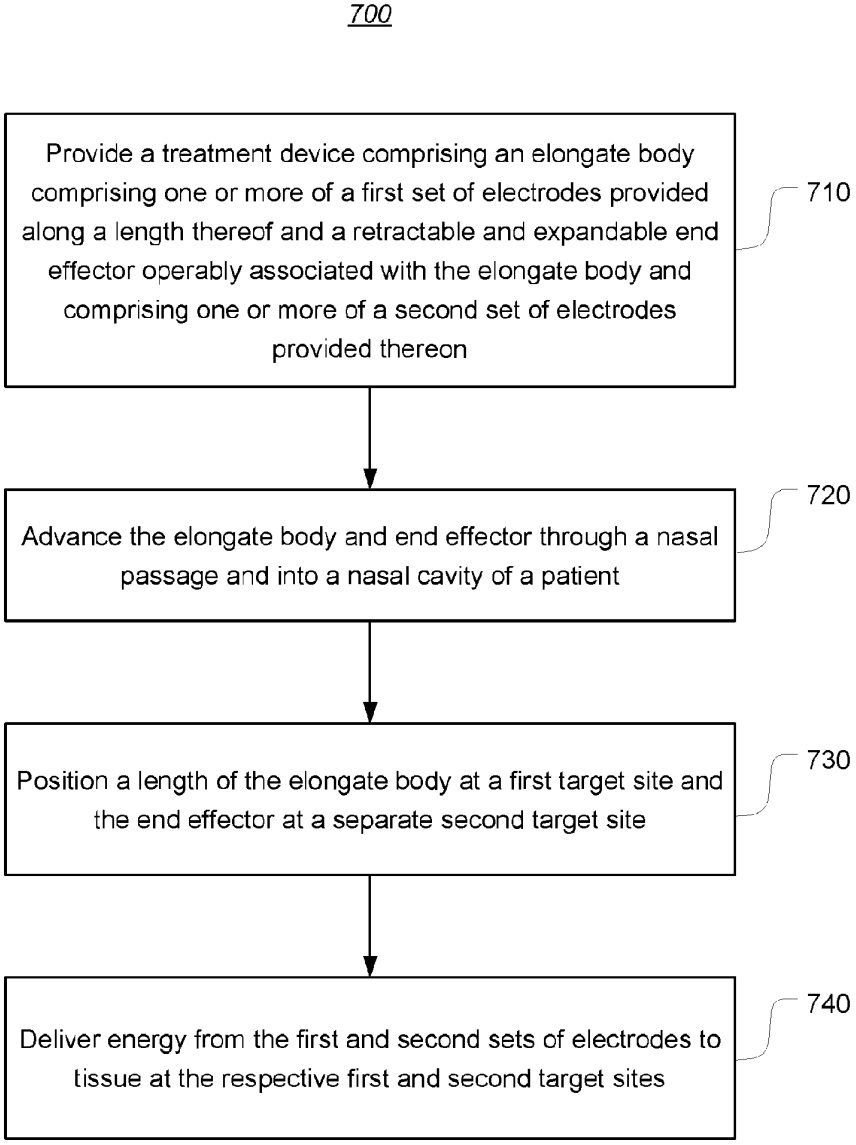

700
Provide a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon
710
Advance the elongate body and end effector through a nasal passage and into a nasal cavity of a patient
720
Position a length of the elongate body at a first target site and the end effector at a separate second target site
730
Deliver energy from the first and second sets of electrodes to tissue at the respective first and second target sites
740

FIG. 16

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000234

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/02 A61B18/08 A61B18/14
ADD. A61B18/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, COMPENDEX, INSPEC, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016/331459 A1 (TOWNLEY DAVID [IE] ET AL) 17 November 2016 (2016-11-17) cited in the application	1-8
Y	paragraphs [0002], [0058], [0066], [0102]; figures 1-5,10	9,10
Y	US 2017/151014 A1 (PERFLER ENRICO [IT]) 1 June 2017 (2017-06-01) paragraphs [0101] - [0104]; figures 11,12	9,10
A	US 2018/125560 A1 (SAADAT VAHID [US] ET AL) 10 May 2018 (2018-05-10) cited in the application the whole document	1-10

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2021	06/08/2021

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Aronsson, Fredrik

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000234

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 11-20
because they relate to subject matter not required to be searched by this Authority, namely:

The subject-matter of claims 11-20 refers to a surgical and therapeutic treatment.According to the PCT neither search (Rule 39.1(iv) PCT) nor examination (Rule 67.1(iv) PCT) is required for such subject-matter.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Aerin Exhibit 1009, Page 770 of 2072
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000234

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2016331459 A1	17-11-2016	AU 2016262085 A1	04-01-2018
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		EP 3471638 A1	24-04-2019
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		US 2018125560 A1	10-05-2018
		WO 2017218854 A1	21-12-2017

Aerin Exhibit 1009, Page 771 of 2072
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 October 2021 (14.10.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/205231 A1

(51) International Patent Classification:
A61B 18/12 (2006.01) *A61B 18/14* (2006.01)
A61B 18/00 (2006.01)

(21) International Application Number:
PCT/IB2021/000243

(22) International Filing Date:
08 April 2021 (08.04.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/007,639 09 April 2020 (09.04.2020) US

(71) Applicant: **NEURENT MEDICAL LIMITED** [IE/IE]; No. 1 Oran Point, Main Street, Oranmore, Galway (IE).

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(54) **Title:** SYSTEMS AND METHODS FOR IDENTIFYING AND CHARACTERIZING TISSUE AND PROVIDING TARGETED TREATMENT THEREOF

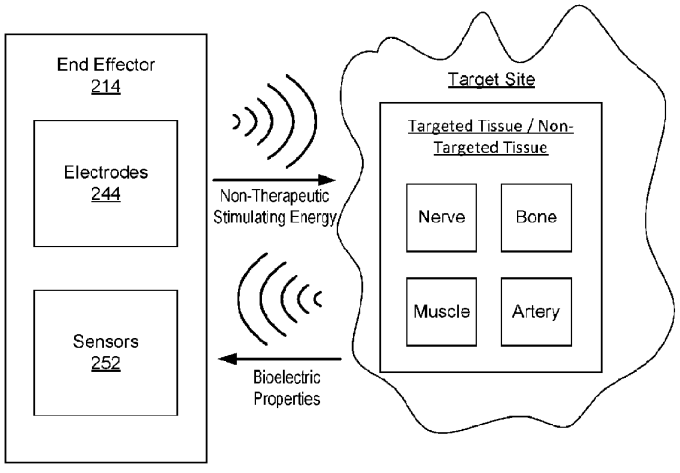


FIG. 9A

(57) **Abstract:** The invention generally relates to systems and methods for providing detection, identification, and precision targeting of specific tissue of interest to undergo a therapeutic treatment while minimizing or avoiding collateral damage to surrounding or adjacent non- targeted tissue.

[Continued on next page]

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SYSTEMS AND METHODS FOR IDENTIFYING AND CHARACTERIZING TISSUE AND PROVIDING TARGETED TREATMENT THEREOF

Cross-reference to Related Applications

This application claims the benefit of, and priority to, U.S. Provisional Patent Application No. 63/007,639, filed April 9, 2020, the contents of which are incorporated by reference.

Field of the Invention

The invention generally relates to systems and methods for providing detection, identification, and precision targeting of specific tissue(s) of interest to undergo a therapeutic treatment while minimizing or avoiding collateral damage to surrounding or adjacent non-targeted tissue.

Background

Certain surgical procedures, such as ablation therapy, require a surgeon to apply precise treatment to the intended target site (i.e., tissue intended to receive treatment) at appropriate levels so as to avoid collateral damage to surrounding tissue, which can lead to further complications and even death. For example, certain procedures require increased precision due to the nature tissue to be treated and the location of such tissue in relation to any nearby or underlying tissue that may be highly sensitive and/or is critical to keep intact and free of unintended damage (i.e., blood vessels, nerves, etc.).

For example, many neuromodulation procedures require such precision. Neuromodulation refers to the alteration, or modulation, of nerve activity by delivering electrical (or sometimes pharmaceutical) agents directly to a target area. The delivery of electrical stimulation can result in partial or complete incapacitation, or other effective disruption, of neural activity. Therapeutic neuromodulation, for example, can include partially or completely inhibiting, reducing, and/or blocking neural communication along neural fibers for the treatment of certain conditions and disorders, specifically for pain relief and/or restoration of function. Some conditions and disorders that may be treated via neuromodulation include, but are not limited to, epilepsy, migraine headaches, spinal cord injuries, Parkinson's disease, and urinary incontinence, to name a few. Neuromodulation can also be used to treat certain conditions

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associated with the nose, such as rhinosinusitis, including, but not limited to, allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, recurrent rhinitis, chronic sinusitis, acute sinusitis, recurrent sinusitis, and medical resistant rhinitis and/or sinusitis, in addition to combinations of one or more of the preceding conditions.

Neuromodulation treatment procedures may generally involve the application of electrodes to the brain, the spinal cord, or peripheral nerves for subsequent treatment of conditions or disorders associated therewith. The electrodes are coupled, via an extension cable, to a pulse generator and power source, which generates the necessary electrical stimulation. An electrical current passes from the generator to the nerve, and can either inhibit pain signals or stimulate neural impulses where they were previously absent. Importantly, electrodes must be precisely placed and the level of electrical stimulation must be controlled so as to avoid or minimize creating collateral damage to surrounding or adjacent non-neural structures, such as bone and blood vessels, as well as non-targeted neural tissue.

Peripheral nerve stimulation is a commonly used approach to treat peripheral neurological conditions and conditions, including chronic pain. In order to establish accurate placement of electrodes and level of electrical stimulation to the targeted peripheral nerve, peripheral nerve stimulation treatment typically requires an initial testing or trial period. For example, a small electrical device (a wire-like electrode) is surgically implanted and placed next to one of the peripheral nerves. The electrode delivers rapid electrical pulses during the initial testing period (trial) to determine whether the electrical pulses result in the desired effect. Once the desired effect is established (via repositioning and/or adjusting of electrical stimulation levels) a more permanent electrode may be implanted into a patient's body. Accordingly, a drawback to current neuromodulation procedures, notably neuromodulation of peripheral nerves, is that such procedures cannot precisely target neural tissue, thereby presenting risk of causing significant collateral damage to surrounding non-neural tissue (such as blood vessels), and/or other non-targeted neural tissue.

Another exemplary procedure requiring precision includes interventional cardiac electrophysiology (EP) procedures, for example. In such a procedure, it is often necessary for the surgeon to determine the condition of cardiac tissue at a target ablation site in or near the heart. During some EP procedures, the surgeon may deliver a mapping catheter through a main vein or artery into an interior region of the heart to be treated. Using the mapping catheter, the

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surgeon may then determine the source of a cardiac rhythm disturbance or abnormality by placing a number of mapping elements carried by the catheter into contact with the adjacent cardiac tissue and then operating the catheter to generate an electrophysiology map of the interior region of the heart based on sensed electrical cardiac signals. Once a map of the heart is generated, the surgeon may then advance an ablation catheter into the heart, and position an ablation electrode carried by the catheter tip near the targeted cardiac tissue to ablate the tissue and form a lesion, thereby treating the cardiac rhythm disturbance or abnormality. In some techniques, the ablation catheter itself may include a number of mapping electrodes, allowing the same device to be used for both mapping and ablation.

Various ultrasound-based imaging catheters and probes have been developed for visualizing body tissue in applications such as interventional cardiology, interventional radiology, and electrophysiology. For interventional cardiac electrophysiology procedures, for example, ultrasound imaging devices have been developed that permit the visualization of anatomical structures of the heart directly and in real-time. While such imaging-based products allow some form of visualization of the targeted tissue, such procedures still lack the ability to precisely target and apply treatment to the tissue of interest while reducing or eliminating the risk of further treatment non-targeted, adjacent tissue.

Summary

The invention recognizes that knowing certain bioelectric properties of tissue, both active and passive, specifically interfacial polarization, dielectric dispersion, and dielectric relaxation phenomena/behavior of tissue, at a given target site prior to electrotherapeutic treatment (i.e., neuromodulation, ablation, etc.) provides an ability to more precisely target a specific tissue of interest (i.e., targeted tissue) and minimize and/or prevent collateral damage to adjacent or surrounding non-targeted tissue.

For example, certain target sites intended to undergo treatment may consist of more than one type of tissue (i.e., nerves, muscles, bone, blood vessels, etc.). In particular, a tissue of interest (i.e., the specific tissue to undergo treatment) may be adjacent to one or more tissues that are not of interest (i.e., tissue that is not intended to undergo treatment). In one scenario, a surgeon may wish to provide electrotherapeutic stimulation to a nerve tissue, while avoiding providing any such stimulation to an adjacent blood vessel, for example, as unintended collateral

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damage may result in damage to the blood vessel and cause further complications. In such a scenario, the specific type of targeted tissue may generally dictate the level of electrical stimulation required to elicit a desired effect. Furthermore, physical properties of the targeted tissue, including the specific location and depth of the targeted tissue, in relation to the non-targeted tissue, further impacts the level of electrical stimulation necessary to result in effective therapeutic treatment.

The invention provides systems and methods with an ability to characterize, prior to an electrotherapeutic treatment, tissue at a target site by sensing bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present and further determining a interfacial polarization, or dielectric dispersion and relaxation phenomena/behavior pattern for the identified types of tissue. For example, different tissue types include different physiological and histological characteristics (e.g., cell components, proteins, etc.). As a result of the different characteristics, different tissue types have different associated bioelectrical properties and thus exhibit different associated electrical behavior in response to application of energy and frequencies applied thereto. One change in such electrical behavior is referred to as relaxation phenomena. The relaxation phenomena of a given tissue occurs at a particular electrical frequency in which the membranes of cells of the given tissue become permeable to thereby allow electrical stimulation current (at the particular frequency) to flow through the membrane to thereby elicit a desired effect upon the tissue. When a tissue is not exhibiting the relaxation phenomena (i.e., when electrical stimulation current is tuned to a different frequency that does not correlate to the relaxation phenomena), the membranes of cells of the given tissue may or may not be permeable to that specific electrical stimulation current and thus do not elicit an effect. The systems and methods are further configured to tune energy output (i.e., delivery of electrotherapeutic stimulation) based on the these relaxation patterns of a tissue of interest such that the energy delivered is at a specific frequency configured to target the tissue of interest while avoiding the non-targeted tissue (i.e., the energy is tuned to a frequency level associated with the dielectric relaxation phenomena of the targeted tissue only).

Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types. In particular, the systems and methods are able to, prior to treatment, characterize and identify tissue types and further identify

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specific levels of energy (i.e., specific target frequencies) to be delivered so as to cause only those intended, targeted tissues to exhibit dielectric relaxation phenomena and thus receive the energy for treatment, while non-targeted tissues remain intact and avoid collateral damage.

One aspect of the present invention provides a system for treating a condition. The system includes a device comprising an end effector including a plurality of electrodes and a controller operably associated with the device. The controller is configured to receive data from the device associated with bioelectric properties of one or more tissues at the target site and process the data to identify a type of each of the one or more tissues at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types. The controller is further configured to determine an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, complex, real and imaginary dielectric permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, induced electromotive force, and combinations thereof. The dielectric properties may include, for example, at least a complex dielectric permittivity. It should be noted that, in some embodiments, a subset of the plurality of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site.

The processing of the data may include, but is not limited to, comparing the data received from the device with electric signatures, as well as data with different dielectric models (e.g., Havriliak–Negami (HN) relaxation) to determine the dielectric parameters associated with a plurality of known tissue types. For example, the controller may be configured to compare the tissue data (i.e., data received from the treatment device associated with tissue at the target site) with profiles of known tissue types stored in a database, for example. Each profile may generally include electric signature data that generally characterizes a known tissue type, including physiological, histological, and bioelectric properties of a known tissue type, including

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dielectric relaxation phenomena/behavior of the tissue and the specific frequency value at which the tissue exhibits the dielectric relaxation phenomena/behavior.

In some embodiments, the ablation energy is tuned to a target frequency associated with a dielectric relaxation pattern of the targeted tissue. The target frequency comprises a frequency at which the targeted tissue exhibits relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior. In particular, delivery of the ablation energy, tuned to the target frequency, penetrates a membrane of one or more cells associated only with the targeted tissue.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient. Additionally, or alternatively, the resulting local hypoxia may cause neuronal degeneration.

Another aspect of the invention provides a method for treating a condition. The method includes providing a device comprising an end effector including a plurality of electrodes and a controller operably associated with the device. The method further includes positioning the end effector at a target site associated with a patient and receiving, via the controller, data from the device associated with bioelectric properties of one or more tissues at the target site. The method

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further includes processing, via the controller, the data to identify a type of each of the one or more tissues at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types. The method further includes determining, via the controller, an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, complex, real and imaginary dielectric permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, induced electromotive force, and combinations thereof. The dielectric properties may include, for example, at least a dielectric modulus or a complex dielectric permittivity. It should be noted that, in some embodiments, a subset of the plurality of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site.

The processing of the data may include, but is not limited to, comparing the data received from the device with electric signature, and training of the data with different dielectric models (e.g., Havriliak–Negami (HN) relaxation) to determine the dielectric parameters associated with a plurality of known tissue types. For example, the controller may be configured to compare the tissue data (i.e., data received from the treatment device associated with tissue at the target site) with profiles of known tissue types stored in a database, for example. Each profile may generally include electric signature data that generally characterizes a known tissue type, including physiological, histological, and bioelectric properties of a known tissue type, including dielectric relaxation phenomena/behavior of the tissue and the specific frequency value at which the tissue exhibits the dielectric relaxation phenomena/behavior.

In some embodiments, the ablation energy is tuned to a target frequency associated with a dielectric relaxation pattern of the targeted tissue. The target frequency comprises a frequency at which the targeted tissue exhibits relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior. In particular, delivery of the ablation energy,

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tuned to the target frequency, penetrates a membrane of one or more cells associated only with the targeted tissue.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient. Additionally, or alternatively, the resulting local hypoxia may cause neuronal degeneration.

Brief Description of the Drawings

FIGS. 1A and 1B are diagrammatic illustrations of a system for treating a condition of a patient using a handheld device according to some embodiments of the present disclosure.

FIG. 2 is a diagrammatic illustration of the console coupled to the handheld device consistent with the present disclosure, further illustrating one embodiment of an end effector of the handheld device for delivering energy to tissue at one or more target sites.

FIG. 3 is a side view of one embodiment of a handheld device for providing therapeutic treatment consistent with the present disclosure.

FIG. 4 is an enlarged, perspective view of one embodiment of an end effector consistent with the present disclosure.

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FIGS. 5A-5F are various views of the multi-segment end effector consistent with the present disclosure.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment and second (distal) segment. FIG. 5B is an exploded, perspective view of the multi-segment end effector. FIG. 5C is an enlarged, top view of the multi-segment end effector. FIG. 5D is an enlarged, side view of the multi-segment end effector. FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment of the multi-segment end effector. FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment of the multi-segment end effector.

FIG. 6 is a perspective view, partly in section, of a portion of a support element illustrating an exposed conductive wire serving as an energy delivery element or electrode element.

FIG. 7 is a cross-sectional view of a portion of the shaft of the handheld device taken along lines 7-7 of FIG. 3.

FIG. 8A is a side view of the handle of the handheld device.

FIG. 8B is a side view of the handle illustrating internal components enclosed within.

FIG. 9A is a block diagram illustrating delivery of non-therapeutic energy from electrodes of the end effector at a frequency/waveform for sensing one or more properties associated with one or more tissues at a target site in response to the non-therapeutic energy.

FIG. 9B is a block diagram illustrating communication of sensor data from the handheld device to the controller and subsequent tuning, via the controller, of energy output based on the sensor data for precision targeting of tissue of interest and to be treated.

FIG. 9C is a block diagram illustrating delivery of energy to the target site tuned to a specific frequency to elicit dielectric relaxation phenomena/behavior in the targeted tissue (based on the ablation pattern output from the controller).

FIG. 10 is a block diagram illustrating delivery of energy to the target site, and specifically illustrating flow of current through membranes of cells of the targeted tissue (which is exhibit dielectric relaxation phenomena/behavior) and flow of current around membranes of cells of non-targeted tissue (which is not exhibiting dielectric relaxation phenomena/behavior) as a result of the energy being tuned to a target frequency.

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FIG. 11 is a flow diagram illustrating one embodiment of a method for treating a condition.

FIG. 12 is a schematic of an exemplary probe/electrode setup for performing some of the methods described herein, most notably for characterizing tissue at a target site by sensing bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present and further determining a dielectric relaxation phenomena/behavior pattern for the identified types of tissue. FIG. 12A is a schematic diagram of one embodiment of a 3-probe/electrode system for sensing bioelectric properties of tissue for subsequent characterization of tissue at a target site, wherein such characterization includes identifying specific types of tissue present and further determining a dielectric relaxation phenomena/behavior pattern for the identified types of tissue.

FIGS. 13A and 13B are graphs illustrating dielectric properties of two tissue types (spinal cord and muscle tissues), including the plotting of loss tangent value relative to frequency (FIG. 13A) and the plotting of an imaginary electric modulus relative to frequency (FIG. 13B).

FIGS. 14A-14H are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity (based on the Havriliak–Negami (HN) relaxation phenomena model) relative to frequency for the two tissue types of FIGS. 13A and 13B (spinal cord and muscle tissues).

FIGS. 14A and 14B illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for upper spinal cord tissue.

FIGS. 14C and 14D illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for lower spinal cord tissue.

FIGS. 14E and 14F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for lower back muscle tissue.

FIGS. 14G and 14H are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for upper back muscle tissue.

FIGS. 15A and 15B are graphs illustrating dielectric properties of different portions of a tissue (turbinate tissue), including the plotting of loss tangent value relative to frequency (FIG. 15A) and the plotting of an imaginary electric modulus relative to frequency (FIG. 15B).

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FIGS. 16A-16F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity (based on the HN relaxation phenomena model) relative to frequency for the different portions of the turbinate tissue of FIGS. 15A and 15B.

FIGS. 16A and 16B illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for the end of a turbinate tissue.

FIGS. 16C and 16D illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for the center of the turbinate tissue.

FIGS. 16E and 16F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for portions of the turbinate tissue near blood vessels.

Detailed Description

The invention recognizes that knowing certain bioelectric properties of tissue, both active and passive, specifically interfacial polarization, dielectric dispersion, and dielectric relaxation phenomena/behavior of tissue, at a given target site prior to electrotherapeutic treatment (i.e., neuromodulation, ablation, etc.) provides an ability to more precisely target a specific tissue of interest (i.e., targeted tissue) and minimize and/or prevent collateral damage to adjacent or surrounding non-targeted tissue.

For example, certain target sites intended to undergo treatment may consist of more than one type of tissue (i.e., nerves, muscles, bone, blood vessels, etc.). In particular, a tissue of interest (i.e., the specific tissue to undergo treatment) may be adjacent to one or more tissues that are not of interest (i.e., tissue that is not intended to undergo treatment). In one scenario, a surgeon may wish to provide electrotherapeutic stimulation to a nerve tissue, while avoiding providing any such stimulation to an adjacent blood vessel, for example, as unintended collateral damage may result in damage to the blood vessel and cause further complications. In such a scenario, the specific type of targeted tissue may generally dictate the level of electrical stimulation required to elicit a desired effect. Furthermore, physical properties of the targeted tissue, including the specific location and depth of the targeted tissue, in relation to the non-targeted tissue, further impacts the level of electrical stimulation necessary to result in effective therapeutic treatment.

Neuromodulation, for example, is technology that acts directly upon nerves. It is the

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alteration, or modulation, of nerve activity by delivering electrical or pharmaceutical agents directly to a target area. Neuromodulation devices and treatments have been shown to be highly effective at treating a variety of conditions and disorders. The most common indication for neuromodulation is treatment of chronic pain. However, the number of neuromodulation applications over the years has increased to include more than just the treatment of chronic pain, such as deep brain stimulation (DBS) treatment for Parkinson's disease, sacral nerve stimulation for pelvic disorders and incontinence, and spinal cord stimulation for ischemic disorders (angina, peripheral vascular disease).

Neuromodulation is particularly useful in the treatment of peripheral neurological disorders. There are currently over 100 kinds of peripheral nerve disorders, which can affect one nerve or many nerves. Some are the result of other diseases, like diabetic nerve problems. Others, like Guillain-Barre syndrome, happen after a virus infection. Still others are from nerve compression, like carpal tunnel syndrome or thoracic outlet syndrome. In some cases, like complex regional pain syndrome and brachial plexus injuries, the problem begins after an injury. However, some people are born with peripheral neurological disorders.

Peripheral nerve stimulation has become established for very specific clinical indications, including certain complex regional pain syndromes, pain due to peripheral nerve injuries, and the like. Some of the common applications of peripheral nerve stimulation include treatment of back pain, occipital nerve stimulation for treatment of migraine headaches, and pudendal nerve stimulation that is being investigated for use in urinary bladder incontinence.

The invention provides systems and methods with an ability to characterize, prior to an electrotherapeutic treatment such as neuromodulation, tissue at a target site by sensing bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present and further determining a dielectric relaxation phenomena/behavior pattern for the identified types of tissue. For example, different tissue types include different physiological and histological characteristics (e.g., cell components, extracellular proteins, etc.). As a result of the different characteristics, different tissue types have different associated electrical and electrochemical properties and thus exhibit different associated behavior in response to application of energy and/or frequency applied thereto. The electrical behavior of tissue type (capacitive to resistive or vice versa) alters at specific frequencies due to the relaxation phenomena. The interfacial polarization , dielectric dispersion and relaxation phenomenon of a

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given tissue occurs at a particular electrical frequency in which the membranes of cells of the given tissue become permeable to thereby allow electrical stimulation current (at the particular frequency) to flow through the membrane to thereby elicit a desired effect upon the tissue.

For example, the alternating current (AC) energy transfer through the tissue type takes place either through capacitive or resistive means and is highly dependent on the frequency of an energy used. For example, if the transfer of energy at specific frequency in tissue type taking place though relatively higher resistive means, these phenomena will slowly alter upon changing frequency and, at certain frequency, the conduction though capacitive behavior becomes active. These phenomena are generally represented Maxwell-Wagner-Sillar (MWS) relaxation. Similarly, the permeability of current types (direct current or alternating current) depends on the specific frequency and varies with the cell types, constituency and morphology. The dielectric permittivity and dielectric relaxation frequency heighten when a tissue is stimulated at specific frequency. Below the specific relaxation frequency such as dielectric relaxation, the tissue is highly permeable to the alternating current. However, at the region of relaxation frequency, the heating effects become dominant. Hence, when a tissue is not exhibiting the dielectric relaxation phenomena (i.e., when electrical stimulation current is tuned to a different frequency (i.e., below and above the relaxation frequency) that does not correlate to the dielectric relaxation phenomena), the membranes of cells of the given tissue are not permeable to that specific electrical stimulation current and thus do not elicit an effect. The systems and methods are further configured to tune energy output (i.e., delivery of electrotherapeutic stimulation) based on the dielectric relaxation pattern of a tissue of interest such that the energy delivered is at a specific frequency configured to target the tissue of interest while avoiding the non-targeted tissue (i.e., the energy is tuned to a frequency level associated with the dielectric relaxation phenomena of the targeted tissue only).

Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types. In particular, the systems and methods are able to, prior to treatment, characterize and identify tissue types and further identify specific levels of energy (i.e., specific target frequencies) to be delivered so as to cause only those intended, targeted tissues to exhibit dielectric relaxation phenomena and thus receive the energy for treatment, while non-targeted tissues remain intact and avoid collateral damage.

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It should be noted that, although many of the embodiments are described with respect to devices, systems, and methods for therapeutically modulating nerves associated with the peripheral nervous system (PNS) and thus the treatment of peripheral neurological conditions or disorders, other applications and other embodiments in addition to those described herein are within the scope of the present disclosure. For example, at least some embodiments of the present disclosure may be useful for the treatment of other disorders, such as the treatment of disorders associated with the central nervous system.

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic system 100 for treating a condition of a patient using a handheld device 102 according to some embodiments of the present disclosure. The system 100 generally includes a device 102 and a console 104 to which the device 102 is to be connected. FIG. 2 is a diagrammatic illustrations of the console 104 coupled to the handheld device 102 illustrating an exemplary embodiment of an end effector 114 for delivering energy to tissue at the one or more target sites of a patient for the treatment of a neurological disorder. As illustrated, the device 102 is a handheld device, which includes end effector 114, a shaft 116 operably associated with the end effector 114, and a handle 118 operably associated with the shaft 116. The end effector 114 may be collapsible/retractable and expandable, thereby allowing for the end effector 114 to be minimally invasive (i.e., in a collapsed or retracted state) upon delivery to one or more target sites within a patient and then expanded once positioned at the target site. It should be noted that the terms "end effector" and "therapeutic assembly" may be used interchangeably throughout this disclosure.

For example, a surgeon or other medical professional performing a procedure can utilize the handle 118 to manipulate and advance the shaft 116 to a desired target site, wherein the shaft 116 is configured to locate at least a distal portion thereof intraluminally at a treatment or target site within a portion of the patient associated with tissue to undergo electrotherapeutic stimulation for subsequent treatment of an associated condition or disorder. In the event that the tissue to be treated is a nerve, such that electrotherapeutic stimulation thereof results in treatment of an associated neurological condition, the target site may generally be associated with peripheral nerve fibers. The target site may be a region, volume, or area in which the target nerves are located and may differ in size and shape depending upon the anatomy of the patient. Once positioned, the end effector 114 may be deployed and subsequently deliver energy to the one or more target sites. The energy delivered may be non-therapeutic stimulating energy at a

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frequency for locating neural tissue and further sensing one or more properties of the neural tissue. For example, the end effector 114 may include an electrode array, which includes at least a subset of electrodes configured to sense the presence of neural tissue at a respective position of each of the electrodes, as well as morphology of the neural tissue, wherein such data may be used for determining, via the console 104, the type of neural tissue as well as a dielectric relaxation phenomena/behavior pattern for the identified neural tissue.

Based on the identification of the neural tissue type and a dielectric relaxation phenomena/behavior pattern of the neural tissue, the console 104 is configured to tune energy output (i.e., delivery of electrotherapeutic stimulation) based on the dielectric relaxation pattern of the targeted tissue such that the energy delivered from the end effector 114 upon the target site is at a specific frequency so as to therapeutically modulate the neural tissue (i.e., the energy is tuned to a frequency level associated with the dielectric relaxation phenomena of the targeted tissue only) and minimize and/or prevent damage to non-target neural tissue and/or non-target anatomical structures at the target site, such as blood vessels and/or bone. Accordingly, the end effector 114 is able to therapeutically modulating nerves of interest, particularly nerves associated with a peripheral neurological conditional or disorder so as to treat such condition or disorder, while minimizing and/or preventing collateral damage.

For example, the end effector 114 may include at least one energy delivery element, such as an electrode, configured to delivery energy to the target tissue which may be used for sensing presence and/or specific properties of tissue (such tissue including, but not limited to, muscle, nerves, blood vessels, bones, etc.) for therapeutically modulating tissues of interest, such as neural tissue. For example, one or more electrodes may be provided by one or more portions of the end effector 114, wherein the electrodes may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the end effector 114 may include other energy delivery elements configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power.

In some embodiments, the end effector 114 may include one or more sensors (not shown), such as one or more temperature sensors (e.g., thermocouples, thermistors, etc.),

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impedance sensors, and/or other sensors. The sensors and/or the electrodes may be connected to one or more wires extending through the shaft 116 and configured to transmit signals to and from the sensors and/or convey energy to the electrodes.

As shown, the device 102 is operatively coupled to the console 104 via a wired connection, such as cable 120. It should be noted, however, that the device 102 and console 104 may be operatively coupled to one another via a wireless connection. The console 104 is configured to provide various functions for the device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the device 102. For example, when the device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 may include an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-

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transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via evaluation/feedback algorithms 110. For example, the evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the temperature of the tissue at the treatment site, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to monitor temperature at the treatment site during therapy and automatically shut off the energy delivery when the temperature reaches a predetermined maximum (e.g., when applying RF energy) or predetermined minimum (e.g., when applying cryotherapy). In other embodiments, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a graphical user interface (GUI) 112 provided via a display on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104, such as a tablet or monitor. The GUI 112 may generally provide operational instructions for the procedure, such as indicating when the device 102 is primed and ready to perform the treatment, and further providing status of therapy during the procedure, including indicating when the treatment is complete.

For example, as previously described, the end effector 114 and/or other portions of the system 100 can be configured to detect various parameters of a tissue of interest at the target site to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate nerves and/or other structures, and allow for neural mapping. For example, the end effector 114 may be configured to detect impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural tissue or fibers in the target region, as described in greater detail herein.

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As shown in FIG. 1A, the console 104 further includes a monitoring system 108 configured to receive data from the end effector 114 (i.e., detected electrical and/or thermal measurements of tissue at the target site), specifically sensed by appropriate sensors (e.g., temperature sensors and/or impedance sensors, or the like), and process this information to identify the presence of nerves, the location of nerves, neural activity at *the* target site, and/or other properties of the neural tissue, such a physiological properties (e.g., depth), bioelectric properties, and thermal properties. The nerve monitoring system 108 can be operably coupled to the electrodes and/or other features of the end effector 114 via signal wires (e.g., copper wires) that extend through the cable 120 and through the length of the shaft 116. In other embodiments, the end effector 114 can be communicatively coupled to the nerve monitoring system 108 using other suitable communication means.

The nerve monitoring system 108 can determine neural locations and activity before therapeutic neuromodulation to determine precise treatment regions corresponding to the positions of the desired nerves. The nerve monitoring system 108 can further be used during treatment to determine the effect of the therapeutic neuromodulation, and/or after treatment to evaluate whether the therapeutic neuromodulation treated the target nerves to a desired degree. This information can be used to make various determinations related to the nerves proximate to the target site, such as whether the target site is suitable for neuromodulation. In addition, the nerve monitoring system 108 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site. For example, the nerve monitoring system 108 can further determine electroneurogram (ENG) signals based on recordings of electrical activity of neurons taken by the end effector 114 before and after therapeutic neuromodulation. Statistically meaningful (e.g., measurable or noticeable) decreases in the ENG signal(s) taken after neuromodulation can serve as an indicator that the nerves were sufficiently ablated. Additional features and functions of the nerve monitoring system 108, as well as other functions of the various components of the console 104, including the evaluation/feedback algorithms 110 for providing real-time feedback capabilities for ensuring optimal therapy for a given treatment is administered, are described in at least U.S. Publication No. 2016/0331459 and U.S. Publication No. 2018/0133460, the contents of each of which are incorporated by reference herein in their

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entireties.

The device 102 provides access to target sites associated with peripheral nerves for the subsequent neuromodulation of such nerves and treatment of a corresponding peripheral neurological condition or disorder. The peripheral nervous system is one of two components that make up the nervous system of bilateral animals, with the other part being the central nervous system (CNS). The PNS consists of the nerves and ganglia outside the brain and spinal cord. The main function of the PNS is to connect the CNS to the limbs and organs, essentially serving as a relay between the brain and spinal cord and the rest of the body. The peripheral nervous system is divided into the somatic nervous system and the autonomic nervous system. In the somatic nervous system, the cranial nerves are part of the PNS with the exception of the optic nerve (cranial nerve II), along with the retina. The second cranial nerve is not a true peripheral nerve but a tract of the diencephalon. Cranial nerve ganglia originated in the CNS. However, the remaining ten cranial nerve axons extend beyond the brain and are therefore considered part of the PNS. The autonomic nervous system exerts involuntary control over smooth muscle and glands. The connection between CNS and organs allows the system to be in two different functional states: sympathetic and parasympathetic. Accordingly, the devices, systems, and methods of the present invention are useful in detecting, identifying, and precision targeting nerves associated with the peripheral nervous system for treatment of corresponding peripheral neurological conditions or disorders.

The peripheral neurological conditions or disorders may include, but are not limited to, chronic pain, movement disorders, epilepsy, psychiatric disorders, cardiovascular disorders, gastrointestinal disorders, genitourinary disorders, to name a few. For example, chronic pain may include headaches, complex regional pain syndrome, neuropathy, peripheral neuralgia, ischemic pain, failed back surgery syndrome, and trigeminal neuralgia. The movement disorders may include spasticity, Parkinson's disease, tremor, dystonia, Tourette syndrome, camptocormia, hemifacial spasm, and Meige syndrome. The psychiatric disorders may include depression, obsessive compulsive disorder, drug addiction, and anorexia/eating disorders. The functional restoration may include restoration of certain functions post traumatic brain injury, hearing impairment, and blindness. The cardiovascular disorders may include angina, heart failure, hypertension, peripheral vascular disorders, and stroke. The gastrointestinal disorders may

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include dysmotility and obesity. The genitourinary disorders may include painful bladder syndrome, interstitial cystitis, and voiding dysfunction.

For example, the system 100 may be used for the treatment of a cardiovascular disorder, such as arrhythmias or heart rhythm disorders, including, but not limited to, atrial fibrillation (AF or A-fib). Atrial fibrillation is an irregular and often rapid heart rate that can increase one's risk of stroke, heart failure, and other heart-related complications. Atrial fibrillation occurs when regions of cardiac tissue abnormally conduct electric signals to adjacent tissue, thereby disrupting the normal cardiac cycle and causing asynchronous rhythm. Atrial fibrillation symptoms often include heart palpitations, shortness of breath, and weakness. While episodes of atrial fibrillation can come and go, a person may develop atrial fibrillation that doesn't go away and thus will require treatment. Although atrial fibrillation itself usually isn't life-threatening, it is a serious medical condition that sometimes requires emergency treatment, as it may lead to complications. For example, atrial fibrillation is associated with an increased risk of heart failure, dementia, and stroke.

The normal electrical conduction system of the heart allows the impulse that is generated by the sinoatrial node (SA node) of the heart to be propagated to and stimulate the myocardium (muscular layer of the heart). When the myocardium is stimulated, it contracts. It is the ordered stimulation of the myocardium that allows efficient contraction of the heart, thereby allowing blood to be pumped to the body. In AF, the normal regular electrical impulses generated by the sinoatrial node in the right atrium of the heart are overwhelmed by disorganized electrical impulses usually originating in the roots of the pulmonary veins. This leads to irregular conduction of ventricular impulses that generate the heartbeat. In particular, during AF, the heart's two upper chambers (the atria) beat chaotically and irregularly, out of coordination with the two lower chambers (the ventricles) of the heart.

During atrial fibrillation, the regular impulses produced by the sinus node for a normal heartbeat are overwhelmed by rapid electrical discharges produced in the atria and adjacent parts of the pulmonary veins. Sources of these disturbances are either automatic foci, often localized at one of the pulmonary veins, or a small number of localized sources in the form of either a re-entrant leading circle, or electrical spiral waves (rotors). These localized sources may be found in the left atrium near the pulmonary veins or in a variety of other locations through both the left or right atrium. There are three fundamental components that favor the establishment of a

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leading circle or a rotor: 1) slow conduction velocity of cardiac action potential; 2) short refractory period; and 3) small wavelength. Wavelength is the product of velocity and refractory period. If the action potential has fast conduction, with a long refractory period and/or conduction pathway shorter than the wavelength, an AF focus would not be established. In multiple wavelet theory, a wavefront will break into smaller daughter wavelets when encountering an obstacle, through a process called vortex shedding; but under proper conditions, such wavelets can reform and spin around a center, forming an AF focus.

The system 100 provides for the treatment of AF, in which the device 102 may provide access to and provide treatment of one or more target sites associated with nerves that correspond to, or are otherwise associated with, treating AF. For example, the device 102, in conjunction with the console 104, may detect, identify, and precision target cardiac tissue and subsequently deliver energy at a level or frequency sufficient to therapeutically modulate nerves associated with such cardiac tissue. The therapeutic modulation of such nerves is sufficient to disrupt the origin of the signals causing the AF and/or disrupt the conducting pathway for such signals.

Similar to the conduction system of the heart, a neural network exists which surrounds the heart and plays an important role in formation of the substrate of AF and when a trigger is originated, usually from pulmonary vein sleeves, AF occurs. This neural network includes ganglionated plexi (GP) located adjacent to pulmonary vein ostia which are under control of higher centers in normal people. For example, the heart is richly innervated by the autonomic nerves. The ganglion cells of the autonomic nerves are located either outside the heart (extrinsic) or inside the heart (intrinsic). Both extrinsic and intrinsic nervous systems are important for cardiac function and arrhythmogenesis. The vagal nerves include axons that come from various nuclei in the medulla. The extrinsic sympathetic nerves come from the paravertebral ganglia, including the superior cervical ganglion, middle cervical ganglion, the cervicothoracic (stellate) ganglion and the thoracic ganglia. The intrinsic cardiac nerves are found mostly in the atria, and are intimately involved in atrial arrhythmogenesis cardiovascular disorder, such as arrhythmias or heart rhythm disorders, including, but not limited to, atrial fibrillation. When GP become hyperactive owing to loss of inhibition from higher centers (e.g., in elderly), AF can occur.

The system 100 can be used to control hyperactive GP either by stimulating higher centers and their connections, such as vagus nerve stimulation, or simply by ablating GP.

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Accordingly, the device 102, in conjunction with the console 104, may detect and identify ganglionated plexus (GP) and further determine an energy level sufficient to therapeutically modulate or treat (i.e., ablate) the GP for the treatment of AF (i.e., surgically disrupting the origin of the signals causing the AF and disrupting the conducting pathway for such signals) while minimizing and/or preventing collateral damage to surrounding or adjacent non-neural tissue including bloods vessels and bone and non-targeted neural tissue. It should be noted that other nerves and/or cardiac tissue, or other structures, known to have an impact on or cause AF, may be targeted by the system 100, including, but not limited to, pulmonary veins (e.g., pulmonary vein isolation upon creation of lesions around PV ostia to prevent triggers from reaching atrial substrate).

In addition to treating arrhythmias, the system 100 may also be used for the treatment of other cardiovascular-related conditions, particularly those involving the kidney. The kidneys play a significant role in the progression of CHF, as well as in Chronic Renal Failure (CRF), End-Stage Renal Disease (ESRD), hypertension (pathologically high blood pressure), and other cardio-renal diseases.

The functions of the kidney can be summarized under three broad categories: filtering blood and excreting waste products generated by the body's metabolism; regulating salt, water, electrolyte and acid-base balance; and secreting hormones to maintain vital organ blood flow. Without properly functioning kidneys, a patient will suffer water retention, reduced urine flow and an accumulation of waste toxins in the blood and body. These conditions resulting from reduced renal function or renal failure (kidney failure) are believed to increase the workload of the heart.

For example, in a CHF patient, renal failure will cause the heart to further deteriorate as the water build-up and blood toxins accumulate due to the poorly functioning kidneys and, in turn, cause the heart further harm. CHF is a condition that occurs when the heart becomes damaged and reduces blood flow to the organs of the body. If blood flow decreases sufficiently, kidney function becomes impaired and results in fluid retention, abnormal hormone secretions and increased constriction of blood vessels. These results increase the workload of the heart and further decrease the capacity of the heart to pump blood through the kidney and circulatory system. This reduced capacity further reduces blood flow to the kidney. It is believed that progressively decreasing perfusion of the kidney is a principal non-cardiac cause perpetuating

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the downward spiral of CHF. Moreover, the fluid overload and associated clinical symptoms resulting from these physiologic changes are predominant causes for excessive hospital admissions, reduced quality of life, and overwhelming costs to the health care system due to CHF.

End-stage renal disease is another condition at least partially controlled by renal neural activity. There has been a dramatic increase in patients with ESRD due to diabetic nephropathy, chronic glomerulonephritis and uncontrolled hypertension. Chronic renal failure (CRF) slowly progresses to ESRD. CRF represents a critical period in the evolution of ESRD. The signs and symptoms of CRF are initially minor, but over the course of 2-5 years, become progressive and irreversible. While some progress has been made in combating the progression to, and complications of, ESRD, the clinical benefits of existing interventions remain limited.

Arterial hypertension is a major health problem worldwide. Treatment-resistant hypertension is defined as the failure to achieve target blood pressure despite the concomitant use of maximally tolerated doses of three different antihypertensive medications, including a diuretic. Treatment-resistant hypertension is associated with considerable morbidity and mortality. Patients with treatment-resistant hypertension have markedly increased cardiovascular morbidity and mortality, facing an increase in the risk of myocardial infarction (MI), stroke, and death compared to patients whose hypertension is adequately controlled.

The autonomic nervous system is recognized as an important pathway for control signals that are responsible for the regulation of body functions critical for maintaining vascular fluid balance and blood pressure. The autonomic nervous system conducts information in the form of signals from the body's biologic sensors such as baroreceptors (responding to pressure and volume of blood) and chemoreceptors (responding to chemical composition of blood) to the central nervous system via its sensory fibers. It also conducts command signals from the central nervous system that control the various innervated components of the vascular system via its motor fibers.

It is known from clinical experience and research that an increase in renal sympathetic nerve activity leads to vasoconstriction of blood vessels supplying the kidney, decreased renal blood flow, decreased removal of water and sodium from the body, and increased renin secretion. It is also known that reduction of sympathetic renal nerve activity, e.g., via denervation, may reverse these processes.

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The renal sympathetic nervous system plays a critical influence in the pathophysiology of hypertension. The adventitia of the renal arteries has efferent and afferent sympathetic nerves. Renal sympathetic activation via the efferent nerves initiates a cascade resulting in elevated blood pressure. Efferent sympathetic outflow leads to vasoconstriction with a subsequent reduction in glomerular blood flow, a lowering of the glomerular filtration rate, release of renin by the juxtaglomerular cells, and the subsequent activation of the renin-angiotensin-aldosterone axis leading to increased tubular reabsorption of sodium and water. Decreased glomerular filtration rate also prompts additional systemic sympathetic release of catecholamines. As a consequence, blood pressure increases by a rise in total blood volume and increased peripheral vascular resistance.

The system 100 can be used for the treatment of cardio-renal diseases, including hypertension, by providing renal neuromodulation and/or denervation. For example, the device 102 may be placed at one or more target sites associated with renal nerves other neural fibers that contribute to renal neural function, or other neural features. For example, the device 102, in conjunction with the console 104, may detect, identify, and precision target renal nerve tissue and subsequently deliver energy at a level or frequency sufficient to therapeutically modulate nerves associated with such renal tissue. The therapeutic modulation of such renal nerves and/or renal tissue is sufficient to completely block or denervate the target neural structures and/or disrupt renal nervous activity, while minimizing and/or preventing collateral damage to surrounding or adjacent non-neural tissue including bloods vessels and bone and non-targeted neural tissue.

It should further be noted that the system 100 can be used to determine disease progression. In particular, the present system 100 can obtain measurements at one or more target sites associated with a given disease, disorder, or the like. Such measurements may be based on the active neural parameters (i.e., neuronal firing and active voltage monitoring) and may be used to identify neurons. The active neural parameters (and thus behavior) change with disease progression, thereby allowing the present system to identify such changes and determine a progression of the underlying disease or disorder. Such capabilities are possible based, at least in part, on the fact that the present system 100 is configured to monitor passive electric phenomena (i.e., the present system 100 determines the ohmic conductivity frequency, which remains consistent, while conductivity will be different based on disease or disorder progression).

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FIG. 3 is a side view of one embodiment of a handheld device for providing therapeutic neuromodulation consistent with the present disclosure. As previously described, the device 102 includes an end effector (not shown) transformable between a collapsed/retracted configuration and an expanded deployed configuration, a shaft 116 operably associated with the end effector, and a handle 118 operably associated with the shaft 116. The handle 118 includes at least a first mechanism 126 for deployment of the end effector from collapsed/retracted configuration to the expanded, deployed configuration, and a second mechanism 128, separate from the first mechanism 124, for control of energy output by the end effector, specifically electrodes or other energy elements provided by the end effector. The handheld device 102 may further include an auxiliary line 121, which may provide a fluid connection between a fluid source, for example, and the shaft 116 such that fluid may be provided to a target site via the distal end of the shaft 116. In some embodiments, the auxiliary line 121 may provide a connection between a vacuum source and the shaft 116, such that the device 102 may include suction capabilities (via the distal end of the shaft 116).

FIG. 4 is an enlarged, perspective view of one embodiment of an end effector 214 consistent with the present disclosure. As shown, the end effector 214 is generally positioned at a distal portion 116b of the shaft 116. The end effector 214 is transformable between a low-profile delivery state to facilitate intraluminal delivery of the end effector 214 to a treatment site and an expanded state, as shown. The end effector 214 includes a plurality of struts 240 that are spaced apart from each other to form a frame or basket 242 when the end effector 214 is in the expanded state. The struts 240 can carry one or more energy delivery elements, such as a plurality of electrodes 244. In the expanded state, the struts 240 can position at least two of the electrodes 244 against tissue at a target site within a particular region. The electrodes 244 can apply bipolar or multi-polar RF energy to the target site to therapeutically modulate nerves associated with a peripheral neurological condition or disorder. In various embodiments, the electrodes 244 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

In the embodiment illustrated in FIG. 4, the basket 242 includes eight branches 246 spaced radially apart from each other to form at least a generally spherical structure, and each of the branches 246 includes two struts 240 positioned adjacent to each other. In other embodiments, however, the basket 242 can include fewer than eight branches 246 (e.g., two,

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three, four, five, six, or seven branches) or more than eight branches 246. In further embodiments, each branch 246 of the basket 242 can include a single strut 240, more than two struts 240, and/or the number of struts 240 per branch can vary. In still further embodiments, the branches 246 and struts 240 can form baskets or frames having other suitable shapes for placing the electrodes 244 in contact with tissue at the target site. For example, when in the expanded state, the struts 240 can form an ovoid shape, a hemispherical shape, a cylindrical structure, a pyramid structure, and/or other suitable shapes.

The end effector 214 can further include an internal or interior support member 248 that extends distally from the distal portion 116b of the shaft 116. A distal end portion 250 of the support member 248 can support the distal end portions of the struts 240 to form the desired basket shape. For example, the struts 240 can extend distally from the distal potion 116b of the shaft 116 and the distal end portions of the struts 240 can attach to the distal end portion 250 of the support member 248. In certain embodiments, the support member 248 can include an internal channel (not shown) through which electrical connectors (e.g., wires) coupled to the electrodes 244 and/or other electrical features of the end effector 214 can run. In various embodiments, the internal support member 248 can also carry an electrode (not shown) at the distal end portion 250 and/or along the length of the support member 248.

The basket 242 can transform from the low-profile delivery state to the expanded state (shown in FIG. 4) by either manually manipulating a handle of the device 102, interacting with the first mechanism 126 for deployment of the end effector 214 from collapsed/retracted configuration to the expanded, deployed configuration, and/or other feature at the proximal portion of the shaft 116 and operably coupled to the basket 242. For example, to move the basket 242 from the expanded state to the delivery state, an operator can push the support member 248 distally to bring the struts 240 inward toward the support member 248. An introducer or guide sheath (not shown) can be positioned over the low-profile end effector 214 to facilitate intraluminal delivery or removal of the end effector 214 from or to the target site. In other embodiments, the end effector 214 is transformed between the delivery state and the expanded state using other suitable means, such as the first mechanism 126, as will be described in greater detail herein.

The individual struts 240 can be made from a resilient material, such as a shape-memory material (e.g., Nitinol) that allows the struts 240 to self-expand into the desired shape of the

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basket 242 when in the expanded state. In other embodiments, the struts 240 can be made from other suitable materials and/or the end effector 214 can be mechanically expanded via a balloon or by proximal movement of the support member 248. The basket 242 and the associated struts 240 can have sufficient rigidity to support the electrodes 244 and position or press the electrodes 244 against tissue at the target site. In addition, the expanded basket 242 can press against surrounding anatomical structures proximate to the target site and the individual struts 240 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 214 at the treatment site during energy delivery. In addition, the expansion and conformability of the struts 240 can facilitate placing the electrodes 244 in contact with the surrounding tissue at the target site.

At least one electrode 244 is disposed on individual struts 240. In the illustrated embodiment, two electrodes 244 are positioned along the length of each strut 240. In other embodiments, the number of electrodes 244 on individual struts 240 be only one, more than two, zero, and/or the number of electrodes 244 on the different struts 240 can vary. The electrodes 244 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene ("PEDOT"), titanium, titanium nitride, carbon, carbon nanotubes, platinum grey, Drawn Filled Tubing ("DFT") with a silver core made by Fort Wayne Metals of Fort Wayne, Ind., and/or other suitable materials for delivery RF energy to target tissue.

In certain embodiments, each electrode 444 can be operated independently of the other electrodes 244. For example, each electrode can be individually activated and the waveform, polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 of FIG. 1A). Various embodiments of such independently controlled electrodes 244 are described in greater detail herein. The selective independent control of the electrodes 244 allows the end effector 214 to deliver RF energy to highly customized regions and to further create multiple micro-lesions to selectively modulate a target neural structure by effectively causing multi-point interruption of a neural signal due to the multiple micro-lesions. For example, a select portion of the electrodes 244 can be activated to target neural fibers in a specific region while the other electrodes 244 remain inactive. In certain embodiments, for example, electrodes 244 may be activated across the portion of the basket 242 that is adjacent to tissue at the target site, and the electrodes 244 that are not proximate to the

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target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves along a portion of a target site without applying energy to structures in other portions of the target site.

The electrodes 244 can be electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1A) via wires (not shown) that extend from the electrodes 244, through the shaft 116, and to the RF generator. When each of the electrodes 244 is independently controlled, each electrode 244 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 244 can be controlled together and, therefore, multiple electrodes 244 can be electrically coupled to the same wire extending through the shaft 116. The RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 244. For example, the RF generator can deliver RF power at about 200-300 W to the electrodes 244, and do so while activating the electrodes 244 in a predetermined pattern selected based on the position of the end effector 214 relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the RF generator delivers power at lower levels (e.g., less than 1 W, 2-5W, 5-15 W, 15-50 W, 50-150 W, etc.) and/or higher power levels.

The end effector 214 can further include one or more sensors 252 (e.g., temperature sensors, impedance sensors, etc.) disposed on the struts 240 and/or other portions of the end effector 214 and configured to sense/detect one or more properties associated with tissue at a target site. For example, temperature sensors are configured to detect the temperature adjacent thereto. The sensors 252 can be electrically coupled to a console (e.g., the console 104 of FIG. 1A) via wires (not shown) that extend through the shaft 116. In various embodiments, the sensors 252 can be positioned proximate to the electrodes 244 to detect various properties of targeted tissue and/or the treatment associated therewith. As will be described in greater detail herein, the sensed data can be provided to the console 104, wherein such data is generally related to at least bioelectric properties of tissue at the target site. In turn, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such data and determine to identify a type of each of the one or more tissues at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types. The console (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is further configured to determine an ablation pattern to be

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delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

In some embodiments, the device 102 may further be configured to provide the console 104 with sensed data in the form of feedback data associated with the effect of the therapeutic stimulation on the targeted tissue. For example, feedback data may be associated with efficacy of ablation upon targeted tissue (e.g., neural tissue) during and/or after delivery of initial energy from one or more of the plurality of electrodes. Accordingly, in certain embodiments, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such feedback data to determine if certain properties of the targeted tissue undergoing treatment (e.g., tissue temperature, tissue impedance, etc.) reach predetermined thresholds for irreversible tissue damage. The controller 107 can tune energy output individually for the one or more electrodes after an initial level of energy has been delivered based, at least in part, on feedback data. For example, once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact. In certain embodiments, the energy delivery can automatically be tuned based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 110 of FIG. 1A) stored on a console (e.g., the console 104 of FIG. 1A) operably coupled to the end effector 214.

FIGS. 5A-5F are various views of another embodiment of an end effector 314 consistent with the present disclosure. As generally illustrated, the end effector 314 is a multi-segmented end effector, which includes at least a first segment 322 and a second segment 324 spaced apart from one another. The first segment 322 is generally positioned closer to a distal portion of the shaft 116, and is thus sometimes referred to herein as the proximal segment 322, while the second segment 324 is generally positioned further from the distal portion of the shaft 116 and is thus sometimes referred to herein as the distal segment 324. Each of the first and second segments 322 and 324 is transformable between a retracted configuration, which includes a low-profile delivery state and a deployed configuration, which includes an expanded state, as shown in the figures. The end effector 314 is generally designed to be positioned within a nasal region of the patient for the treatment of a rhinosinusitis condition while minimizing or avoiding collateral damage to surrounding tissue, such as blood vessels or bone. In particular, the end

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effector 314 is configured to be advanced within the nasal cavity and be positioned at one or more target sites generally associated with postganglionic parasympathetic fibers that innervate the nasal mucosa. In turn, the end effector 314 is configured to therapeutically modulate the postganglionic parasympathetic nerves.

It should be noted, however, that an end effector consistent with the present disclosure may be multi-segmented in a similar fashion as end effector 314 and may be used to provide treatment in other regions of the patient outside of the nasal cavity and thus is not limited to the particular design/configuration as the end effector 314 nor the intended treatment site (e.g., nasal cavity). Rather, other multi-segmented designs are contemplated for use in particular regions of a patient, particularly regions in which the use of multiple and distinct segments would be advantageous, as is the case with the end effector 314 design due to the anatomy of the nasal cavity.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment 322 and second (distal) segment 324. FIG. 5B is an exploded, perspective view of the multi-segment end effector 314. FIG. 5C is an enlarged, top view of the multi-segment end effector 314. FIG. 5D is an enlarged, side view of the multi-segment end effector 314. FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment 322 of the multi-segment end effector 314 and FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment 324 of the multi-segment end effector 314.

As illustrated, the first segment 322 includes at least a first set of flexible support elements, generally in the form of wires, arranged in a first configuration, and the second segment 324 includes a second set of flexible support elements, also in the form of wires, arranged in a second configuration. The first and second sets of flexible support elements include composite wires having conductive and elastic properties. For example, in some embodiments, the composite wires include a shape memory material, such as Nitinol. The flexible support elements may further include a highly lubricious coating, which may allow for desirable electrical insulation properties as well as desirable low friction surface finish. Each of the first and second segments 322, 324 is transformable between a retracted configuration and an expanded deployed configuration such that the first and second sets of flexible support elements are configured to position one or more electrodes provided on the respective segments (see

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electrodes 336 in FIGS. 5E and 5F) into contact with one or more target sites when in the deployed configuration.

As shown, when in the expanded deployed configuration, the first set of support elements of the first segment 322 includes at least a first pair of struts 330a,330b, each comprising a loop (or leaflet) shape and extending in an upward direction and a second pair of struts 332a, 332b, each comprising a loop (or leaflet) shape and extending in a downward direction, generally in an opposite direction relative to at least the first pair of struts 330a, 330b. It should be noted that the terms upward and downward are used to describe the orientation of the first and second segments 322, 324 relative to one another. More specifically, the first pair of struts 330a, 330b generally extend in an outward inclination in a first direction relative to a longitudinal axis of the multi-segment end effector 314 and are spaced apart from one another. Similarly, the second pair of struts 332a, 332b extend in an outward inclination in a second direction substantially opposite the first direction relative to the longitudinal axis of the multi-segment end effector and spaced apart from one another.

The second set of support elements of the second segment 324, when in the expanded deployed configuration, includes a second set of struts 334(1), 334(2), 334(n) (approximately six struts), each comprising a loop shape extending outward to form an open-ended circumferential shape. As shown, the open-ended circumferential shape generally resembles a blooming flower, wherein each looped strut 334 may generally resemble a flower petal. It should be noted that the second set of struts 334 may include any number of individual struts and is not limited to six, as illustrated. For example, in some embodiments, the second segment 124 may include two, three, four, five, six, seven, eight, nine, ten, or more struts 334.

The first and second segments 322, 324, specifically struts 330, 332, and 334 include one or more energy delivery elements, such as a plurality of electrodes 336. It should be noted that any individual strut may include any number of electrodes 336 and is not limited to one electrode, as shown. In the expanded state, the struts 330, 332, and 334 can position any number of electrodes 336 against tissue at a target site within the nasal region (e.g., proximate to the palatine bone inferior to the SPF). The electrodes 336 can apply bipolar or multi-polar radiofrequency (RF) energy to the target site to therapeutically modulate postganglionic parasympathetic nerves that innervate the nasal mucosa proximate to the target site. In various embodiments, the electrodes 336 can be configured to apply pulsed RF energy with a desired

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duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

The first and second segments 322, 324 and the associated struts 330, 332, and 334 can have sufficient rigidity to support the electrodes 336 and position or press the electrodes 336 against tissue at the target site. In addition, each of the expanded first and second segments 322, 324 can press against surrounding anatomical structures proximate to the target site (e.g., the turbinates, the palatine bone, etc.) and the individual struts 330, 332, 334 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 314. In addition, the expansion and conformability of the struts 330, 332, 334 can facilitate placing the electrodes 336 in contact with the surrounding tissue at the target site. The electrodes 336 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene (PEDOT), titanium, titanium nitride, carbon, carbon nanotubes, platinum grey, Drawn Filled Tubing (DFT) with a silver core, and/or other suitable materials for delivery RF energy to target tissue. In some embodiments, such as illustrated in FIG. 6, a strut may include an outer jacket surrounding a conductive wire, wherein portions of the outer jacket are selectively absent along a length of the strut, thereby exposing the underlying conductive wire so as to act as an energy delivering element (i.e., an electrode) and/or sensing element, as described in greater detail herein.

In certain embodiments, each electrode 336 can be operated independently of the other electrodes 336. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein). The selective independent control of the electrodes 336 allows the end effector 314 to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 336 can be activated to target neural fibers in a specific region while the other electrodes 336 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 324 that is adjacent to tissue at the target site, and the electrodes 336 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves on the lateral nasal wall within one nostril without applying energy to structures in other portions of the nasal cavity.

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The electrodes 336 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1A) via wires (not shown) that extend from the electrodes 336, through the shaft 116, and to the RF generator. When each of the electrodes 336 is independently controlled, each electrode 336 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 336 can be controlled together and, therefore, multiple electrodes 336 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 336. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 336, and do so while activating the electrodes 336 in a predetermined pattern selected based on the position of the end effector 314 relative to the treatment site and/or the identified locations of the target tissues. It should further be noted that the electrodes 336 may be individually activated and controlled (i.e., controlled level of energy output and delivery) based, at least in part, on feedback data. The RF generator is able to provide bipolar low power (10 watts with maximum setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

Once deployed, the first and second segments 322, 324 contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments 322, 324 become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes 336, precise and focused application of RF thermal energy or non-thermal energy to the one or more target sites to thereby therapeutically modulate associated neural tissue. More specifically, the first and second segments 322, 324 have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments 322, 324, and thus one or more electrodes associated therewith 336, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

For example, the first set of flexible support elements of the first segment 322 conforms to and complements a shape of a first anatomical structure at the first location when the first segment 322 is in the deployed configuration and the second set of flexible support elements of the second segment 124 conforms to and complements a shape of a second anatomical structure

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at the second location when the second segment is in the deployed configuration. The first and second anatomical structures may include, but are not limited to, inferior turbinate, middle turbinate, superior turbinate, inferior meatus, middle meatus, superior meatus, pterygopalatine region, pterygopalatine fossa, sphenopalatine foramen, accessory sphenopalatine foramen(ae), and sphenopalatine micro-foramen(ae).

In some embodiments, the first segment 322 of the multi-segment end effector 314 is configured in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to the middle turbinate and the second segment 324 of the multi-segment end effector is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the middle turbinate.

For example, the first set of flexible support elements of the first segment (i.e., struts 330 and 332) conforms to and complements a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 322 is in the deployed configuration and the second set of flexible support elements (i.e., struts 334) of the second segment 324 contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of middle turbinate when the second segment 324 is in the deployed configuration. Accordingly, when in the deployed configuration, the first and second segments 322, 324 are configured to position one or more associated electrodes 336 at one or more target sites relative to either of the middle turbinate and the plurality of tissue locations in the cavity behind the middle turbinate. In turn, electrodes 336 are configured to deliver RF energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

As illustrated in FIG. 5E, the first segment 322 comprises a bilateral geometry. In particular, the first segment 322 includes two identical sides, including a first side formed of struts 330a, 332a and a second side formed of struts 330b, 332b. This bilateral geometry allows at least one of the two sides to conform to and accommodate an anatomical structure within the nasal cavity when the first segment 322 is in an expanded state. For example, when in the expanded state, the plurality of struts 330a, 332a contact multiple locations along multiple portions of the anatomical structure and electrodes provided by the struts are configured to emit energy at a level sufficient to create multiple micro-lesions in tissue of the anatomical structure that interrupt neural signals to mucus producing and/or mucosal engorgement elements. In

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particular, struts 330a, 332a conform to and complement a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 322 is in the deployed configuration, thereby allowing for both sides of the anatomical structure to receive energy from the electrodes. By having this independence between first and second side (i.e., right and left side) configurations, the first segment 322 is a true bilateral device. By providing a bilateral geometry, the multi-segment end effector 314 does not require a repeat use configuration to treat the other side of the anatomical structure, as both sides of the structure are accounted at the same time due to the bilateral geometry. The resultant micro-lesion pattern can be repeatable and is predictable in both macro element (depth, volume, shape parameter, surface area) and can be controlled to establish low to high effects of each, as well as micro elements (the thresholding of effects within the range of the macro envelope can be controlled), as well be described in greater detail herein. The systems of the present invention are further able to establish gradients within allowing for control over neural effects without having widespread effect to other cellular bodies, as will be described in greater detail herein.

FIG. 7 is a cross-sectional view of a portion of the shaft 116 of the handheld device taken along lines 7-7 of FIG. 3. As illustrated, the shaft 116 may be constructed from multiple components so as to have the ability to constrain the end effector in the retracted configuration (i.e., the low-profile delivery state) when the end effector is retracted within the shaft 116, and to further provide an atraumatic, low profile and durable means to deliver the end effector to the target site. The shaft 116 includes coaxial tubes which travel from the handle 118 to a distal end of the shaft 116. The shaft 116 assembly is low profile to ensure adequate delivery of therapy in areas requiring low-profile access. The shaft 116 includes an outer sheath 138, surrounding a hypotube 140, which is further assembled over electrode wires 129 which surround an inner lumen 142. The outer sheath 138 serves as the interface between the anatomy and the device 102. The outer sheath 138 may generally include a low friction PTFE liner to minimize friction between the outer sheath 138 and the hypotube 140 during deployment and retraction. In particular the outer sheath 138 may generally include an encapsulated braid along a length of the shaft 116 to provide flexibility while retaining kink resistance and further retaining column and/or tensile strength. For example, the outer sheath 138 may include a soft Pebax material, which is atraumatic and enables smooth delivery through a passageway.

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The hypotube 140 is assembled over the electrode wires starting within the handle 118 and travelling to the proximal end of the end effector. The hypotube 140 generally acts to protect the wires during delivery and is malleable to enable flexibility without kinking to thereby improve trackability. The hypotube 140 provides stiffness and enables torqueability of the device 102 to ensure accurate placement of the end effector 314. The hypotube 140 also provides a low friction exterior surface which enables low forces when the outer sheath 138 moves relative to the hypotube 140 during deployment and retraction or constraint. The shaft 116 may be pre-shaped in such a manner so as to complement a given anatomy (e.g., nasal cavity). For example, the hypotube 140 may be annealed to create a bent shaft 116 with a pre-set curve. The hypotube 140 may include a stainless-steel tubing, for example, which interfaces with a liner in the outer sheath 138 for low friction movement.

The inner lumen 142 may generally provide a channel for fluid extraction during a treatment procedure. For example, the inner lumen 142 extends from the distal end of the shaft 116 through the hypotube 140 and to atmosphere via a fluid line (line 121 of FIG. 3). The inner lumen 142 materials are chosen to resist forces of external components acting thereon during a procedure.

FIG. 8A is a side view of the handle of the handheld 118 and FIG. 8B is a side view of the handle 118 illustrating internal components enclosed within. The handle 118 generally includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. For example, the handle 118 may include specific contours, including recesses 144, 146, and 148 which are designed to naturally receive one or more of an operator's fingers in either of an overhand grip or underhand grip style and provide a comfortable feel for the operator. For example, in an underhand grip, recess 144 may naturally receive an operator's index finger, recess 146 may naturally receive an operator's middle finger, and recess 148 may naturally receive an operator's ring and little (pinkie or pinky) fingers which wrap around the proximal protrusion 150 and the operator's thumb naturally rests on a top portion of the handle 118 in a location adjacent to the first mechanism 126. In an overhand grip, the operator's index finger may naturally rest on the top portion of the handle 118, adjacent to the first mechanism 126, while recess 144 may naturally receive the operator's middle finger, recess 146 may naturally receive a portion of the

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operator's middle and/or ring fingers, and recess 148 may naturally receive and rest within the space (sometimes referred to as the purlicue) between the operator's thumb and index finger.

As previously described, the handle includes multiple user-operated mechanisms, including at least a first mechanism 126 for deployment of the end effector from the collapsed/retracted configuration to the expanded deployed configuration and a second mechanism 128 for controlling of energy output by the end effector, notably energy delivery from one or more electrodes. As shown, the user inputs for the first and second mechanisms 126, 128 are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. For example, user input for the first mechanism 126 is positioned on a top portion of the handle 118 adjacent the grip portion and user input for the second mechanism 128 is positioned on side portions of the handle 118 adjacent the grip portion. As such, in an underhand grip style, the operator's thumb rests on the top portion of the handle adjacent to the first mechanism 126 and at least their middle finger is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. In an overhand grip system, the operator's index finger rests on the top portion of the handle adjacent to the first mechanism 126 and at least their thumb is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

Referring to FIG. 8B, the various components provided within the handle 118 are illustrated. As shown, the first mechanism 126 may generally include a rack and pinion assembly providing movement of end effector between the retracted and deployed configurations in response to input from a user-operated controller. The rack and pinion assembly generally includes a set of gears 152 for receiving input from the user-operated controller and converting the input to linear motion of a rack member 154 operably associated with at least one of the shaft 116 and the end effector. The rack and pinion assembly comprises a gearing ratio sufficient to balance a stroke length and retraction and deployment forces, thereby improving control over the deployment of the end effector. As shown, the rack member 154 may be coupled to a portion of the shaft 116, for example, such that movement of the rack member 154 in a direction towards a proximal end of the handle 118 results in corresponding movement of the shaft 116 while the end

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effector remains stationary, thereby exposing the end effector and allowing the end effector to transition from the constrained, retracted configuration to the expanded, deployed configuration. Similarly, movement of the rack member 154 in a direction towards a distal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector remains stationary, and thereby encloses the end effector within the shaft 116. It should be noted that, in other embodiments, the rack member 154 may be directly coupled to a portion of the end effector such that movement of the rack member 154 results in corresponding movement of the end effector while the shaft 116 remains stationary, thereby transitioning the end effector between the retracted and deployed configurations.

The user-operated controller associated with the first mechanism 126 may include a slider mechanism operably associated with the rack and pinion rail assembly. Movement of the slider mechanism in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and movement of the slider mechanism in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration. In other embodiment, the user-operated controller associated with the first mechanism 126 may include a scroll wheel mechanism operably associated with the rack and pinion rail assembly. Rotation of the wheel in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and rotation of the wheel in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration.

FIGS. 9A, 9B, and 9C are block diagrams illustrating the process of sensing, via an end effector, data associated with one or more tissues at a target site, notably bioelectric electric properties of one more tissues at the target site, and the subsequent processing of such data (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) to determine the type of tissue(s) at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types, and further determining an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

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It should be noted that, while the block diagrams of FIGS. 9A, 9B, and 9C include reference to end effector 214, other end effector embodiments, including end effector 314, are similarly configured with respect to sensing data associated with at least the presence of neural tissue and other properties of the neural tissue, including neural tissue depth. Accordingly, the following process is not limited to end effector 214.

FIG. 9A is a block diagram illustrating delivery of non-therapeutic energy from electrodes 244 of the end effector at a frequency for sensing one or more properties associated with tissue at a target site in response to the non-therapeutic energy.

As previously described, the handheld treatment device includes an end effector comprising a micro-electrode array arranged about a plurality of struts. For example, end effector 214 includes a plurality of struts 240 that are spaced apart from each other to form a frame or basket 242 when the end effector 214 is in the expanded state. The struts 240 include a plurality of energy delivery elements, such as a plurality of electrodes 244. In the expanded state, each of the plurality of struts is able to conform to and accommodate an anatomical structure at a target site. When positioned, the struts may contact multiple locations along multiple portions of a target site and thereby position one or more electrodes 244 against tissue at a target site. At least a subset of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site, and further convey such data to the console 104. In addition to bioelectric properties, the data may also include at least one of physiological properties and thermal properties of tissue at the target site.

For example, upon delivering non-therapeutic stimulating energy (via one or more electrodes 244) to respective positions, various properties of the tissue at the one or more target sites can be detected. This information can then be transmitted to the console 104, particularly the controller 107, monitoring system 108, and evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate a tissue of interest (targeted tissue to receive electric therapeutic stimulation), such as neural tissue, differentiate between different types of neural tissue, and map the anatomical and/or neural structure at the target site. For example, the end effector 214 can be used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in

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the target region. In certain embodiments, the end effector 214, together with the console 104 components, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. For example, the evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes 244).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-50Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures, including the firing of neural tissue, differences between neural tissue and other anatomical structures (e.g., blood vessels), and even different types of neural tissue. This information can be analyzed by the evaluation/feedback algorithms 110 and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural tissue and other anatomy at the treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode 244 can be operated independently of the other electrodes 244. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes 244 allows the end effector 214 to detect information (i.e., the presence of neural tissue, depth of neural tissue, and other physiological and bioelectrical properties) and subsequently deliver RF energy to highly customized regions. For example, a select portion of the electrodes 244 can be activated to target specific neural fibers in a specific region while the other electrodes 244 remain inactive. In addition, the electrodes 244 can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

As previously described, the system 100 can identify tissue type of one or more tissues at a target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types prior to therapy such that the therapeutic stimulation can be applied to

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precise regions including targeted tissue, while avoiding negative effects on non-targeted tissue and structures (e.g., blood vessels). For example, the system 100 can detect various bioelectrical parameters in an interest zone to determine the location and morphology of various tissue types (e.g., different types of neural tissue, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony regions, etc.). The system 100 is further configured to measure bioelectric potential.

To do so, one or more of the electrodes 244 is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies, and/or alternating (sine, square, triangle, sawtooth, etc.) wave or direct constant current/power/voltage source at one or more frequencies) are applied to the tissue by one or more electrodes 244 at or near the treatment site, and the voltage and/or current differences based on the wave applied at various different frequencies between various pairs of electrodes 244 of the end effector 214 may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural tissue, and/or other types of tissue) in the region of interest. For example, a fixed current (i.e., direct or alternating current) can be applied to a pair of electrodes 244 adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes 244 are measured. Conversely, a fixed voltage (i.e. mono or bi-phasic) can be applied to a pair of electrodes 244 adjacent to each other and the resultant current between other pairs of adjacent electrodes 244 are measured. It will be appreciated that the current injection electrodes 244 and measurement electrodes 244 need not be adjacent, and that modifying the spacing between the two current injection electrodes 244 can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes 244 provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes 244 that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric potential measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector 114), and this information can be used to map the neural and anatomical structures

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by the use of frequency differentiation reconstruction. In particular, current-voltage data may be observed with the difference in dielectric and conductive properties of tissue type when different levels of current frequencies are applied.

Furthermore, applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters, which can further be used to identify specific tissue type and respective dielectric relaxation phenomena/behavior of the identified tissue types.

For example, different tissue types include different physiological and histological characteristics (e.g., cell components, extracellular proteins, etc.). As a result of the different characteristics, different tissue types have different associated bioelectrical properties and thus exhibit different associated behavior in response to application of energy applied thereto. It should be noted that active bioelectrical properties may generally include the influx and outflux of ions into and out of a cell, while passive bioelectrical properties may include resistive, capacitive, and inductive properties of the cell. One such behavior is referred to as dielectric relaxation phenomena. The energy conduction behavior of tissue differs with frequency/energy applied as tissue passive electrical components activate and de-active depending on frequency applied. This switching action of activating and deactivating of these electrically passive components depends on the energy and frequency applied is known as relaxation phenomena. This relaxation can take place either on ionic or dielectric or atomic or electronic level (highly dependent on frequency). For example, the ionic resistive component of a tissue is relative to active more than capacitive or inductive component of the tissue and, in dielectric, the capacitive component is relatively more active than resistive component.

As a result, the relaxation phenomena of a given tissue occurs at a particular electrical frequency in which the membranes of cells of the given tissue become permeable to thereby allow electrical stimulation current (at the particular frequency) to flow through the membrane to thereby elicit a desired effect upon the tissue. When a tissue is not exhibiting the dielectric relaxation phenomena (i.e., when electrical stimulation current is tuned to a different frequency that does not correlate to the dielectric relaxation phenomena), the membranes of cells of the given tissue are not permeable to that specific electrical stimulation current and thus do not elicit an effect.

For example, at relatively high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of neural tissue do not impede current flow, and the

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current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes and morphologies of the cells, cell density and/or cell spacing. The stimulation frequencies can be in the megahertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), in the hertz range (e.g., 0.2-0.8 Hz, 8-12 Hz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

Further, the inherent morphology and composition of the anatomical structures within a given region or zone of a patient's body react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural tissue, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy.

In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be

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determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes 244 at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, passive bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes 244 and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes 244 are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural tissue that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural tissue that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate neural fibers associated with certain neurological conditions or disorders to be treated. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the

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evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

FIG. 9B is a block diagram illustrating communication of sensor data from the handheld device 102 to the controller and subsequent tuning, via the controller, of energy output based on the sensor data for precision targeting of tissue of interested and to be treated. As shown, the end effector 214 communicates the tissue data (i.e., bioelectric properties of tissue at the target site) to the console 104. The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, induced electromotive force, and combinations thereof. The dielectric properties may include, for example, at least a complex relative dielectric permittivity.

In turn, console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such data and determine a type of tissue at the target site, as well as other properties, including a dielectric relaxation pattern for each of the one or more identified tissue types. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is further configured to determine an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site. More specifically, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to tune energy output (i.e., delivery of electrical therapeutic stimulation) based on the dielectric relaxation pattern of a tissue of interest such that the energy delivered is at a specific frequency configured to target the tissue of interest while avoiding the non-targeted tissue (i.e., the energy is tuned to a frequency level associated with the dielectric relaxation phenomena of the targeted tissue only thereby penetrate the cell membranes of the targeted tissue).

The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is generally configured to determine/calculate a dielectric relaxation pattern of a

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given identified tissue type based on an algorithm utilizing complex relative dielectric permittivity calculations in empirical modeling of relaxation phenomena.

For example, by way of background, a dielectric material is an electrical insulator that can be polarized by an applied electric field. When a dielectric material is placed in an electric field, electric charges do not flow through the material as they do in an electrical conductor, but only slightly shift from their average equilibrium positions causing dielectric polarization. Because of dielectric polarization, positive charges are displaced in the direction of the field and negative charges shift in the direction opposite to the field (for example, if the field is moving in the positive x-axis, the negative charges will shift in the negative x-axis). As a result, dielectric polarization creates an internal electric field that reduces the overall field within the dielectric itself. If a dielectric is composed of weakly bonded molecules, those molecules not only become polarized, but also reorient so that their symmetry axes align to the field.

Accordingly, biological tissue, most notably cells of biological tissue, can essentially be modeled as capacitors with dielectric properties. For example, the phospholipid bilayer of a cell membrane can resemble a parallel-plate capacitor, such that, depending on the frequency applied, a cell membrane will allow an electrical charge/current to flow through. Adding a dielectric allows the capacitor to store more charge for a given potential difference. For example, when a dielectric is inserted into a charged capacitor to increase the capacitance of the capacitor, the dielectric is polarized by the field. The electric field from the dielectric will partially cancel the electric field from the charge on the capacitor plates.

The resulting concepts of relative dielectric permittivity and dielectric constant can be used to further determine complex relative dielectric permittivity of a tissue for the subsequent calculation of dielectric relaxation phenomena of a given tissue. The dielectric constant or relative dielectric permittivity, is understood by the following formula:

$$\kappa = \varepsilon_r = \frac{\varepsilon_m}{\varepsilon_0}$$

Dielectric permittivity (ε) is the ability of a substance to hold an electrical charge and is a function of frequency, temperature, humidity and other physical parameters. The dielectric constant (κ), also referred to as relative dielectric permittivity (ε_r), is the ratio of the permittivity of a substance to free space. In the above formula, ε_m is the complex frequency-dependent permittivity of the material and ε_0 is the vacuum permittivity. The value of ε_0 is $8.85418782 \times$

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$10^{-12}\ m^{-3}\ kg^{-1}\ s^4\ A^2$. Many materials have an ε or κ. For example, the κ or ε_r of air is 1, of water is approximately 80, of glass is between 5 and 10, of paper is between 2 and 4, and of body tissue is approximately 8 at a frequency of 1kHz and at room temperature of 20 degrees Celsius (°C).

By knowing the relative dielectric permittivity of a material, the complex relative dielectric permittivity may be obtained. The complex relative dielectric permittivity is understood by the following formula:

$$\varepsilon_r = \varepsilon'_r - j\varepsilon''_r$$

where ε_r is the relative dielectric permittivity, or dielectric constant, ε'_r is the real part of the complex dielectric constant, ε''_r is the imaginary part of the complex dielectric constant, and j is the imaginary constant. The real part (ε'_r) of the relative dielectric permittivity or dielectric constant defines the polarization capability of the material. The imaginary part (ε''_r) of the relative dielectric permittivity or dielectric constant defines the loss of the material (ionic loss at low frequency around mHz to Hz range, dielectric heat loss at kHz to MHz range, atomic loss and electronic loss at higher frequencies) and the conducting behavior of the polymer. At low to middle frequency range, relaxation phenomena or behavior occurs when the dielectric material starts leaking charge or heat loss at a particular frequency, where the imaginary part of the dielectric constant becomes more dominant compared to that of the real part of the dielectric constant.

Certain parameters can be extracted from complex relative dielectric permittivity of a given tissue, including, for example, loss tangent (also referred to as dielectric loss) with respect to impedance measurements of a tissue. Dielectric loss quantifies a dielectric material's inherent dissipation of electromagnetic energy (e.g. heat). It can be parameterized in terms of either the loss angle δ or the corresponding loss tangent tan δ (i.e., loss tangent). Both refer to the phasor in the complex plane whose real and imaginary parts are the resistive (lossy) component of an electromagnetic field and its reactive (lossless) counterpart. Loss tangent is defined as:

$$\tan\delta = \frac{\varepsilon''_r}{\varepsilon'_r}$$

where δ always refers to the angle of complex dielectric permittivity and θ always refers to impedance phase angle, so $\tan\theta = X_c/R$. X_c is the reactive part of complex impedance and R is

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the real part of impedance. The relationship between loss tangent tan δ and impedance phase angle θ is: $\delta = 90° - \theta$. Accordingly:

$$\tan\delta = \cot\theta = \frac{1}{2\pi R_p C_p}$$

As previously described, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is generally configured to determine/calculate a dielectric relaxation pattern of a given identified tissue type based on an algorithm utilizing complex relative dielectric permittivity calculations in empirical modeling of relaxation phenomena. In some embodiments, the calculation of the dielectric relaxation pattern of a given identified tissue is based, at least in part, on the Havriliak–Negami relaxation model. The Havriliak–Negami relaxation is an empirical modification of the Debye relaxation model in electromagnetism. Unlike the Debye model, the Havriliak–Negami (HN) relaxation accounts for the asymmetry and broadness of the dielectric dispersion curve. The model was first used to describe the dielectric relaxation of some polymers, by adding two exponential parameters to the Debye equation:

$$\varepsilon^* = \varepsilon_\infty + (\varepsilon_0 - \varepsilon_\infty) \times \frac{1}{[1 + (i\omega\tau)^{1-\alpha_{HN}}]^{\beta_{HN}}} - \frac{i\sigma_{dc}}{\varepsilon_0 \omega^s}$$

where ε_∞ and ε_0 represent the total dielectric permittivity at high frequency and low frequency respectively. i is the characteristic complex number $\sqrt{-1}$, ω is the angular frequency (where $\omega = 2\pi f$), τ is the relaxation time and is given by $1/2\pi f_{max}$, f_{max} is the peak frequency of loss modulus and α_{HN} and β_{HN} are shaped characteristics of the fitted curve which describe width and asymmetry of loss peak respectively where $0 \leq \alpha_{HN}, \beta_{HN} \leq 1$. The fitting parameters become 1 for purely ohmic conductivity and decrease with electrode polarization. The parameter $\varepsilon_0 - \varepsilon_\infty$ denotes the dielectric strength (Δε) of nanocomposites. The exponents, α and β, describe the asymmetry and broadness of the corresponding spectra. where $\alpha_{HN}=0$ the HN model reduces to the Cole –Davidson model. The HN relaxation model proposes that the real and imaginary parts of the complex relative permittivity can be expressed as a function of ω (angular frequency) and α and β, as follows:

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$$\varepsilon' = \varepsilon_\infty + (\varepsilon_0 - \varepsilon_\infty) \times \frac{\cos(\beta_{HN}\theta)}{\left[1 + 2(\omega\tau_{HN})^{1-\alpha_{HN}} \sin\left(\frac{\alpha_{HN}\pi}{2}\right) + (\omega\tau)^{2(1-\alpha)}\right]^{\frac{\beta}{2}}}$$

$$\varepsilon'' = (\varepsilon_0 - \varepsilon_\infty) \times \frac{\sin(\beta_{HN}\theta)}{\left[1 + 2(\omega\tau_{HN})^{1-\alpha_{HN}} \sin\left(\frac{\alpha_{HN}\pi}{2}\right) + (\omega\tau)^{2(1-\alpha)}\right]^{\frac{\beta}{2}}}$$

and

$$\theta = \tan^{-1} \frac{(\omega\tau)^{1-\alpha_{HN}} \cos\left(\frac{\alpha_{HN}\pi}{2}\right)}{1 + (\omega\tau)^{1-\alpha_{HN}} \sin\left(\frac{\alpha_{HN}\pi}{2}\right)}$$

Based on the above formulas, calculation of ε'_r and ε''_r as a function of ω (angular frequency) from the data using a capacitance equation, as well as dimensions of the electrodes, for example.

It should be noted that, in some embodiments, the system 100 may include a database 400 containing a plurality of profiles 402(1)-402(n) of identified and known tissue types, wherein each profile may include electric signature data for the associated tissue type. The electric signature data may generally include previously identified bioelectric properties of the tissue type and previously identified dielectric relaxation pattern, and the associated frequency at which the tissue type exhibits different dielectric/MWS/loss factor relaxation and or dielectric relaxation phenomena/behaviors. Accordingly, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process data received from the end effector 114 (i.e., bioelectric properties of one or more tissues at the target site) and determine a type of tissue at the target site a dielectric relaxation pattern for each of the one or more identified tissue types based on a comparison of the data with the electric signature data stored in each of the profiles 402. Upon a positive correlation between data sets, the console 104 is configured to identify a matching profile and thus determine the one or more tissue types at the target site and the respective relaxation and conductivity patterns of each so as to identify an accurate ablation pattern for limiting treatment to that of the targeted tissue.

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As generally understood, in dielectric spectroscopy, large frequency dependent contributions to the dielectric response, especially at low frequencies, may come from build-ups of charge. This Maxwell-Wagner-Sillar polarization, occurs either at inner dielectric boundary layers on a mesoscopic scale, or at the external electrode-sample interface on a macroscopic scale. In both cases this leads to a separation of charges (such as through a depletion layer). The charges are often separated over a considerable distance (relative to the atomic and molecular sizes), and the contribution to dielectric loss can therefore be orders of magnitude larger than the dielectric response due to molecular fluctuations.

Maxwell-Wagner-Sillar polarization (also referred to as the Maxwell-Wagner effect) processes are taken into account during the investigation of inhomogeneous materials like suspensions or colloids, biological materials, phase separated polymers, blends, and crystalline or liquid crystalline polymers. The Maxwell–Wagner effect accounts for charge accumulation at the two-material interface on the basis of the difference of charge carrier relaxation times in these two materials. Macroscopically, basic electrical properties of materials are specified using two physical parameters, dielectric constant ϵ and conductivity σ. The ratio of these two parameters, $\tau=\varepsilon/\sigma$. The simplest model for describing an inhomogenous structure is a double layer arrangement, where each layer is characterized by its permittivity ε'_1, ε'_2 and its conductivity σ_1, σ_2. The relaxation time for such an arrangement is given by:

$$\tau_{MW} = \epsilon_0 \frac{\epsilon_1 + \epsilon_2}{\sigma_1 + \sigma_2}$$

Importantly, since the materials' conductivities are in general frequency dependent, this shows that the double layer composite generally has a frequency dependent relaxation time even if the individual layers are characterized by frequency independent permittivities.

The system 100 of the present invention may utilize Maxwell-Wagner-Sillar (MWS) relaxation model to confirm the target frequencies (frequencies at which relaxation phenomena occurs) of identified tissues. As previously described, relaxation phenomena is important in understanding changes in electric behavior of tissues under different frequencies conditions. At molecular dynamics level, dielectric spectroscopy has proven to be a more improved technique compared to other measurement techniques including Nuclear Magnetic Resonance (NMR), Small angle X-ray scattering (SAXS), Dynamic Mechanical Analysis (DMA), Quasi-elastic light

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scattering and neutron scattering. Cooperative relaxation and Maxwell-Wagner-Sillar (MWS) polarization are the two types of relaxation phenomenon found in biological tissue at low frequency range. Cooperative relaxation occurs due to the relaxation of the backbone chain of biopolymers and is generally termed as glass transition relaxation of those biopolymers. Maxwell-Wagner-Sillar (MWS) relaxation occurs generally at a very low frequency in biological tissues due to charge trapping at the interface of materials having different permittivity-based molecules. Frequency-based MWS are hard to find using imaginary dielectric permittivity. However, electric modulus, an inverse of dielectric permittivity, ε_r, can be used to define different relaxation especially MWS and crystalline loss in polymer and nanocomposites. Mathematically, it is presented by the following:

$$M^* = 1/\varepsilon_r = 1/(\varepsilon^{'} - i\varepsilon^{"}) = \varepsilon^{'}/(\varepsilon^{'2} + \varepsilon^{"2}) + j\varepsilon^{"}/(\varepsilon^{'2} + \varepsilon^{"2}) = M^{'} + jM^{"}$$

where $M^{'}$ and $M^{"}$ are the real and imaginary component of electric modulus, which is analogous to the shear modulus. $\varepsilon^{'}$ and $\varepsilon^{"}$ are real and img. dielectric permittivity of biological tissue.

FIG. 9C is a block diagram illustrating delivery of energy to the target site tuned to a specific frequency to elicit dielectric relaxation phenomena/behavior in the targeted tissue (based on the ablation pattern output from the controller). The level of energy output from the end effector may be at a therapeutic energy level sufficient to therapeutically modulate (e.g. ablate) the targeted tissue while minimizing and/or preventing damage to a surrounding or adjacent non-targeted tissue or structure. In particular, energy to be delivered from the end effector is tuned to a target frequency associated with a specific relaxation pattern of the targeted tissue. The target frequency is a frequency at which the targeted tissue exhibits near relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior. In particular, delivery of the ablation energy, tuned to the target frequency, penetrates (passes through) a membrane of one or more cells associated only with the targeted tissue, while passing around cell membranes of non-targeted tissue and structures at the target site.

For example, in some embodiments, the condition to be treated may include a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition, such as rhinosinusitis. Accordingly, in some embodiments, the target site is within a

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sino-nasal cavity (e.g., proximate or inferior to a sphenopalatine foramen) of the patient and the targeted tissue is neural tissue associated with rhinosinusitis (i.e., neural tissue innervating mucus producing and/or mucosal engorgement elements within the sino-nasal cavity). As a result, the ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue (i.e., neural tissue) and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site. More specifically, as illustrated in FIG. 10, the energy output (i.e., delivery of electrical therapeutic stimulation) is based on the dielectric relaxation pattern of a tissue of interest (i.e., neural tissue in this instance) such that the energy delivered is at a specific frequency configured to target the tissue of interest while avoiding the non-targeted tissue (i.e., the energy is tuned to a frequency level associated with the dielectric relaxation phenomena of the targeted tissue only thereby penetrate the cell membranes of the targeted tissue).

FIG. 10 is a block diagram illustrating delivery of energy to the target site, and specifically illustrating flow of current through membranes of cells of the targeted tissue (near relaxation phenomena/behavior) and flow of current around membranes of cells of non-targeted tissue (which is not exhibiting nearby relaxation phenomena/behavior) as a result of the energy being tuned to a target frequency.

The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient.

Accordingly, the electrical stimulating energy can be applied to the tissue of interest in a highly targeted manner and elicit the desired effect (i.e., neuromodulation, ablation, lesion formation, etc.) to selectively modulate the targeted tissue, while avoiding non-targeted tissue or

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structures (which may include vital organs or tissues, such as blood vessels) and allowing the surrounding tissue structure to remain healthy for effective wound healing.

In that manner, the present invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types. In particular, the systems and methods are able to, prior to treatment, characterize and identify tissue types and further identify specific levels of energy (i.e., specific target frequencies) to be delivered so as to cause only those intended, targeted tissues to exhibit nearby relaxation phenomena and thus receive the energy for treatment, while non-targeted tissues remain intact and avoid collateral damage.

It should further be noted that, with reference to FIG. 9C, the end effector 114 can continue to sense tissue properties during and/or after treatment. Such sensed data from the end effector 214 can further include feedback data associated with the effect of the stimulating energy at the therapeutic level on targeted tissue at any given location. For example, feedback data (sensed during therapeutic neuromodulation of neural tissue) may be associated with efficacy of ablation of the targeted tissue during and/or after delivery of initial energy from one or more of the plurality of electrodes 244. Accordingly, in certain embodiments, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such feedback data to determine if certain properties of the targeted tissue undergoing treatment (i.e., tissue temperature, tissue impedance, etc.) reach predetermined thresholds for irreversible tissue damage.

The electrodes 244 are configured to be independently controlled and activated by the controller 107 (in conjunction with the evaluation/feedback algorithms 110) to thereby deliver energy independent of one another. Accordingly, the controller 107 can tune energy output individually for the one or more electrodes 244 after an initial level of energy has been delivered based, at least in part, on feedback data. For example, once the threshold is reached, the application of therapeutic stimulation energy can be terminated to allow the tissue to remain intact. In other embodiments, if the threshold has not been reached, the controller can maintain, reduce, or increase energy output to a given electrode 244 until such threshold is reached. Accordingly, the energy delivery of any given electrode 244 can automatically be tuned based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 110 of FIG. 1A)

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stored on a console (e.g., the console 104 of FIG. 1A) operably coupled to the end effector 214. For example, at least some of the electrodes 244 may have different levels of energy to be delivered at respective positions sufficient to ablate neural tissue at the respective positions based on the feedback data received for the respective locations.

For example, in some embodiments, the controller 107 is configured to tune energy output from each of the plurality of electrodes 244 after an initial level of energy has been delivered based, at least in part, on feedback data received. The feedback data may be associated with efficacy of ablation of the neural tissue at each position during and/or after delivery of initial energy from each of the plurality of electrodes. The feedback data includes one or more properties associated with neural tissue at respective positions. The one or more properties may include, but are not limited to, physiological properties, bioelectric properties, and thermal properties. For example, the active and passive bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, complex, real and imaginary permittivity, conductivity, nerve firing voltage, nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

FIG. 11 is a flow diagram illustrating one embodiment of a method 500 for treating a condition. The condition may include, for example, a peripheral neurological condition of a patient. The method 500 includes providing a device comprising an end effector including a plurality of electrodes and a controller operably associated with the device (operation 510). The method 500 further includes positioning the end effector at a target site associated with a patient (operation 520) and receiving, via the controller, data from the device associated with bioelectric properties of one or more tissues at the target site (operation 530).

The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, induced electromotive force, and combinations thereof. The dielectric properties may include, for example, at least a complex relative dielectric permittivity. It should be noted that, in some embodiments, a subset of the plurality of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site.

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The method 500 further includes processing, via the controller, the data to identify a type of each of the one or more tissues at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types (operation 540).

The processing of the data may include, for example: a) comparing the data received from the device with electric signature data associated with a plurality of known tissue types; and (b) use of (i) a supervised and/or (ii) an unsupervised trained neural network. For example, the controller may be configured to compare the tissue data (i.e., data received from the treatment device associated with tissue at the target site) with profiles of known tissue types stored in a database, for example. Each profile may generally include electric signature data that generally characterizes a known tissue type, including physiological, histological, and bioelectric properties of a known tissue type, including different relaxation phenomena/behavior of the tissue and the specific frequency value at which the tissue exhibits these relaxation phenomena/behavior.

The method 500 further includes determining, via the controller, an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site (operation 550). The ablation energy is tuned to a target frequency associated with a relaxation pattern of the targeted tissue. The target frequency comprises a frequency at which the targeted tissue exhibits relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior. In particular, delivery of the ablation energy, tuned to the target frequency, penetrates the plasma membrane of one or more cells associated only with the targeted tissue.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still,

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delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient.

FIG. 12 is a schematic of an exemplary probe/electrode setup for performing some of the methods described herein, most notably for characterizing tissue at a target site by sensing bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present and further determining a dielectric relaxation phenomena/behavior pattern for the identified types of tissue.

FIG. 12A is a schematic diagram of one embodiment of a 3-probe/electrode system for sensing bioelectric properties of tissue for subsequent characterization of tissue at a target site, wherein such characterization includes identifying specific types of tissue present and further determining a dielectric relaxation phenomena/behavior pattern for the identified types of tissue.

It should be noted that, while the diagrams of FIGS. 12 and 12A illustrate a 3-probe/electrode system, the systems and methods of the present invention may include any number of probes/electrodes for obtaining bioelectric data from tissue of interest (either targeted tissue or non-targeted tissue) for the purposes of determining dielectric relaxation phenomena/behavior patterns or other properties, as described herein. For example, experimental setups may include the use of 2, 3, 4, or more probes/electrodes.

Referring to FIGS. 12 and 12A, the experimental setup includes a 3-electrode assembly (a reference electrode, a counter electrode, and an active working electrode). Such a setup which includes the 3-probe/electrode assembly is used to obtain dielectric properties of various tissue types, wherein such data is described in greater detail herein with reference to FIGS. 13, 14, 15, and 16.

FIGS. 13A and 13B are graphs illustrating dielectric properties of two tissue types (spinal cord and muscle tissues), including the plotting of loss tangent value relative to frequency (FIG.

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13A) and the plotting of an imaginary electric modulus relative to frequency (FIG. 13B). As illustrated, the relaxation phenomena/behavior is generally observed around 10 kHz earlier for nervous tissue as compared to muscle tissue.

FIGS. 14A-14H are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity (based on the Havriliak–Negami (HN) relaxation phenomena model) relative to frequency for the two tissue types of FIGS. 13A and 13B (spinal cord and muscle tissues).

FIGS. 14A and 14B illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for upper spinal cord tissue. FIGS. 14C and 14D illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for lower spinal cord tissue. FIGS. 14E and 14F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for lower back muscle tissue. FIGS. 14G and 14H are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for upper back muscle tissue.

Below is a table (Table 1) providing the specific data points for each of the tissues with respect to the real and imaginary dielectric permittivity values or specific HN relaxation parameters obtained for specific tissue types when data obtained from 10 kHz to 80 kHz are trained.

TABLE 1

Tissue Type	Parameters	Value	Standard Error
Upper Spinal Cord	α	0	0.008
	β	0.875	0.009
	f0	1012.70	130.20
	$\varepsilon 0$-$\varepsilon\infty$	5.811E7	6.12E6
	$\varepsilon\infty$	431140.35	26246.9
Lower Spinal Cord	α	0.011	0.01
	β	0.98	0.01
	f0	2629.47	208.63
	$\varepsilon 0$-$\varepsilon\infty$	1.72E7	1.0E6
	$\varepsilon\infty$	375317.95	25581.28
Lower Back Muscle	α	0	0.004

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	β	0.72	0.004
	f0	63.23	81.80
	ε0-ε∞	3.15E8	2.89E8
	ε∞	241267.91	18021.86
Upper Back Muscle	α	0	0.00467
	β	0.71561	0.0044
	f0	63.16	81.80
	ε0-ε∞	3.1E8	2.9E8
	ε∞	241256.79	18021.68

It was observed that HN relaxation frequency of upper spinal cord occurs around 1 kHz when two independent equations of real and imaginary dielectric permittivity values are trained for 10 kHz to 80 kHz. It was further observed that HN relaxation of lower spinal cord occurs around 2.6 kHz when two independent equation of real and imaginary dielectric permittivity value are trained for 10 kHz to 80 kHz.

A notable feature of spinal cord is that the conduction behavior is ohmic conductivity when data is train between 10 kHz to 80 kHz as the fitting parameter α is near to 0 and β is near to 1. FIGS. 15A and 15B are graphs illustrating dielectric properties of different portions of a tissue (turbinate tissue), including the plotting of loss tangent value relative to frequency (FIG. 15A) and the plotting of an imaginary electric modulus relative to frequency (FIG. 15B). The different portions of turbinate include an end of the turbinate, center of the turbinate, and portions of the turbinate adjacent to blood vessels. From the data observed (based on peak of tan delta and relaxation), only the center of turbinate appeared to follow the relaxation behavior of nervous tissue, as the center of the turbinate generally includes a bundle of nervous tissue, similar in nature to the lower spinal cord.

FIGS. 16A-16F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity (based on the HN relaxation phenomena) relative to frequency for the different portions of the turbinate tissue of FIGS. 15A and 15B.

FIGS. 16A and 16B illustrate plotting of real and imaginary values of the complex relative permittivity relative to frequency for the end of a turbinate tissue. FIGS. 16C and 16D illustrate plotting of real and imaginary values of the complex relative permittivity relative to

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frequency for the center of the turbinate tissue. FIGS. 16E and 16F are graphs illustrating the plotting of real and imaginary values of the complex relative permittivity relative to frequency for portions of the turbinate tissue near blood vessels.

Below is a table (Table 2) providing the specific data points for each of the tissues with respect to the real and imaginary dielectric permittivity values or specific HN relaxation parameters obtained for specific tissue types when data obtained from 10 kHz to 80 kHz are trained.

TABLE 2

Tissue Type	Parameters	Value	Standard Error
End of Turbinate	α	0.082	0.009
	β	0.681	0.007
	f0	4539.116	193.596
	$\varepsilon 0$-$\varepsilon\infty$	9.858E6	170687.48
	$\varepsilon\infty$	1.54761E-10	--
Center of Turbinate	α	0	0.05358
	β	1	0.07788
	f0	3290.96	859.79
	$\varepsilon 0$-$\varepsilon\infty$	1.60E6	298682.17
	$\varepsilon\infty$	149101.39	11446.76
Near Blood Vessels	α	0.008	0.0118
	β	0.974	0.0174
	f0	3148.04	189.86
	$\varepsilon 0$-$\varepsilon\infty$	1.64E7	685597.97
	$\varepsilon\infty$	244034.20	26444.04
Upper Back Muscle	α	0	0.00467
	β	0.71561	0.0044
	f0	63.16	81.80
	$\varepsilon 0$-$\varepsilon\infty$	3.1E8	2.9E8
	$\varepsilon\infty$	241256.79	18021.68

Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic

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stimulation at a target site composed of a variety of tissue types. In particular, the systems and methods are able to, prior to treatment, characterize and identify tissue types and further identify specific levels of energy (i.e., specific target frequencies) to be delivered so as to cause only those intended, targeted tissues to exhibit dielectric relaxation phenomena and thus receive the energy for treatment, while non-targeted tissues remain intact and avoid collateral damage.

The following provides a detailed description of the various capabilities of systems and methods of the present invention, including, but not limited to, neuromodulation monitoring, feedback, and mapping capabilities, which, in turn, allowing for detection of anatomical structures and function, neural identification and mapping, and anatomical mapping, for example.

Neuromodulation Monitoring, Feedback, and Mapping Capabilities

As previously described, the system 100 includes a console 104 to which the device 102 is to be connected. The console 104 is configured to provide various functions for the device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the device 102. The console 104 can further be configured to generate a selected form and/or magnitude of energy for delivery to tissue or nerves at the target site via the end effector (214, 314), and therefore the console 104 may have different configurations depending on the treatment modality of the device 102. For example, when device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 includes an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy. When the device 102 is configured for cryotherapeutic treatment, the console 104 can include a refrigerant reservoir (not shown), and can be configured to supply the device 102 with refrigerant. Similarly, when the device 102 is configured for chemical-based treatment (e.g., drug infusion), the console 104 can include a chemical reservoir (not shown) and can be configured to supply the device 102 with one or more chemicals.

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In some embodiments, the console 104 may include a controller 107 communicatively coupled to the device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector (214, 314) directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, perform nerve mapping, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via mapping/evaluation/feedback algorithms 110. For example, the mapping/evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the location of other anatomical structures (e.g., vessels) at the treatment site, the temperature at the treatment site during monitoring and modulation, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the mapping/evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107 and the end effector (214, 314), can be configured to monitor neural activity and/or temperature at the treatment site during therapy and automatically shut off the energy delivery when the neural activity and/or temperature reaches a predetermined threshold (e.g., a threshold reduction in neural activity, a threshold maximum temperature when

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applying RF energy, or a threshold minimum temperature when applying cryotherapy). In other embodiments, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance or resistance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a display 112 (e.g., a monitor, touchscreen, user interface, etc.) on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104.

In various embodiments, the end effector (214, 314) and/or other portions of the system 100 can be configured to detect various bioelectric-parameters of the tissue at the target site, and this information can be used by the mapping/evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate neural tissue, differentiate between different types of neural tissue, map the anatomical and/or neural structure at the target site, and/or identify neuromodulation patterns of the end effector (214, 314) with respect to the patient's anatomy. For example, the end effector (214, 314) can be used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in the target region. In certain embodiments, the end effector (214, 314), together with the mapping/evaluation/feedback algorithms 110, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. The mapping/evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes (244, 336)).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-2000Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures and events, including the firing of neural tissue, differences between neural tissue and other anatomical structures (e.g., blood vessels), and event different types of neural tissue. This

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information can be analyzed by the mapping/evaluation/feedback algorithms and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural tissue and other anatomy at the treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode (244, 336) can be operated independently of the other electrodes (244, 336). For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes (244, 336) allows the end effector (214, 314) to detect information and deliver RF energy to highly customized regions. For example, a select portion of the electrodes (244, 336) can be activated to target specific neural fibers in a specific region while the other electrodes (244, 336) remain inactive. In certain embodiments, for example, electrodes (244, 336) may be activated across the portion of a strut that is adjacent to tissue at the target site, and the electrodes (244, 336) that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. In addition, the electrodes (244, 336) can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

The electrodes (244, 336) can be electrically coupled to the energy generator 106 via wires (not shown) that extend from the electrodes (244, 336), through the shaft 116, and to the energy generator 106. When each of the electrodes (244, 336) is independently controlled, each electrode (244, 336) couples to a corresponding wire that extends through the shaft 116. This allows each electrode (244, 336) to be independently activated for stimulation or neuromodulation to provide precise ablation patterns and/or individually detected via the console 104 to provide information specific to each electrode (244, 336) for neural or anatomical detection and mapping. In other embodiments, multiple electrodes (244, 336) can be controlled together and, therefore, multiple electrodes (244, 336) can be electrically coupled to the same wire extending through the shaft 116. The energy generator 16 and/or components (e.g., a control module) operably coupled thereto can include custom algorithms to control the activation of the electrodes (244, 336). For example, the RF generator can deliver RF power at about 200-

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100 W to the electrodes (244, 336), and do so while activating the electrodes (244, 336) in a predetermined pattern selected based on the position of the end effector (214, 314) relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the energy generator 106 delivers power at lower levels (e.g., less than 1 W, 1-5 W, 5-15 W, 15-50 W, 50-150 W, etc.) for stimulation and/or higher power levels. For example, the energy generator 106 can be configured to delivery stimulating energy pulses of 1-3 W via the electrodes (244, 336) to stimulate specific targets in the tissue.

As previously described, the end effector (214, 314) can further include one or more temperature sensors disposed on the struts and/or other portions of the end effector (214, 314) and electrically coupled to the console 104 via wires (not shown) that extend through the shaft 116. In various embodiments, the temperature sensors can be positioned proximate to the electrodes (244, 336) to detect the temperature at the interface between tissue at the target site and the electrodes (244, 336). In other embodiments, the temperature sensors can penetrate the tissue at the target site (e.g., a penetrating thermocouple) to detect the temperature at a depth within the tissue. The temperature measurements can provide the operator or the system with feedback regarding the effect of the therapeutic neuromodulation on the tissue. For example, in certain embodiments the operator may wish to prevent or reduce damage to the tissue at the treatment site, and therefore the temperature sensors can be used to determine if the tissue temperature reaches a predetermined threshold for irreversible tissue damage. Once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and avoid significant tissue sloughing during wound healing. In certain embodiments, the energy delivery can automatically terminate based on the mapping/evaluation/feedback algorithm 110 stored on the console 104 operably coupled to the temperature sensors.

In certain embodiments, the system 100 can determine the locations and/or morphology of neural tissue and/or other anatomical structures before therapy such that the therapeutic neuromodulation can be applied to precise regions including target neural tissue, while avoiding negative effects on non-target structures, such as blood vessels. As described in further detail below, the system 100 can detect various bioelectrical parameters in an interest zone to determine the location and morphology of various neural tissue (e.g., different types of neural tissue, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony

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regions, etc.). In some embodiments, the system 100 is configured to measure bioelectric potential. To do so, one or more of the electrodes (244, 336) is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies) are applied to the tissue by one or more electrodes (244, 336) at or near the treatment site, and the voltage and/or current differences at various different frequencies between various pairs of electrodes (244, 336) of the end effector (214, 314) may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural tissue, and/or other types of tissue) in the region of interest. For example, current (i.e., direct or alternating current) can be applied to a pair of electrodes (244, 336) adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes (244, 336) are measured. It will be appreciated that the current injection electrodes (244, 336) and measurement electrodes (244, 336) need not be adjacent, and that modifying the spacing between the two current injection electrodes (244, 336) can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes (244, 336) provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes (244, 336) that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector (214, 314)), and this information can be used to map the neural and anatomical structures by the use of frequency differentiation reconstruction. Applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters. At high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of the neural tissue do not impede current flow, and the current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids, ions, proteins and polysaccharides. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes and morphologies of

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the cells or cell densities or cell spacing. The stimulation frequencies can be in the megahertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

Further, the inherent morphology and composition of the anatomical structures in a given region or zone of the patient react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural tissue, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy. In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes (244, 336) at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces

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the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes (244, 336) and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes (244, 336) are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural tissue that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural tissue that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate the postganglionic parasympathetic neural fibers that innervate the mucosa at numerous neural entrance points within a given zone or region of a patient. Further, because there are not any clear anatomical markers denoting the location of the SPF, accessory foramen, and microforamina, the neural mapping allows the operator to identify and therapeutically modulate nerves that would otherwise be unidentifiable without intricate dissection of the mucosa. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the mapping/evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural

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activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

In various embodiments, the system 100 can also be configured to map the expected therapeutic modulation patterns of the electrodes (244, 336) at specific temperatures and, in certain embodiments, take into account tissue properties based on the anatomical mapping of the target site. For example, the system 100 can be configured to map the ablation pattern of a specific electrode ablation pattern at the 45° C. isotherm, the 55° C. isotherm, the 65° C. isotherm, and/or other temperature/ranges (e.g., temperatures ranging from 45° C. to 70° C. or higher) depending on the target site and/or structure.

The system 100 may provide, via the display 112, three-dimensional views of such projected ablation patterns of the electrodes (244, 336) of the end effector (214, 314). The ablation pattern mapping may define a region of influence that each electrode (244, 336) has on the surrounding tissue. The region of influence may correspond to the region of tissue that would be exposed to therapeutically modulating energy based on a defined electrode activation pattern (i.e., one, two, three, four, or more electrodes on any given strut). In other words, the ablation pattern mapping can be used to illustrate the ablation pattern of any number of electrodes (244, 336), any geometry of the electrode layout, and/or any ablation activation protocol (e.g., pulsed activation, multi-polar/sequential activation, etc.).

In some embodiments, the ablation pattern may be configured such that each electrode (244, 336) has a region of influence surrounding only the individual electrode (244, 336) (i.e., a "dot" pattern). In other embodiments, the ablation pattern may be such that two or more electrodes (244, 336) may link together to form a sub-grouped regions of influence that define peanut-like or linear shapes between two or more electrodes (244, 336). In further embodiments, the ablation pattern can result in a more expansive or contiguous pattern in which the region of influence extends along multiple electrodes (244, 336) (e.g., along each strut). In still further embodiments, the ablation pattern may result in different regions of influence depending upon the electrode activation pattern, phase angle, target temperature, pulse duration, device structure, and/or other treatment parameters. The three-dimensional views of the ablation patterns can be output to the display 112 and/or other user interfaces to allow the clinician to visualize the changing regions of influence based on different durations of energy application, different electrode activation sequences (e.g., multiplexing), different pulse sequences, different

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temperature isotherms, and/or other treatment parameters. This information can be used to determine the appropriate ablation algorithm for a patient's specific anatomy. In other embodiments, the three-dimensional visualization of the regions of influence can be used to illustrate the regions from which the electrodes (244, 336) detect data when measuring bioelectrical properties for anatomical mapping. In this embodiment, the three dimensional visualization can be used to determine which electrode activation pattern should be used to determine the desired properties (e.g., impedance, resistance, etc.) in the desired area. In certain embodiments, it may be better to use dot assessments, whereas in other embodiments it may be more appropriate to detect information from linear or larger contiguous regions.

In some embodiments, the mapped ablation pattern is superimposed on the anatomical mapping to identify what structures (e.g., neural tissue, vessels, etc.) will be therapeutically modulated or otherwise affected by the therapy. An image may be provided to the surgeon which includes a digital illustration of a predicted or planned neuromodulation zone in relation to previously identified anatomical structures in a zone of interest. For example, the illustration may show numerous neural tissue and, based on the predicted neuromodulation zone, identifies which neural tissue are expected to be therapeutically modulated. The expected therapeutically modulated neural tissue may be shaded to differentiate them from the non-affected neural tissue. In other embodiments, the expected therapeutically modulated neural tissue can be differentiated from the non-affected neural tissue using different colors and/or other indicators. In further embodiments, the predicted neuromodulation zone and surrounding anatomy (based on anatomical mapping) can be shown in a three dimensional view (and/or include different visualization features (e.g., color-coding to identify certain anatomical structures, bioelectric properties of the target tissue, etc.). The combined predicted ablation pattern and anatomical mapping can be output to the display 112 and/or other user interfaces to allow the clinician to select the appropriate ablation algorithm for a patient's specific anatomy.

The imaging provided by the system 100 allows the clinician to visualize the ablation pattern before therapy and adjust the ablation pattern to target specific anatomical structures while avoiding others to prevent collateral effects. For example, the clinician can select a treatment pattern to avoid blood vessels, thereby reducing exposure of the vessel to the therapeutic neuromodulation energy. This reduces the risk of damaging or rupturing vessels and, therefore, prevents immediate or latent bleeding. Further, the selective energy application

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provided by the neural mapping reduces collateral effects of the therapeutic neuromodulation, such as tissue sloughing off during wound healing (e.g., 1-3 weeks post ablation), thereby reducing the aspiration risk associated with the neuromodulation procedure.

The system 100 can be further configured to apply neuromodulation energy (via the electrodes (244, 336)) at specific frequencies attuned to the target neural structure and, therefore, specifically target desired neural tissue over non-target structures. For example, the specific neuromodulation frequencies can correspond to the frequencies identified as corresponding to the target structure during neural mapping. As described above, the inherent morphology and composition of the anatomical structures react differently to different frequencies. Thus, frequency-tuned neuromodulation energy tailored to a target structure does not have the same modulating effects on non-target structures. More specifically, applying the neuromodulation energy at the target-specific frequency causes ionic agitation in the target neural structure, leading to differentials in osmotic potentials of the targeted neural tissue and dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure). This causes degeneration, possibly resulting in vacuolar degeneration and, eventually, necrosis at the target neural structure, but is not expected to functionally affect at least some non-target structures (e.g., blood vessels). Accordingly, the system 100 can use the neural-structure specific frequencies to both (1) identify the locations of target neural tissue to plan electrode ablation configurations (e.g., electrode geometry and/or activation pattern) that specifically focus the neuromodulation on the target neural structure; and (2) apply the neuromodulation energy at the characteristic neural frequencies to selectively ablate the neural tissue responsive to the characteristic neural frequencies. For example, the end effector (214, 314) of the system 100 may selectively stimulate and/or modulate parasympathetic fibers, sympathetic fibers, sensory fibers, alpha/beta/delta fibers, C-fibers, anoxic terminals of one or more of the foregoing, insulated over non-insulated fibers (regions with fibers), and/or other neural tissue. In some embodiments, the system 100 may also selectively target specific cells or cellular regions during anatomical mapping and/or therapeutic modulation, such as smooth muscle cells, sub-mucosal glands, goblet cells, and stratified cellular regions within a given tissue type. Therefore, the system 100 provides highly selective neuromodulation therapy specific to targeted neural tissue, and reduces the collateral effects of neuromodulation therapy to non-target structures (e.g., blood vessels).

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The present disclosure provides a method of anatomical mapping and therapeutic neuromodulation. The method includes expanding an end effector (i.e., end effector (214, 314)) at a zone of interest ("interest zone"). For example, the end effector (214, 314) can be expanded such that at least some of the electrodes (244, 336) are placed in contact with tissue at the interest zone. The expanded device can then take bioelectric measurements via the electrodes (244, 336) and/or other sensors to ensure that the desired electrodes are in proper contact with the tissue at the interest zone. In some embodiments, for example, the system 100 detects the impedance and/or resistance across pairs of the electrodes (244, 336) to confirm that the desired electrodes have appropriate surface contact with the tissue and that all of the electrodes are (244, 336) functioning properly.

The method continues by optionally applying an electrical stimulus to the tissue, and detecting bioelectric properties of the tissue to establish baseline norms of the tissue. For example, the method can include measuring resistance, complex impedance, current, voltage, nerve firing rate, neuromagnetic field, muscular activation, and/or other parameters that are indicative of the location and/or function of neural tissue and/or other anatomical structures (e.g., glandular structures, blood vessels, etc.). In some embodiments, the electrodes (244, 336) send one or more stimulation signals (e.g., pulsed signals or constant signals) to the interest zone to stimulate neural activity and initiate action potentials. The stimulation signal can have a frequency attuned to a specific target structure (e.g., a specific neural structure, a glandular structure, a vessel) that allows for identification of the location of the specific target structure. The specific frequency of the stimulation signal is a function of the host permeability and, therefore, applying the unique frequency alters the tissue attenuation and the depth into the tissue the RF energy will penetrate. For example, lower frequencies typically penetrate deeper into the tissue than higher frequencies.

Pairs of the non-stimulating electrodes (244, 336) of the end effector (214, 314) can then detect one or more bioelectric properties of the tissue that occur in response to the stimulus, such as impedance or resistance. For example, an array of electrodes (e.g., the electrodes (244, 336)) can be selectively paired together in a desired pattern (e.g., multiplexing the electrodes (244, 336)) to detect the bioelectric properties at desired depths and/or across desired regions to provide a high level of spatial awareness at the interest zone. In certain embodiments, the electrodes (244, 336) can be paired together in a time-sequenced manner according to an

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algorithm (e.g., provided by the mapping/evaluation/feedback algorithms 110). In various embodiments, stimuli can be injected into the tissue at two or more different frequencies, and the resultant bioelectric responses (e.g., action potentials) in response to each of the injected frequencies can be detected via various pairs of the electrodes (244, 336). For example, an anatomical or neural mapping algorithm can cause the end effector (214, 314) to deliver pulsed RF energy at specific frequencies between different pairs of the electrodes (244, 336) and the resultant bioelectric response can be recorded in a time sequenced rotation until the desired interest zone is adequately mapped (i.e., "multiplexing"). For example, the end effector (214, 314) can deliver stimulation energy at a first frequency via adjacent pairs of the electrodes (244, 336) for a predetermined time period (e.g., 1-50 milliseconds), and the resultant bioelectric activity (e.g., resistance) can be detected via one or more other pairs of electrodes (244, 336) (e.g., spaced apart from each other to reach varying depths within the tissue). The end effector (214, 314) can then apply stimulation energy at a second frequency different from the first frequency, and the resultant bioelectric activity can be detected via the other electrodes. This can continue when the interest zone has been adequately mapped at the desired frequencies. As described in further detail below, in some embodiments the baseline tissue bioelectric properties (e.g., nerve firing rate) are detected using static detection methods (without the injection of a stimulation signal).

After detecting the baseline bioelectric properties, the information can be used to map anatomical structures and/or functions at the interest zone. For example, the bioelectric properties detected by the electrodes (244, 336) can be amazed via the mapping/evaluation/feedback algorithms 110, and an anatomical map can be output to a user via the display 112. In some embodiments, complex impedance, dielectric, or resistance measurements can be used to map parasympathetic nerves and, optionally, identify neural tissue in a diseased state of hyperactivity. The bioelectric properties can also be used to map other non-target structures and the general anatomy, such as blood vessels, bone, and/or glandular structures. The anatomical locations can be provided to a user (e.g., on the display 112) as a two-dimensional map (e.g., illustrating relative intensities, illustrating specific sites of potential target structures) and/or as a three-dimensional image. This information can be used to differentiate structures on a submicron, cellular level and identify very specific target structures (e.g., hyperactive parasympathetic nerves). The method can also predict the ablation patterns of

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the end effector (214, 314) based on different electrode neuromodulation protocol and, optionally, superimpose the predicted neuromodulation patterns onto the mapped anatomy to indicate to the user which anatomical structures will be affected by a specific neuromodulation protocol. For example, when the predicted neuromodulation pattern is displayed in relation to the mapped anatomy, a clinician can determine whether target structures will be appropriately ablated and whether non-target structures (e.g., blood vessels) will be undesirably exposed to the therapeutic neuromodulation energy. Thus, the method can be used for planning neuromodulation therapy to locate very specific target structures, avoid non-target structures, and select electrode neuromodulation protocols.

Once the target structure is located and a desired electrode neuromodulation protocol has been selected, the method continues by applying therapeutic neuromodulation to the target structure. The neuromodulation energy can be applied to the tissue in a highly targeted manner that forms micro-lesions to selectively modulate the target structure, while avoiding non-targeted blood vessels and allowing the surrounding tissue structure to remain healthy for effective wound healing. In some embodiments, the neuromodulation energy can be applied in a pulsed manner, allowing the tissue to cool between modulation pulses to ensure appropriate modulation without undesirably affecting non-target tissue. In some embodiments, the neuromodulation algorithm can deliver pulsed RF energy between different pairs of the electrodes (244, 336) in a time sequenced rotation until neuromodulation is predicted to be complete (i.e., "multiplexing"). For example, the end effector (214, 314) can deliver neuromodulation energy (e.g., having a power of 5-10 W (e.g., 7 W, 8 W, 9 W) and a current of about 50-100 mA) via adjacent pairs of the electrodes (244, 336) until at least one of the following conditions is met: (a) load resistance reaches a predefined maximum resistance (e.g., 350Ω); (b) a thermocouple temperature associated with the electrode pair reaches a predefined maximum temperature (e.g., 80° C.); or (c) a predetermined time period has elapsed (e.g., 10 seconds). After the predetermined conditions are met, the end effector (214, 314) can move to the next pair of electrodes in the sequence, and the neuromodulation algorithm can terminate when all of the load resistances of the individual pairs of electrodes is at or above a predetermined threshold (e.g., 100Ω). In various embodiments, the RF energy can be applied at a predetermined frequency (e.g., 450-500 kHz) and is expected to initiate ionic agitation of the specific target structure, while avoiding functional disruption of non-target structures.

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During and/or after neuromodulation therapy, the method continues by detecting and, optionally, mapping the post-therapy bioelectric properties of the target site. This can be performed in a similar manner as described above. The post-therapy evaluation can indicate if the target structures (e.g., hyperactive parasympathetic nerves) were adequately modulated or ablated. If the target structures are not adequately modulated (i.e., if neural activity is still detected in the target structure and/or the neural activity has not decreased), the method can continue by again applying therapeutic neuromodulation to the target. If the target structures were adequately ablated, the neuromodulation procedure can be completed.

Detection of Anatomical Structures and Function

Various embodiments of the present technology can include features that measure bio-electric, dielectric, and/or other properties of tissue at target sites to determine the presence, location, and/or activity of neural tissue and other anatomical structures and, optionally, map the locations of the detected neural tissue and/or other anatomical structures. For example, the present technology can be used to detect glandular structures and, optionally, their mucoserous functions and/or other functions. The present technology can also be configured to detect vascular structures (e.g., arteries) and, optionally, their arterial functions, volumetric pressures, and/or other functions. The mapping features discussed below can be incorporated into any the system 100 and/or any other devices disclosed herein to provide an accurate depiction of nerves at the target site.

Neural and/or anatomical detection can occur (a) before the application of a therapeutic neuromodulation energy to determine the presence or location of neural tissue and other anatomical structures (e.g., blood vessels, glands, etc.) at the target site and/or record baseline levels of neural activity; (b) during therapeutic neuromodulation to determine the real-time effect of the energy application on the neural fibers at the treatment site; and/or (c) after therapeutic neuromodulation to confirm the efficacy of the treatment on the targeted structures (e.g., nerves glands, etc.). This allows for the identification of very specific anatomical structures (even to the micro-scale or cellular level) and, therefore, provides for highly targeted neuromodulation. This enhances the efficacy and efficiency of the neuromodulation therapy. In addition, the anatomical mapping reduces the collateral effects of neuromodulation therapy to non-target sites. Accordingly, the targeted neuromodulation inhibits damage or rupture of blood vessels (i.e.,

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inhibits undesired bleeding) and collateral damage to tissue that may be of concern during wound healing (e.g., when damaged tissue sloughs off).

In certain embodiments, the systems disclosed herein can use bioelectric measurements, such as impedance, resistance, voltage, current density, and/or other parameters (e.g., temperature) to determine the anatomy, in particular the neural, glandular, and vascular anatomy, at the target site. The bioelectric properties can be detected after the transmission of a stimulus (e.g., an electrical stimulus, such as RF energy delivered via the electrodes (244, 336); i.e., "dynamic" detection) and/or without the transmission of a stimulus (i.e., "static" detection).

Dynamic measurements include various embodiments to excite and/or detect primary or secondary effects of neural activation and/or propagation. Such dynamic embodiments involve the heightened states of neural activation and propagation and use this dynamic measurement for nerve location and functional identification relative to the neighboring tissue types. For example, a method of dynamic detection can include: (1) delivering stimulation energy to a treatment site via a treatment device (e.g., the end effector) to excite parasympathetic nerves at the treatment site; (2) measuring one or more physiological parameters (e.g., resistance, impedance, etc.) at the treatment site via a measuring/sensing array of the treatment device (e.g., the electrodes (244, 336)); (4) based on the measurements, identifying the relative presence and position of parasympathetic nerves at the treatment site; and (5) delivering ablation energy to the identified parasympathetic nerves to block the detected para-sympathetic nerves.

Static measurements include various embodiments associated with specific native properties of the stratified or cellular composition at or near the treatment site. The static embodiments are directed to inherent biologic and electrical properties of tissue types at or near the treatment site, the stratified or cellular compositions at or near the treatment site, and contrasting both foregoing measurements with tissue types adjacent the treatment site (and that are not targeted for neuromodulation). This information can be used to localize specific targets (e.g., parasympathetic fibers) and non-targets (e.g., vessels, sensory nerves, etc.). For example, a method of static detection can include: (1) before ablation, utilizing a measuring/sensing array of a treatment device (e.g., the electrodes (244, 336)) to determine one or more baseline physiological parameters; (2) geometrically identifying inherent tissue properties within a region of interest based on the measured physiological parameters (e.g., resistance, impedance, etc.); (3) delivering ablation energy to one or more nerves within the region of via treatment device

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interest; (4) during the delivery of the ablation energy, determining one or more mid-procedure physiological parameters via the measuring/sensing array; and (5) after the delivery of ablation energy, determining one or more post-procedure physiological parameters via the measurement/sensing array to determine the effectiveness of the delivery of the ablation energy on blocking the nerves that received the ablation energy.

After the initial static and/or dynamic detection of bioelectric properties, the location of anatomical features can be used to determine where the treatment site(s) should be with respect to various anatomical structures for therapeutically effective neuromodulation of the targeted nerves. The bioelectric and other physiological properties described herein can be detected via electrodes (e.g., the electrodes (244, 336) of the end effector (214, 314)), and the electrode pairings on a device (e.g., end effector (214, 314)) can be selected to obtain the bioelectric data at specific zones or regions and at specific depths of the targeted regions. The specific properties detected at or surrounding target neuromodulation sites and associated methods for obtaining these properties are described below. These specific detection and mapping methods discussed below are described with reference to the system 100 , although the methods can be implemented on other suitable systems and devices that provide for anatomical identification, anatomical mapping and/or neuromodulation therapy.

Neural Identification and Mapping

In many neuromodulation procedures, it is beneficial to identify the portions of the nerves that fall within a zone and/or region of influence (referred to as the "interest zone") of the energy delivered by a device 102, as well as the relative three-dimensional position of the neural tissue relative to the device 102. Characterizing the portions of the neural tissue within the interest zone and/or determining the relative positions of the neural tissue within the interest zone enables the clinician to (1) selectively activate target neural tissue over non-target structures (e.g., blood vessels), and (2) sub-select specific targeted neural tissue (e.g., parasympathetic nerves) over non-target neural tissue (e.g., sensory nerves, subgroups of neural tissue, neural tissue having certain compositions or morphologies). The target structures (e.g., parasympathetic nerves) and non-target structures (e.g., blood vessels, sensory nerves, etc.) can be identified based on the inherent signatures of specific structures, which are defined by the unique morphological compositions of the structures and the bioelectrical properties associated

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with these morphological compositions. For example, unique, discrete frequencies can be associated with morphological compositions and, therefore, be used to identify certain structures. The target and non-target structures can also be identified based on relative bioelectrical activation of the structures to sub-select specific neural structures. Further, target and non-target structures can be identified by the differing detected responses of the structures to a tailored injected stimuli. For example, the systems described herein can detect the magnitude of response of structures and the difference in the responses of anatomical structures with respect to differing stimuli (e.g., stimuli injected at different frequencies).

At least for purposes of this disclosure, a nerve can include the following portions that are defined based on their respective orientations relative to the interest zone: terminating neural tissue (e.g., terminating axonal structures), branching neural tissue (e.g., branching axonal structures), and travelling neural tissue (e.g., travelling axonal structures). For example, terminating neural tissue enter the zone but do not exit. As such, terminating neural tissue are terminal points for neuronal signaling and activation. Branching neural tissue are nerves that enter the interest zone and increase number of nerves exiting the interest zone. Branching neural tissue are typically associated with a reduction in relative geometry of nerve bundle. Travelling neural tissue are nerves that enter the interest zone and exit the zone with no substantially no change in geometry or numerical value.

The system 100 can be used to detect voltage, current, complex impedance, resistance, permittivity, and/or conductivity, which are tied to the compound action potentials of nerves, to determine and/or map the relative positions and proportionalities of nerves in the interest zone. Neuronal cross-sectional area ("CSA") is expected to be due to the increase in axonic structures. Each axon is a standard size. Larger nerves (in cross-sectional dimension) have a larger number of axons than nerves having smaller cross-sectional dimensions. The compound action responses from the larger nerves, in both static and dynamic assessments, are greater than smaller nerves. This is at least in part because the compound action potential is the cumulative action response from each of the axons. When using static analysis, for example, the system 100 can directly measure and map impedance or resistance of nerves and, based on the determined impedance or resistance, determine the location of nerves and/or relative size of the nerves. In dynamic analysis, the system 100 can be used to apply a stimulus to the interest zone and detect the dynamic response of the neural tissue to the stimulus. Using this information, the system 100

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can determine and/or map impedance or resistance in the interest zone to provide information related to the neural positions or relative nerve sizes. Neural impedance mapping can be illustrated by showing the varying complex impedance levels at a specific location at differing cross-sectional depths. In other embodiments, neural impedance or resistance can be mapped in a three-dimensional display.

Identifying the portions and/or relative positions of the nerves within the interest zone can inform and/or guide selection of one or more treatment parameters (e.g., electrode ablation patterns, electrode activation plans, etc.) of the system 100 for improving treatment efficiency and efficacy. For example, during neural monitoring and mapping, the system 100 can identify the directionality of the nerves based at least in part on the length of the neural structure extending along the interest zone, relative sizing of the neural tissue, and/or the direction of the action potentials. This information can then be used by the system 100 or the clinician to automatically or manually adjust treatment parameters (e.g., selective electrode activation, bipolar and/or multipolar activation, and/or electrode positioning) to target specific nerves or regions of nerves. For example, the system 100 can selectively activate specific electrodes (244, 336), electrode combinations (e.g., asymmetric or symmetric), and/or adjust the bi-polar or multi-polar electrode configuration. In some embodiments, the system 100 can adjust or select the waveform, phase angle, and/or other energy delivery parameters based on the nerve portion/position mapping and/or the nerve proportionality mapping. In some embodiments, structure and/or properties of the electrodes (244, 336) themselves (e.g., material, surface roughening, coatings, cross-sectional area, perimeter, penetrating, penetration depth, surface-mounted, etc.) may be selected based on the nerve portion and proportionality mapping.

In various embodiments, treatment parameters and/or energy delivery parameters can be adjusted to target on-axis or near axis travelling neural tissue and/or avoid the activation of traveling neural tissue that are at least generally perpendicular to the end effector (214, 314). Greater portions of the on-axis or near axis travelling neural tissue are exposed and susceptible to the neuromodulation energy provided by the end effector (214, 314) than a perpendicular travelling neural structure, which may only be exposed to therapeutic energy at a discrete cross-section. Therefore, the end effector (214, 314) is more likely to have a greater effect on the on-axis or near axis travelling neural tissue. The identification of the neural structure positions (e.g., via complex impedance or resistance mapping) can also allow targeted energy delivery to

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travelling neural tissue rather than branching neural tissue (typically downstream of the travelling neural tissue) because the travelling neural tissue are closer to the nerve origin and, therefore, more of the nerve is affected by therapeutic neuromodulation, thereby resulting in a more efficient treatment and/or a higher efficacy of treatment. Similarly, the identification of neural structure positions can be used to target travelling and branching neural tissue over terminal neural tissue. In some embodiments, the treatment parameters can be adjusted based on the detected neural positions to provide a selective regional effect. For example, a clinician can target downstream portions of the neural tissue if only wanting to influence partial effects on very specific anatomical structures or positions.

In various embodiments, neural locations and/or relative positions of nerves can be determined by detecting the nerve-firing voltage and/or current over time. An array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone, and the electrodes (244, 336) can measure the voltage and/or current associated with nerve-firing. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves in a hyper state (i.e., excessive parasympathetic tone). Rhinitis is at least in part the result of over-firing nerves because this hyper state drives the hyper-mucosal production and hyper-mucosal secretion. Therefore, detection of nerve firing rate via voltage and current measurements can be used to locate the portions of the interest region that include hyper-parasympathetic neural function (i.e., nerves in the diseased state). This allows the clinician to locate specific nerves (i.e., nerves with excessive parasympathetic tone) before neuromodulation therapy, rather than simply targeting all parasympathetic nerves (including non-diseased state parasympathetic nerves) to ensure that the correct tissue is treated during neuromodulation therapy. Further, nerve firing rate can be detected during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy. For example, recording decreases or elimination of nerve firing rate after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In various embodiments, the system 100 can detect neural activity using dynamic activation by injecting a stimulus signal (i.e., a signal that temporarily activates nerves) via one or more of the electrodes (244, 336) to induce an action potential, and other pairs of electrodes (244, 336) can detect bioelectric properties of the neural response. Detecting neural tissue using dynamic activation involves detecting the locations of action potentials within the interest zone

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by measuring the discharge rate in neurons and the associated processes. The ability to numerically measure, profile, map, and/or image fast neuronal depolarization for generating an accurate index of activity is a factor in measuring the rate of discharge in neurons and their processes. The action potential causes a rapid increase in the voltage across nerve fiber and the electrical impulse then spreads along the fiber. As an action potential occurs, the conductance of a neural cell membrane changes, becoming about 40 times larger than it is when the cell is at rest. During the action potential or neuronal depolarization, the membrane resistance diminishes by about 80 times, thereby allowing an applied current to enter the intracellular space as well. Over a population of neurons, this leads to a net decrease in the resistance during coherent neuronal activity, such as chronic para-sympathetic responses, as the intracellular space will provide additional conductive ions. The magnitude of such fast changes has been estimated to have local resistivity changes with recording near DC is 2.8-3.7% for peripheral nerve bundles.

Detecting neural tissue using dynamic activation includes detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The basis of each this discharge is the action potential, during which there is a depolarization of the neuronal membrane of up to 110 mV or more, lasting approximately 2 milliseconds, and due to the transfer of micromolar quantities of ions (e.g., sodium and potassium) across the cellular membrane. The complex impedance or resistance change due to the neuronal membrane falls from 1000 to 25 Ωcm. The introduction of a stimulus and subsequent measurement of the neural response can attenuate noise and improve signal to noise ratios to precisely focus on the response region to improve neural detection, measurement, and mapping.

In some embodiments, the difference in measurements of physiological parameters (e.g., complex impedance, resistance, voltage) over time, which can reduce errors, can be used to create a neural profiles, spectrums, or maps. For example, the sensitivity of the system 100 can be improved because this process provides repeated averaging to a stimulus. As a result, the mapping function outputs can be a unit-less ratio between the reference and test collated data at a single frequency and/or multiple frequencies and/or multiple amplitudes. Additional considerations may include multiple frequency evaluation methods that consequently expand the parameter assessments, such as resistivity, admittivity, center frequency, or ratio of extra- to intracellular resistivity.

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In some embodiments, the system 100 may also be configured to indirectly measure the electrical activity of neural tissue to quantify the metabolic recovery processes that accompany action potential activity and act to restore ionic gradients to normal. These are related to an accumulation of ions in the extracellular space. The indirect measurement of electrical activity can be approximately a thousand times larger (in the order of millimolar), and thus are easier to measure and can enhance the accuracy of the measured electrical properties used to generate the neural maps.

The system 100 can perform dynamic neural detection by detecting nerve-firing voltage and/or current and, optionally, nerve firing rate over time, in response to an external stimulation of the nerves. For example, an array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone, one or more of the electrodes (244, 336) can be activated to inject a signal into the tissue that stimulates the nerves, and other electrodes (244, 336) of the electrode array can measure the neural voltage and/or current due to nerve firing in response to the stimulus. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves and, in certain embodiments, identify parasympathetic nerves in a hyper state (e.g., indicative of Rhinitis or other diseased state). The dynamic detection of neural activity (voltage, current, firing rate, etc.) can be performed before neuromodulation therapy to detect target nerve locations to select the target site and treatment parameters to ensure that the correct tissue is treated during neuromodulation therapy. Further, dynamic detection of neural activity can be performed during or after neuromodulation therapy to allow the clinician to monitor changes in neural activity to validate treatment efficacy. For example, recording decreases or elimination of neural activity after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In some embodiments, a stimulating signal can be delivered to the vicinity of the targeted nerve via one or more penetrating electrodes (e.g., microneedles that penetrate tissue) associated with the end effector (214, 314) and/or a separate device. The stimulating signal generates an action potential, which causes smooth muscle cells or other cells to contract. The location and strength of this contraction can be detected via the penetrating electrode(s) and, thereby, indicate to the clinician the distance to the nerve and/or the location of the nerve relative to the stimulating needle electrode. In some embodiments, the stimulating electrical signal may have a voltage of typically 1-2 mA or greater and a pulse width of typically 100-200 microseconds or

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greater. Shorter pulses of stimulation result in better discrimination of the detected contraction, but may require more current. The greater the distance between the electrode and the targeted nerve, the more energy is required to stimulate. The stimulation and detection of contraction strength and/or location enables identification of how close or far the electrodes are from the nerve, and therefore can be used to localize the nerve spatially. In some embodiments, varying pulse widths may be used to measure the distance to the nerve. As the needle becomes closer to the nerve, the pulse duration required to elicit a response becomes less and less.

To localize nerves via muscle contraction detection, the system 100 can vary pulse-width or amplitude to vary the energy (Energy=pulse-width*amplitude) of the stimulus delivered to the tissue via the penetrating electrode(s). By varying the stimulus energy and monitoring muscle contraction via the penetrating electrodes and/or other type of sensor, the system 100 can estimate the distance to the nerve. If a large amount of energy is required to stimulate the nerve/contract the muscle, the stimulating/penetrating electrode is far from the nerve. As the stimulating/penetrating electrode, moves closer to the nerve, the amount of energy required to induce muscle contraction will drop. For example, an array of penetrating electrodes can be positioned in the tissue at the interest zone and one or more of the electrodes can be activated to apply stimulus at different energy levels until they induce muscle contraction. Using an iterative process, localize the nerve (e.g., via the mapping/evaluation/feedback algorithm 110).

In some embodiments, the system 100 can measure the muscular activation from the nerve stimulus (e.g., via the electrodes (244, 336)) to determine neural positioning for neural mapping, without the use of penetrating electrodes. In this embodiment, the treatment device targets the smooth muscle cells' varicosities surrounding the submucosal glands and the vascular supply, and then the compound muscle action potential. This can be used to summate voltage response from the individual muscle fiber action potentials. The shortest latency is the time from stimulus artifact to onset of the response. The corresponding amplitude is measured from baseline to negative peak and measured in millivolts (mV). Nerve latencies (mean±SD) in adults typically range about 2-6 milliseconds, and more typically from about 3.4±0.8 to about 4.0±0.5 milliseconds.

In some embodiments, the system 100 can record a neuromagnetic field outside of the nerves to determine the internal current of the nerves without physical disruption of the nerve membrane. Without being bound by theory, the contribution to the magnetic field from the

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current inside the membrane is two orders of magnitude larger than that from the external current, and that the contribution from current within the membrane is substantially negligible. Electrical stimulation of the nerve in tandem with measurements of the magnetic compound action fields ("CAFs") can yield sequential positions of the current dipoles such that the location of the conduction change can be estimated (e.g., via the least-squares method). Visual representation (e.g., via the display 112) using magnetic contour maps can show normal or non-normal neural characteristics (e.g., normal can be equated with a characteristic quadrupolar pattern propagating along the nerve), and therefore indicate which nerves are in a diseases, hyperactive state and suitable targets for neuromodulation.

During magnetic field detection, an array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes (244, 336) can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire), and therefore changing magnetic fields are indicative of the nerve nerve-firing rate. The changing magnetic field caused by neural firing can induce a current detected by nearby sensor wire (e.g., the sensor 314) and/or wires associated with the nearby electrodes (244, 336). By measuring this current, the magnetic field strength can be determined. The magnetic fields can optionally be mapped (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. Further, the magnetic field information can be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In other embodiments, the neuromagnetic field is measured with a Hall Probe or other suitable device, which can be integrated into the end effector (214, 314) and/or part of a separate device delivered to the interest zone. Alternatively, rather than measuring the voltage in the second wire, the changing magnetic field can be measured in the original wire (i.e. the nerve) using a Hall probe. A current going through the Hall probe will be deflected in the semi-conductor. This will cause a voltage difference between the top and bottom portions, which can be measured. In some aspects of this embodiments, three orthogonal planes are utilized.

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In some embodiments, the system 100 can be used to induce electromotive force ("EMF") in a wire (i.e., a frequency-selective circuit, such as a tunable/LC circuit) that is tunable to resonant frequency of a nerve. In this embodiment, the nerve can be considered to be a current carrying wire, and the firing action potential is a changing voltage. This causes a changing current which, in turn, causes a changing magnetic flux (i.e., the magnetic field that is perpendicular to the wire). Under Faraday's Law of Induction/Faraday's Principle, the changing magnetic flux induces EMF (including a changing voltage) in a nearby sensor wire (e.g., integrated into the end effector (214, 314), the sensor 314, and/or other structure), and the changing voltage can be measured via the system 100.

In further embodiments, the sensor wire (e.g., the sensor 314) is an inductor and, therefore, provides an increase of the magnetic linkage between the nerve (i.e., first wire) and the sensor wire (i.e., second wire), with more turns for increasing effect. (e.g., $V2,rms=V1,rms(N2/N1)$). Due to the changing magnetic field, a voltage is induced in the sensor wire, and this voltage can be measured and used to estimate current changes in the nerve. Certain materials can be selected to enhance the efficiency of the EMF detection. For example, the sensor wire can include a soft iron core or other high permeability material for the inductor.

During induced EMF detection, the end effector (214, 314) and/or other device including a sensor wire is positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes (244, 336) can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire) that induces a current in the sensor wire (e.g., the sensor 314). This information can be used to determine neural location and/or map the nerves (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. EMF information can also be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In some embodiments, the system 100 can detect magnetic fields and/or EMF generated at a selected frequency that corresponds to a particular type of nerve. The frequency and, by extension, the associated nerve type of the detected signal can be selected based on an external resonant circuit. Resonance occurs on the external circuit when it is matched to the frequency of

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the magnetic field of the particular nerve type and that nerve is firing. In manner, the system 100 can be used to locate a particular sub-group/type of nerves.

In some embodiments, the system 100 can include a variable capacitor frequency-selective circuit to identify the location and/or map specific nerves (e.g., parasympathetic nerve, sensory nerve, nerve fiber type, nerve subgroup, etc.). The variable capacitor frequency-selective circuit can be defined by the sensor 314 and/or other feature of the end effector (214, 314). Nerves have different resonant frequencies based on their function and structure. Accordingly, the system 100 can include a tunable LC circuit with a variable capacitor (C) and/or variable inductor (L) that can be selectively tuned to the resonant frequency of desired nerve types. This allows for the detection of neural activity only associated with the selected nerve type and its associated resonant frequency. Tuning can be achieved by moving the core in and out of the inductor. For example, tunable LC circuits can tune the inductor by: (i) changing the number of coils around the core; (ii) changing the cross-sectional area of the coils around the core; (iii) changing the length of the coil; and/or (iv) changing the permeability of the core material (e.g., changing from air to a core material). Systems including such a tunable LC circuit provide a high degree of dissemination and differentiation not only as to the activation of a nerve signal, but also with respect to the nerve type that is activated and the frequency at which the nerve is firing.

Anatomical Mapping

In various embodiments, the system 100 is further configured to provide minimally-invasive anatomical mapping that uses focused energy current/voltage stimuli from a spatially localized source (e.g., the electrodes (244, 336)) to cause a change in the conductivity of the of the tissue at the interest zone and detect resultant biopotential and/or bioelectrical measurements (e.g., via the electrodes (244, 336)). The current density in the tissue changes in response to changes of voltage applied by the electrodes (244, 336), which creates a change in the electric current that can be measured with the end effector (214, 314) and/or other portions of the system 100. The results of the bioelectrical and/or biopotential measurements can be used to predict or estimate relative absorption profilometry to predict or estimate the tissue structures in the interest zone. More specifically, each cellular construct has unique conductivity and absorption profiles that can be indicative of a type of tissue or structure, such as bone, soft tissue, vessels, nerves,

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types of nerves, and/or certain neural tissue. For example, different frequencies decay differently through different types of tissue. Accordingly, by detecting the absorption current in a region, the system 100 can determine the underlying structure and, in some instances, to a sub-microscale, cellular level that allows for highly specialized target localization and mapping. This highly specific target identification and mapping enhances the efficacy and efficiency of neuromodulation therapy, while also enhancing the safety profile of the system 100 to reduce collateral effects on non-target structures.

To detect electrical and dielectric tissue properties (e.g., resistance, complex impedance, conductivity, and/or, permittivity as a function of frequency), the electrodes (244, 336) and/or another electrode array is placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli (current/voltage) to the tissue. The electrical properties of the tissue between the source and the receiver electrodes (244, 336) are measured, as well as the current and/or voltage at the individual receiver electrodes (244, 336). These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest and, in certain embodiments, the location of firing nerves. For example, the anatomical mapping can be provided as a color-coded or gray-scale three-dimensional or two-dimensional map showing differing intensities of certain bioelectric properties (e.g., resistance, impedance, etc.), or the information can be processed to map the actual anatomical structures for the clinician. This information can also be used during neuromodulation therapy to monitor treatment progression with respect to the anatomy, and after neuromodulation therapy to validate successful treatment. In addition, the anatomical mapping provided by the bioelectrical and/or biopotential measurements can be used to track the changes to non-target tissue (e.g., vessels) due to neuromodulation therapy to avoid negative collateral effects. For example, a clinician can identify when the therapy begins to ligate a vessel and/or damage tissue, and modify the therapy to avoid bleeding, detrimental tissue ablation, and/or other negative collateral effects.

Furthermore, the threshold frequency of electric current used to identify specific targets can subsequently be used when applying therapeutic neuromodulation energy. For example, the neuromodulation energy can be applied at the specific threshold frequencies of electric current that are target neuronal-specific and differentiated from other non-targets (e.g., blood vessels, non-target nerves, etc.). Applying ablation energy at the target-specific frequency results in an

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electric field that creates ionic agitation in the target neural structure, which leads to differentials in osmotic potentials of the targeted neural tissue. These osmotic potential differentials cause dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure) that lead to vacuolar degeneration of the targeted neural tissue and, eventually, necrosis. Using the highly targeted threshold neuromodulation energy to initiate the degeneration allows the system 100 to deliver therapeutic neuromodulation to the specific target, while surrounding blood vessels and other non-target structures are functionally maintained.

In some embodiments, the system 100 can further be configured to detect bioelectrical properties of tissue by non-invasively recording resistance changes during neuronal depolarization to map neural activity with electrical impedance, resistance, bio-impedance, conductivity, permittivity, and/or other bioelectrical measurements. Without being bound by theory, when a nerve depolarizes, the cell membrane resistance decreases (e.g., by approximately 80×) so that current will pass through open ion channels and into the intracellular space. Otherwise the current remains in the extracellular space. For non-invasive resistance measurements, tissue can be stimulated by applying a current of less than 100 Hz, such as applying a constant current square wave at 1 Hz with an amplitude less than 25% (e.g., 10%) of the threshold for stimulating neuronal activity, and thereby preventing or reducing the likelihood that the current does not cross into the intracellular space or stimulating at 2 Hz. In either case, the resistance and/or complex impedance is recorded by recording the voltage changes. A complex impedance or resistance map or profile of the area can then be generated.

For impedance/conductivity/permittivity detection, the electrodes (244, 336) and/or another electrode array are placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli to the tissue, and the current and/or voltage at the individual receiver electrodes (244, 336) is measured. The stimuli can be applied at different frequencies to isolate different types of nerves. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest. The neural mapping can also be used during neuromodulation therapy to select specific nerves for therapy, monitor treatment progression with respect to the nerves and other anatomy, and validate successful treatment.

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In some embodiments of the neural and/or anatomical detection methods described above, the procedure can include comparing the mid-procedure physiological parameter(s) to the baseline physiological parameter(s) and/or other, previously-acquired mid-procedure physiological parameter(s) (within the same energy delivery phase). Such a comparison can be used to analyze state changes in the treated tissue. The mid-procedure physiological parameter(s) may also be compared to one or more predetermined thresholds, for example, to indicate when to stop delivering treatment energy. In some embodiments of the present technology, the measured baseline, mid-, and post-procedure parameters include a complex impedance. In some embodiments of the present technology, the post-procedure physiological parameters are measured after a pre-determined time period to allow the dissipation of the electric field effects (ionic agitation and/or thermal thresholds), thus facilitating accurate assessment of the treatment.

In some embodiments, the anatomical mapping methods described above can be used to differentiate the depth of soft tissues within the nasal mucosa. The depth of mucosa on the turbinates is relatively deep while the depth off the turbinate is relatively shallow and, therefore, identifying the tissue depth in the present technology also identifies positions within the nasal mucosa and where precisely to target. Further, by providing the micro-scale spatial impedance mapping of epithelial tissues as described above, the inherent unique signatures of stratified layers or cellular bodies can be used as identifying the region of interest. For example, different regions have larger or small populations of specific structures, such as submucosal glands, so target regions can be identified via the identification of these structures.

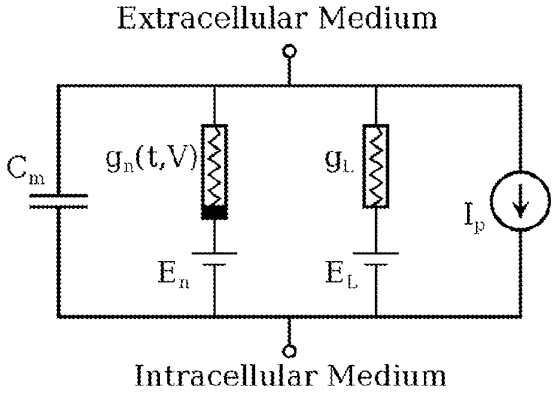
In some embodiments, the system 100 includes additional features that can be used to detect anatomical structures and map anatomical features. For example, the system 100 can include an ultrasound probe for identification of neural tissue and/or other anatomical structures. Higher frequency ultrasound provides higher resolution, but less depth of penetration. Accordingly, the frequency can be varied to achieve the appropriate depth and resolution for neural/anatomical localization. Functional identification may rely on the spatial pulse length ("SPL") (wavelength multiplied by number of cycles in a pulse). Axial resolution (SPL/2) may also be determined to locate nerves.

In some embodiments, the system 100 can further be configured to emit stimuli with selective parameters that suppress rather than fully stimulate neural activity. For example, in

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embodiments where the strength-duration relationship for extracellular neural stimulation is selected and controlled, a state exists where the extracellular current can hyperpolarize cells, resulting in suppression rather than stimulation spiking behavior (i.e., a full action potential is not achieved). Both models of ion channels, Hodgkin–Huxley (HH) and Retinol Ganglion Cell (RGC), suggest that it is possible to hyperpolarize cells with appropriately designed burst extracellular stimuli, rather than extending the stimuli. This phenomenon could be used to suppress, rather than stimulate, neural activity during any of the embodiments of neural detection and/or modulation described herein.

As generally understood , the Hodgkin–Huxley (HH) model, or conductance-based model, is a mathematical model that describes how action potentials in neurons are initiated and propagated. It is a set of nonlinear differential equations that approximates the electrical characteristics of excitable cells such as neurons and cardiac myocytes and is a continuous-time dynamical system. A Hodgkin–Huxley type model represents the biophysical characteristic of cell membranes, as illustrated in the schematic diagram below:



The lipid bilayer is represented as a capacitance (C_m). Voltage-gated and leak ion channels are represented by nonlinear (g_n) and linear (g_L) conductances, respectively. The electrochemical gradients driving the flow of ions are represented by batteries (E), and ion pumps and exchangers are represented by current sources (I_p).

A retinal ganglion cell (RGC) is a type of neuron located near the inner surface (the ganglion cell layer) of the retina of the eye. It receives visual information from photoreceptors via two intermediate neuron types: bipolar cells and retina amacrine cells. Retina amacrine cells, particularly narrow field cells, are important for creating functional subunits within the ganglion

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cell layer and making it so that ganglion cells can observe a small dot moving a small distance. Retinal ganglion cells collectively transmit image-forming and non-image forming visual information from the retina in the form of action potential to several regions in the thalamus, hypothalamus, and mesencephalon, or midbrain. The six types of retinal neurons are bipolar cells, ganglion cells, horizontal cells, retina amacrine cells, and rod and cone photoreceptors.

In various embodiments, the system 100 could apply the anatomical mapping techniques disclosed herein to locate or detect the targeted vasculature and surrounding anatomy before, during, and/or after treatment.

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes.

Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein. The subject matter herein contains important information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment. Thus, appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments.

The terms and expressions which have been employed herein are used as terms of description and not of limitation, and there is no intention, in the use of such terms and expressions, of excluding any equivalents of the features shown and described (or portions

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thereof), and it is recognized that various modifications are possible within the scope of the claims. Accordingly, the claims are intended to cover all such equivalents.

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Claims

What is claimed is:

1. A method for treating a condition, the method comprising:

providing a device comprising an end effector including a plurality of electrodes and a controller operably associated with the device;

positioning the end effector at a target site associated with a patient;

receiving, via the controller, data from the device associated with bioelectric properties of one or more tissues at the target site;

processing, via the controller, the data to identify a type of each of the one or more tissues at the target site and further identify a dielectric relaxation pattern for each of the one or more identified tissue types; and

determining, via the controller, an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified dielectric relaxation patterns, wherein ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

2. The method of claim 1, wherein a subset of the plurality of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site.

3. The method of claim 1, wherein the bioelectric properties comprise at least one of complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

4. The method of claim 3, wherein the dielectric properties comprise at least a complex, real and imaginary relative dielectric permittivity.

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5. The method of claim 1, wherein the processing of the data, via the controller, comprises comparing the data received from the device with electric signature data associated with a plurality of known tissue types.

6. The method of claim 5, wherein the electric signature data comprises at least bioelectric properties and dielectric relaxation patterns of known tissue types.

7. The method of claim 6, wherein the dielectric relaxation patterns comprise at least one of a Maxwell-Wagner-Sillar (MWS) relaxation pattern, ionic relation pattern, and dielectric relaxation pattern.

8. The method of claim 5, wherein the comparison comprises correlating the data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

9. The method of claim 1, wherein the ablation energy is tuned to a target frequency associated with relaxation patterns of the targeted tissue.

10. The method of claim 9, wherein the target frequency comprises a frequency at which the targeted tissue exhibits relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior.

11. The method of claim 10, wherein delivery of the ablation energy, tuned to the target frequency, penetrates a membrane of one or more cells associated only with the targeted tissue.

12. The method of claim 1, wherein condition comprises a peripheral neurological condition.

13. The method of claim 12, wherein the peripheral neurological condition is associated with a nasal condition or a non-nasal condition of the patient.

14. The method of claim 13, wherein the non-nasal condition comprises atrial fibrillation (AF).

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15. The method of claim 13, wherein the nasal condition comprises rhinosinusitis.

16. The method of claim 15, wherein the target site is within a sino-nasal cavity of the patient.

17. The method of claim 16, wherein delivery of the ablation energy results in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient.

18. The method of claim 17, wherein the targeted tissue is proximate or inferior to a sphenopalatine foramen.

19. The method of claim 18, wherein delivery of the ablation energy results in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient.

20. The method of claim 19, wherein delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone.

21. The method of claim 17, wherein delivery of the ablation energy causes thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose.

22. The method of claim 21, wherein the resulting local hypoxia of the mucus producing and/or mucosal engorgement elements results in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient.

23. A system for treating a condition, the system comprising:

a device comprising an end effector including a plurality of electrodes; and

a controller operably associated with the device and configured to:

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receive data from the device associated with bioelectric properties of one or more tissues at the target site;

process the data to identify a type of each of the one or more tissues at the target site and further identify a relaxation pattern(s) for each of the one or more identified tissue types; and

determine an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified relaxation patterns, wherein ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

24. The system of claim 23, wherein a subset of the plurality of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site.

25. The system of claim 23, wherein the bioelectric properties comprise at least one of complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

26. The system of claim 25, wherein the dielectric properties comprise at least a complex relative dielectric permittivity.

27. The system of claim 23, wherein the processing of the data comprises comparing the data received from the device with electric signature data associated with a plurality of known tissue types.

28. The system of claim 27, wherein the electric signature data comprises at least bioelectric properties and relaxation patterns of known tissue types.

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29. The method of claim 28, wherein the dielectric relaxation patterns comprise at least one of a Maxwell-Wagner-Sillar (MWS) relaxation pattern, ionic relation pattern, and dielectric relaxation pattern.

30. The method of claim 27, wherein the comparison comprises correlating the data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

31. The system of claim 23, wherein the ablation energy is tuned to a target frequency associated with a dielectric relaxation pattern of the targeted tissue.

32. The system of claim 31, wherein the target frequency comprises a frequency at which the targeted tissue exhibits relaxation phenomena behavior and the non-targeted tissue does not exhibit relaxation phenomena behavior.

33. The system of claim 32, wherein delivery of the ablation energy, tuned to the target frequency, penetrates a membrane of one or more cells associated only with the targeted tissue.

34. The system of claim 23, wherein condition comprises a peripheral neurological condition.

35. The system of claim 34, wherein the peripheral neurological condition is associated with a nasal condition or a non-nasal condition of the patient.

36. The system of claim 35, wherein the non-nasal condition comprises atrial fibrillation (AF).

37. The system of claim 35, wherein the nasal condition comprises rhinosinusitis.

38. The system of claim 37, wherein the target site is within a sino-nasal cavity of the patient.

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39. The system of claim 38, wherein delivery of the ablation energy results in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient.

40. The system of claim 39, wherein the targeted tissue is proximate or inferior to a sphenopalatine foramen.

41. The system of claim 40, wherein delivery of the ablation energy results in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient.

42. The system of claim 41, wherein delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone.

43. The system of claim 39, wherein delivery of the ablation energy causes thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose.

44. The system of claim 43, wherein the resulting local hypoxia of the mucus producing and/or mucosal engorgement elements results in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient.

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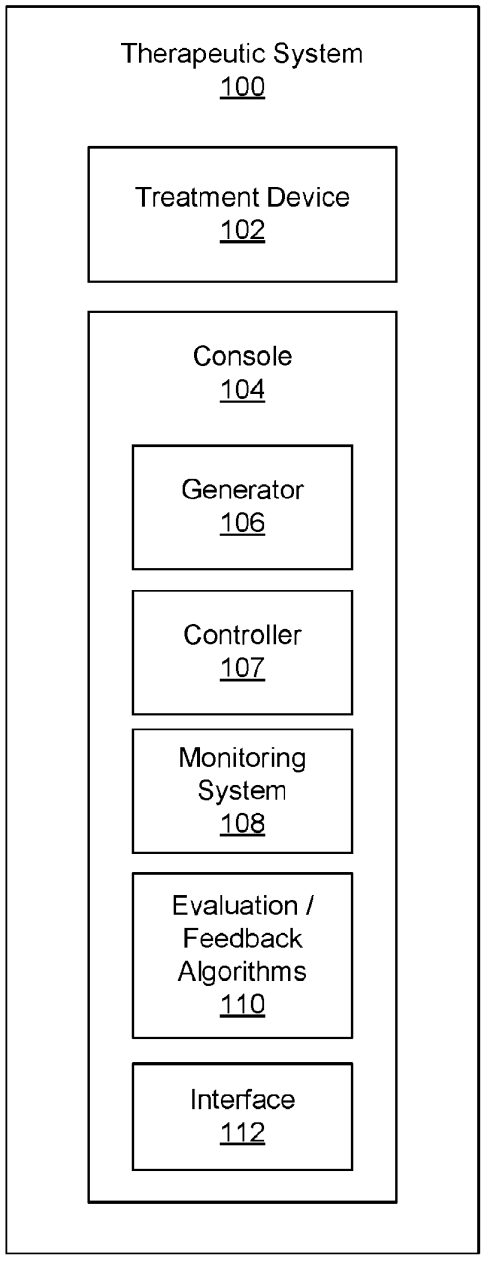


FIG. 1A

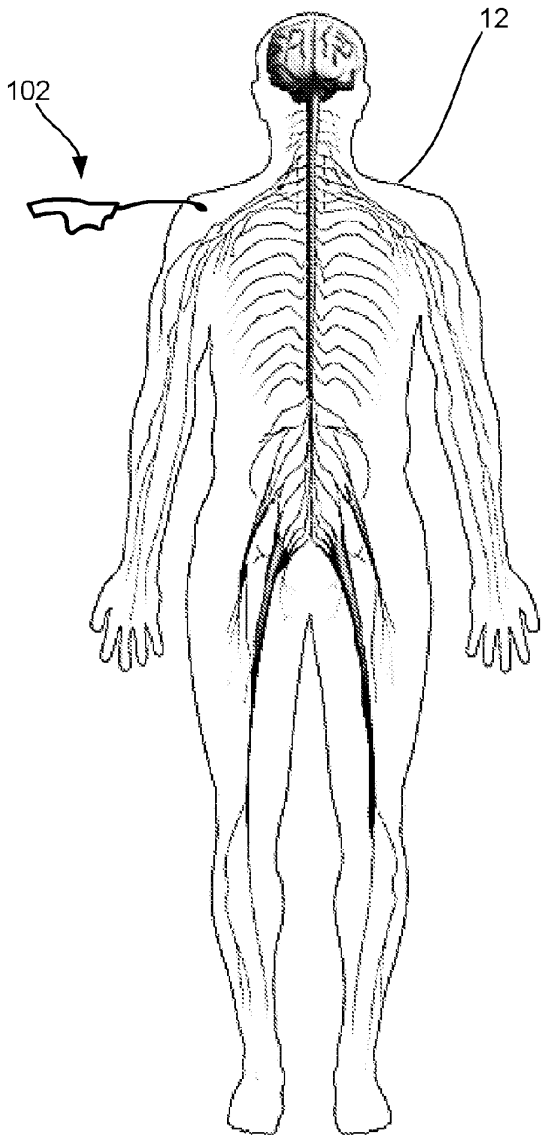


FIG. 1B

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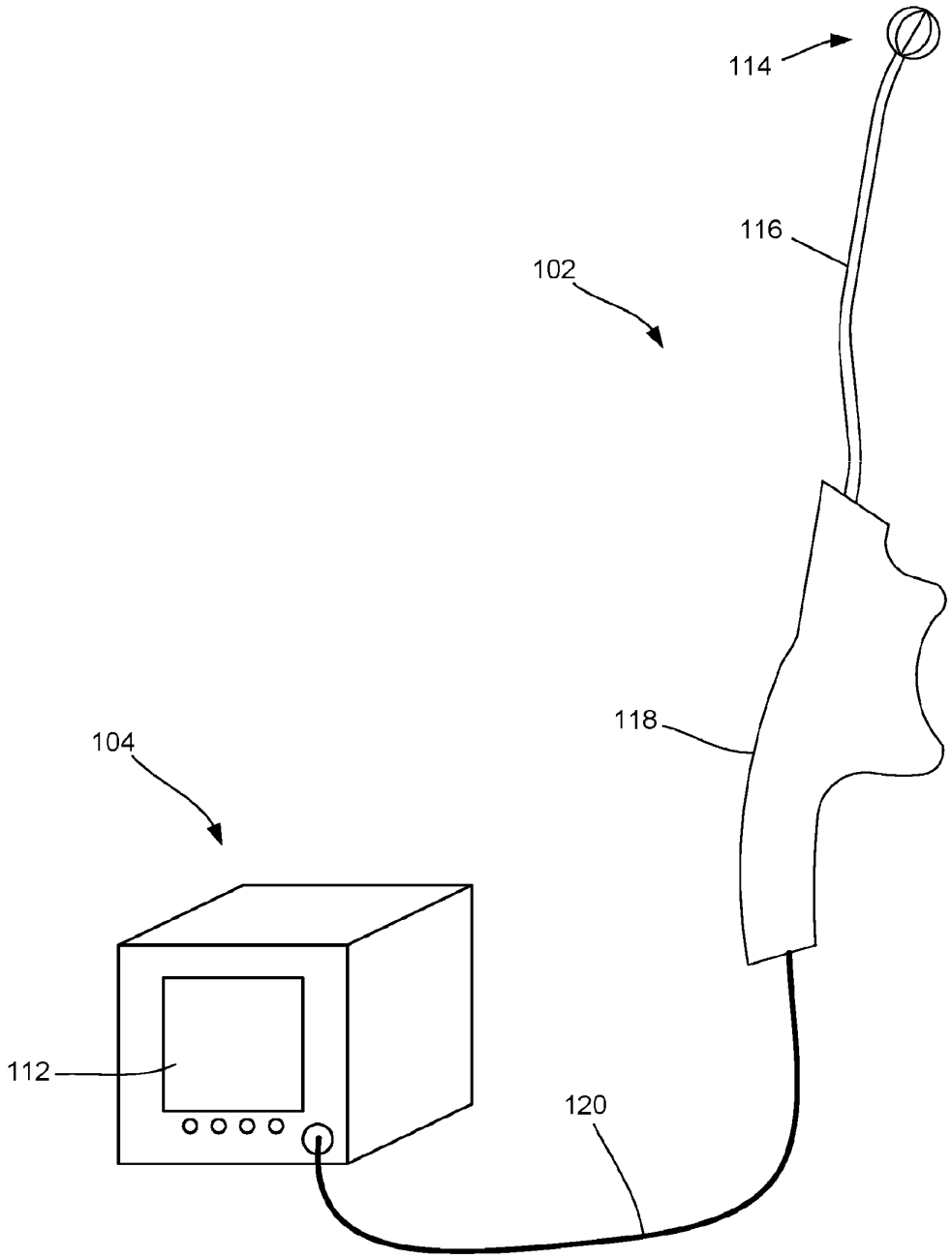


FIG. 2

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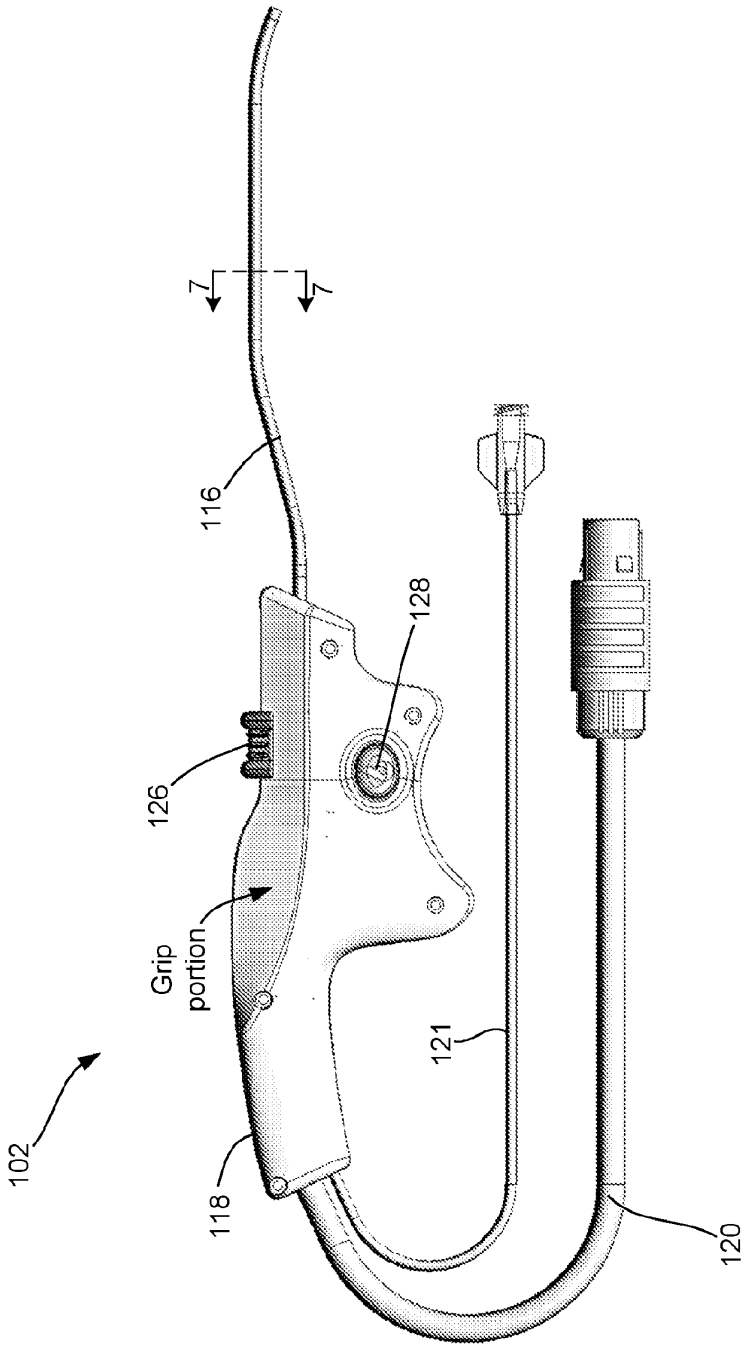


FIG. 3

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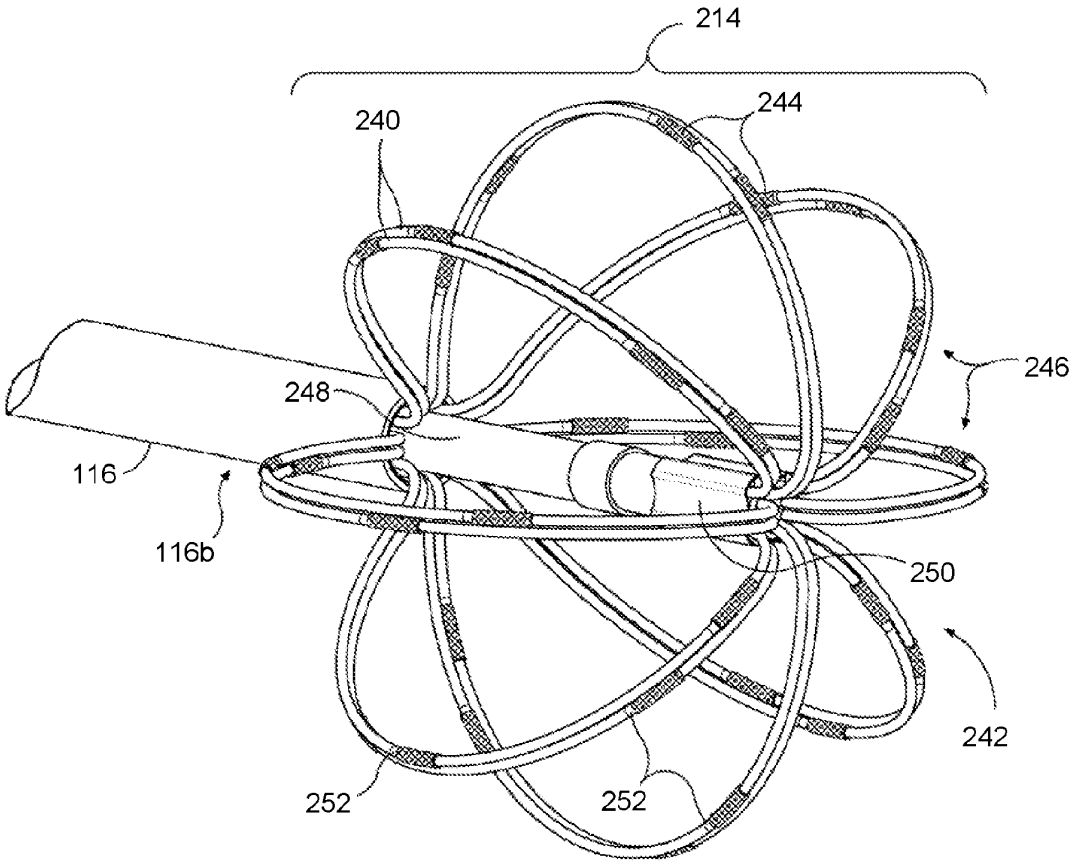


FIG. 4

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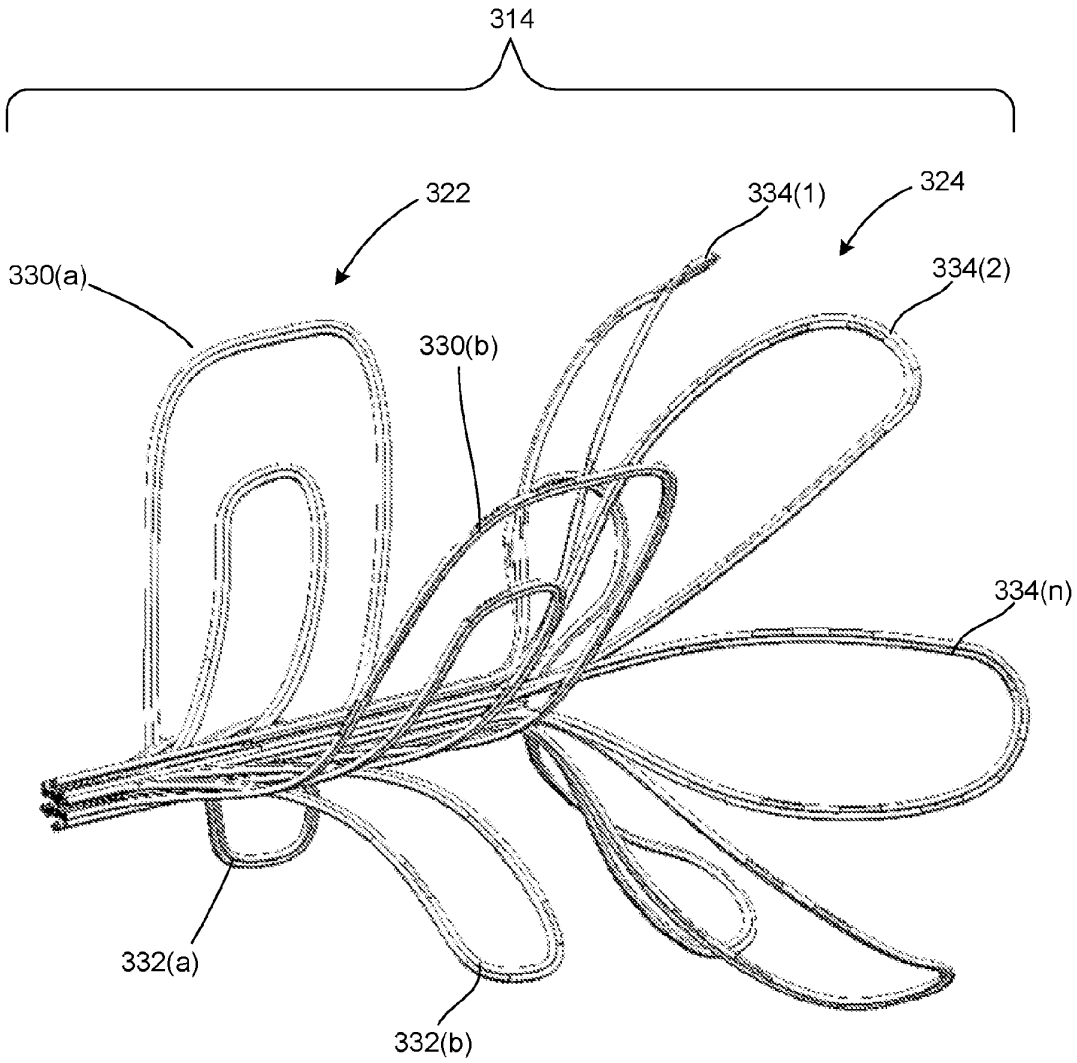


FIG. 5A

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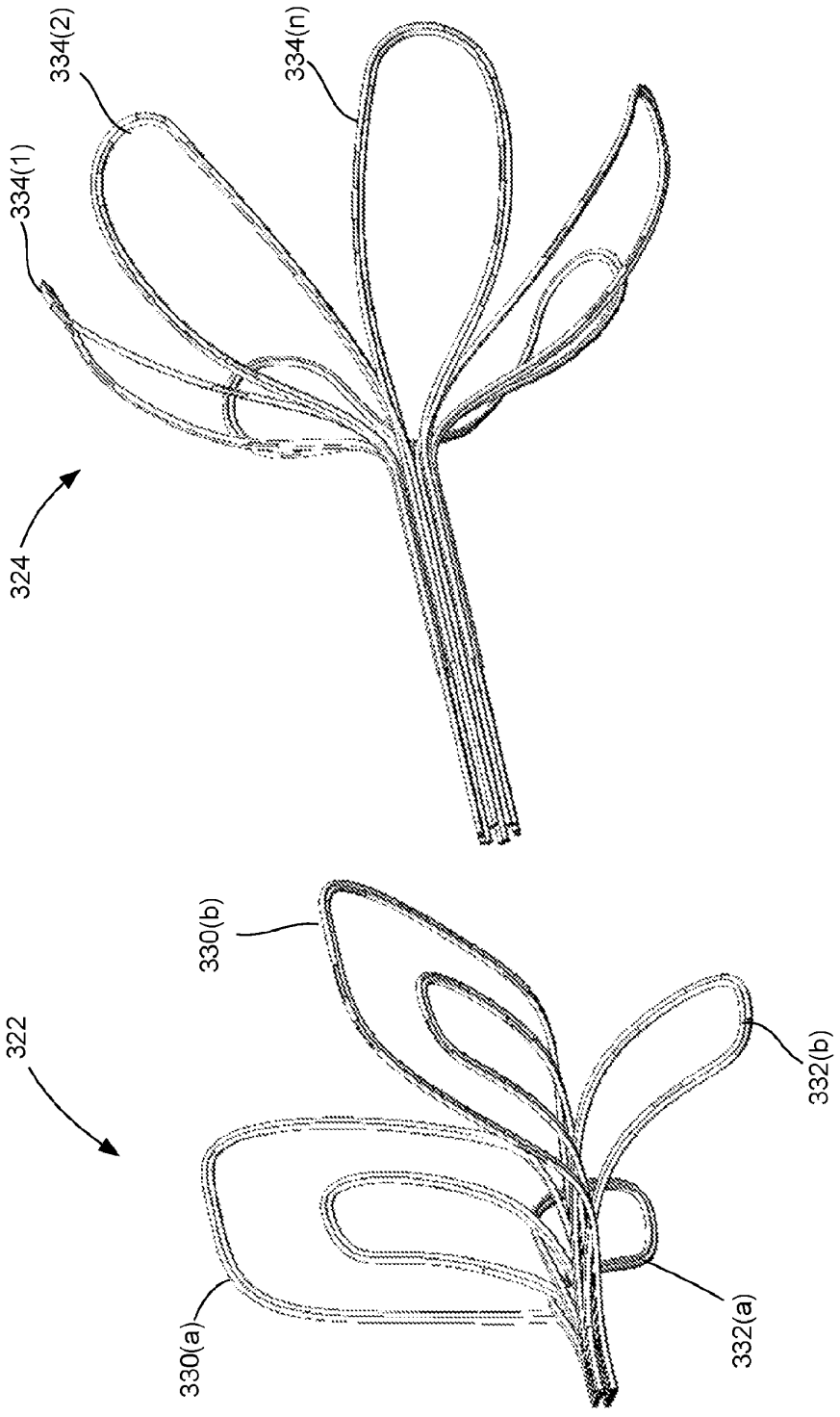


FIG. 5B

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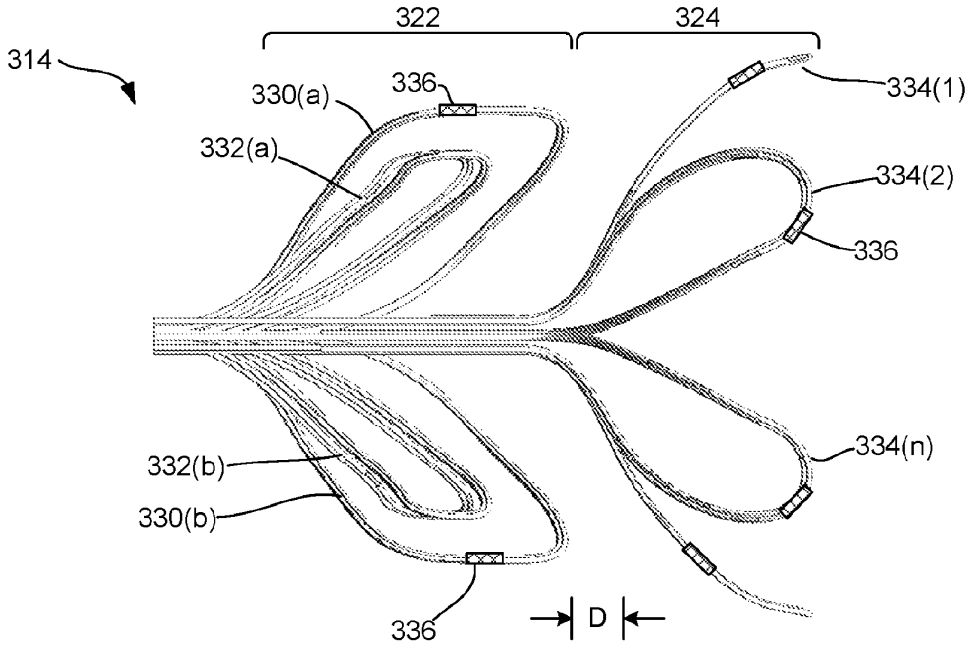


FIG. 5C

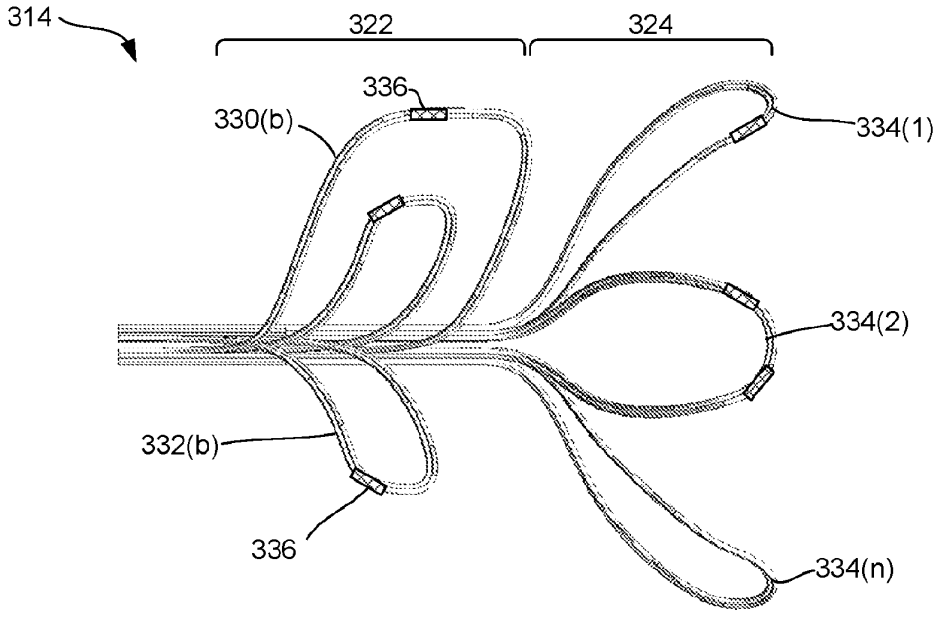


FIG. 5D

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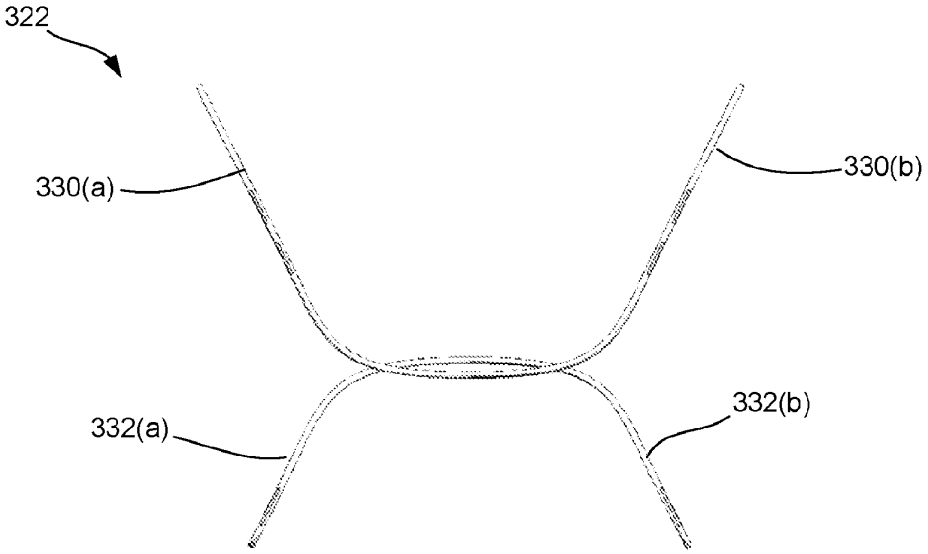


FIG. 5E

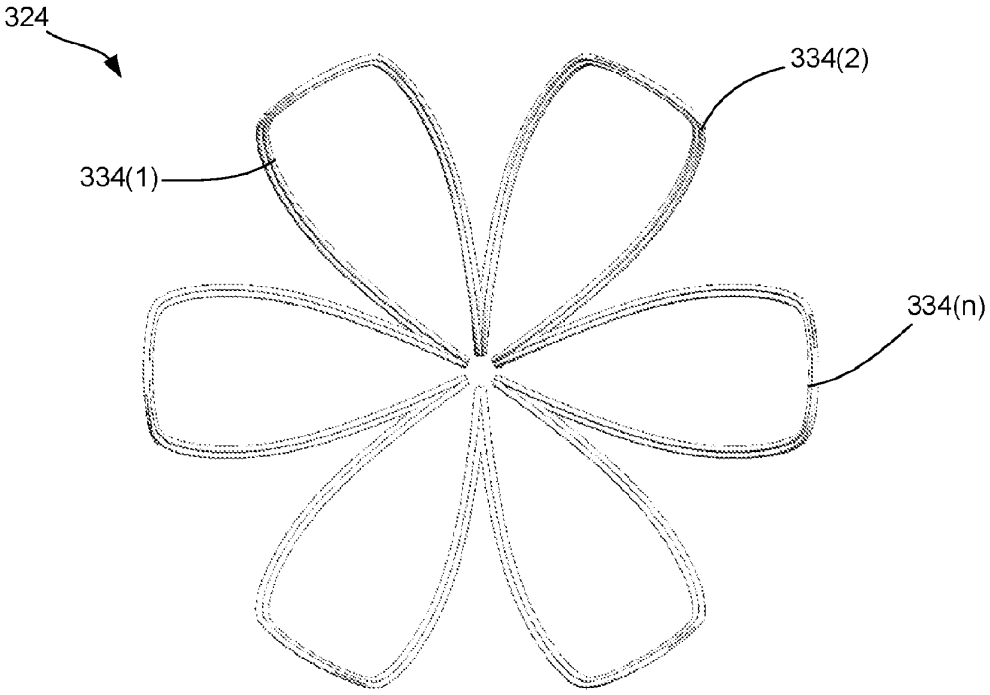


FIG. 5F

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IPR2025-01125

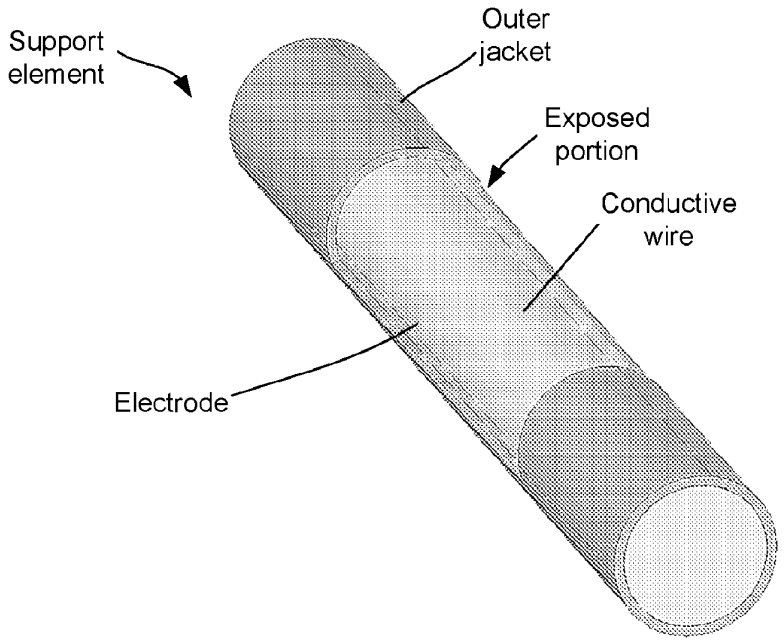


FIG. 6

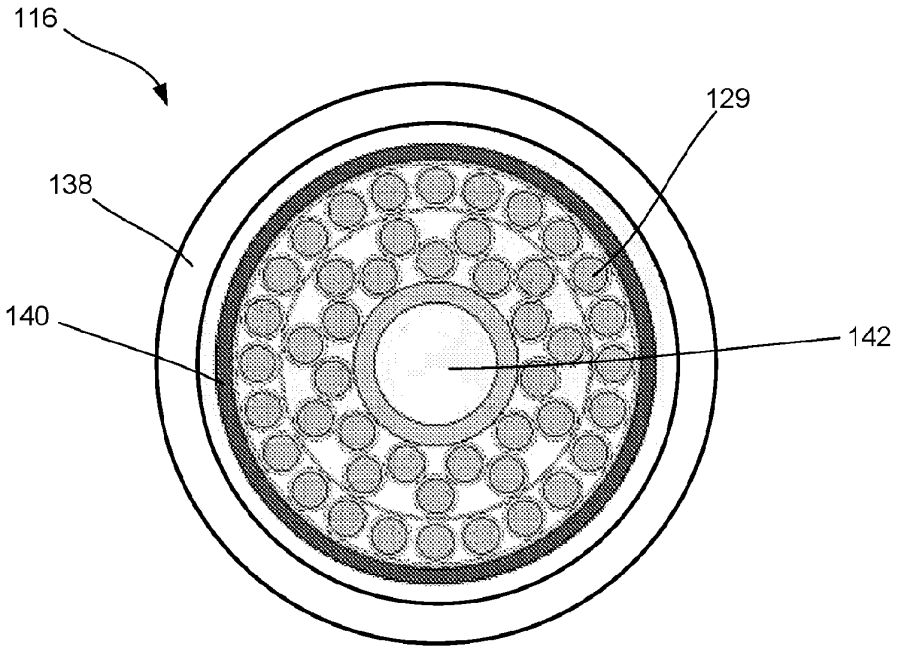


FIG. 7

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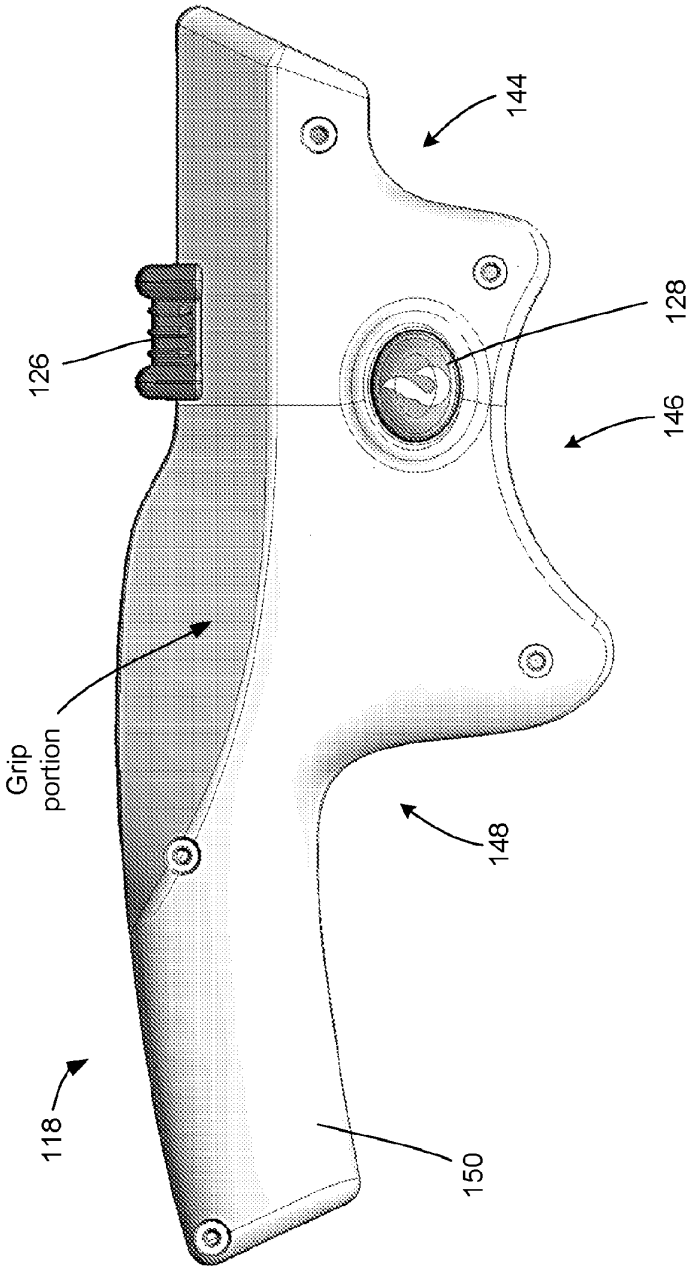


FIG. 8A

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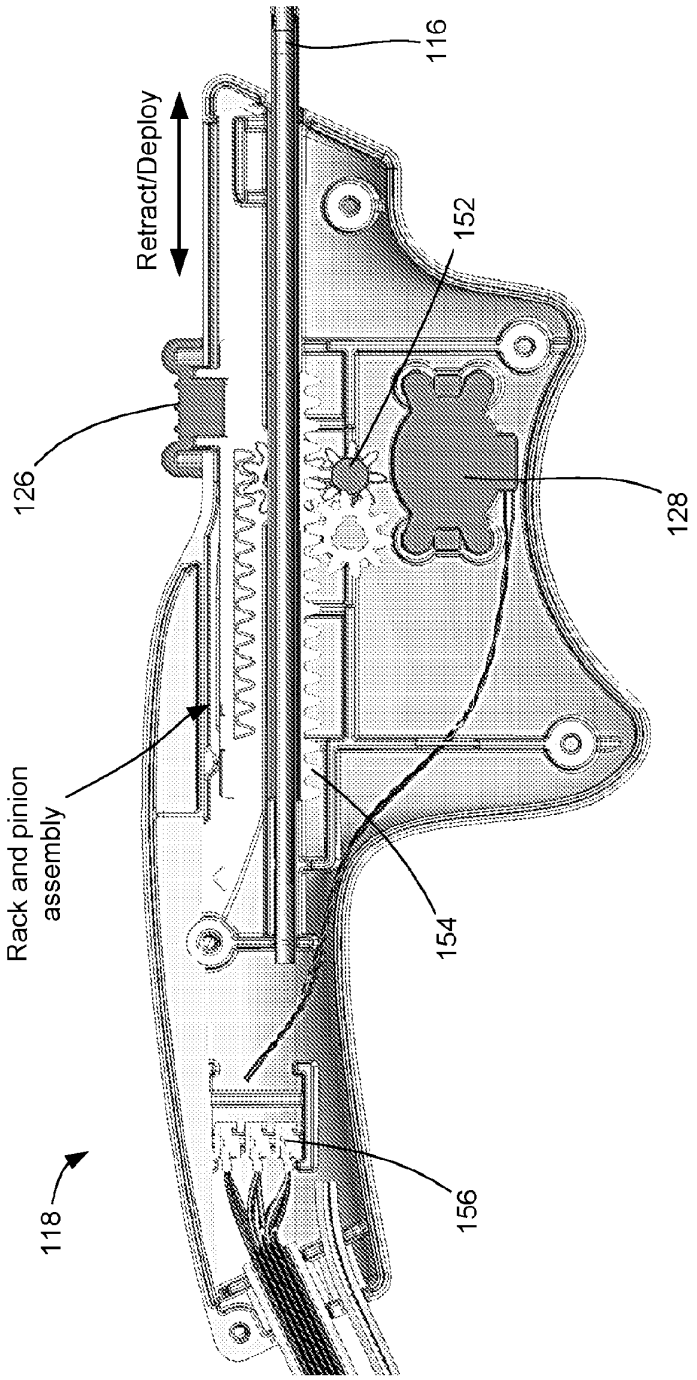


FIG. 8B

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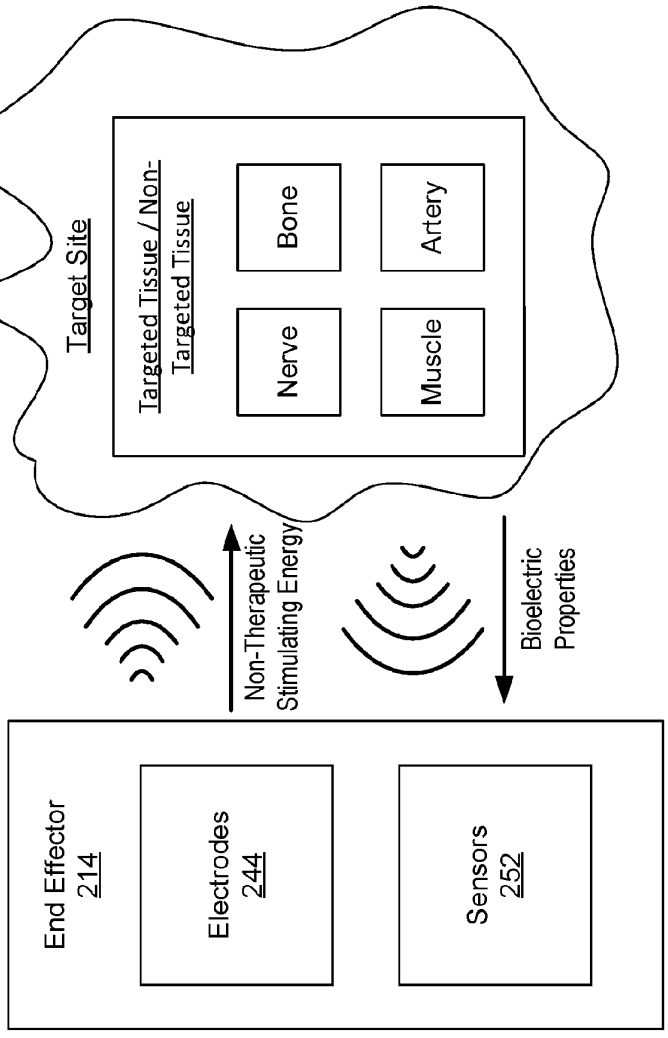


FIG. 9A

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IPR2025-01125

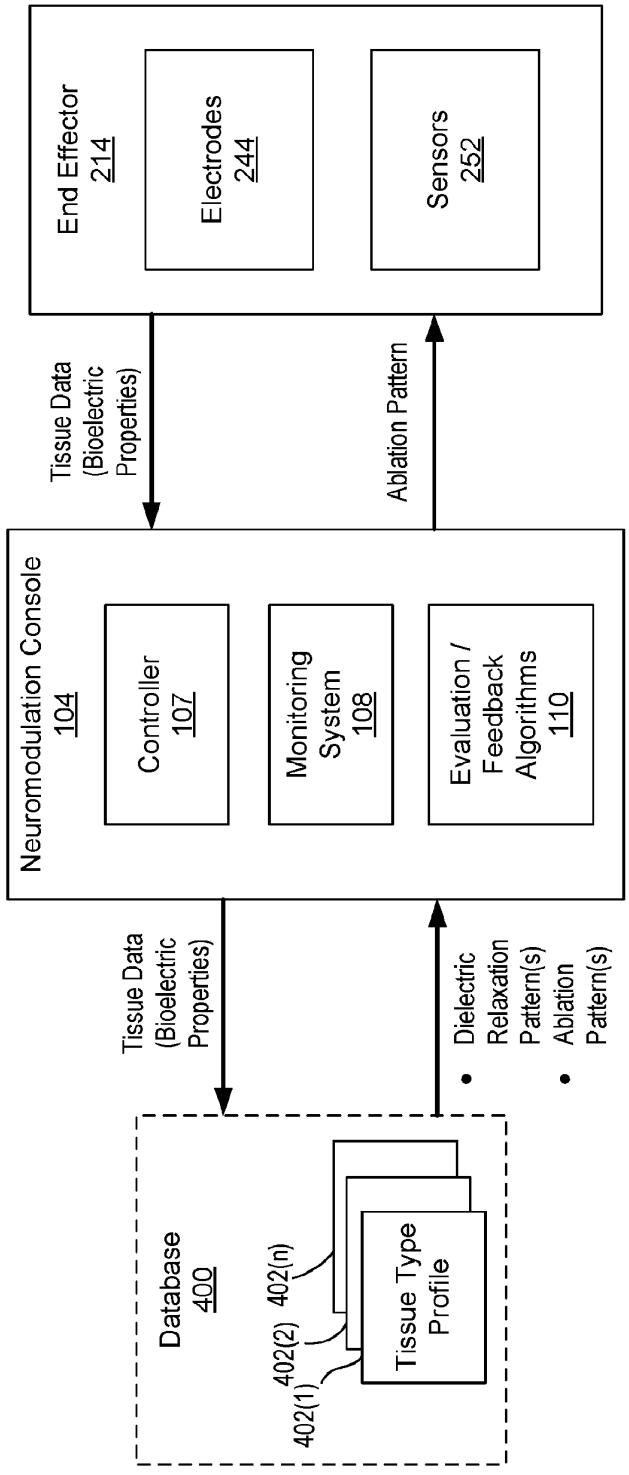


FIG. 9B

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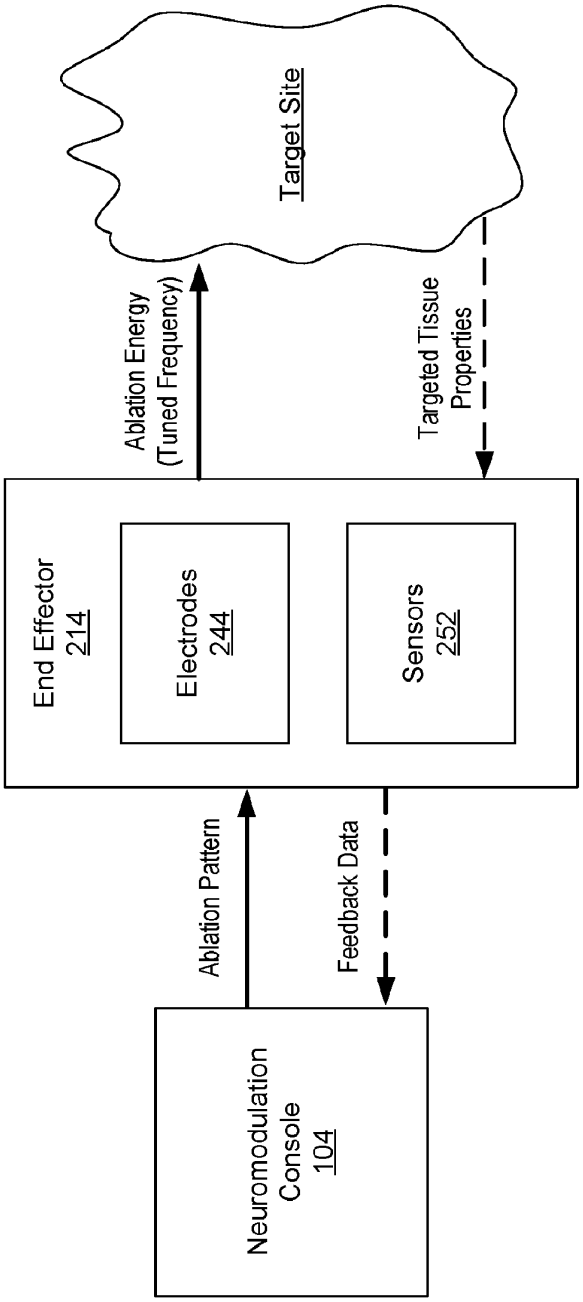


FIG. 9C

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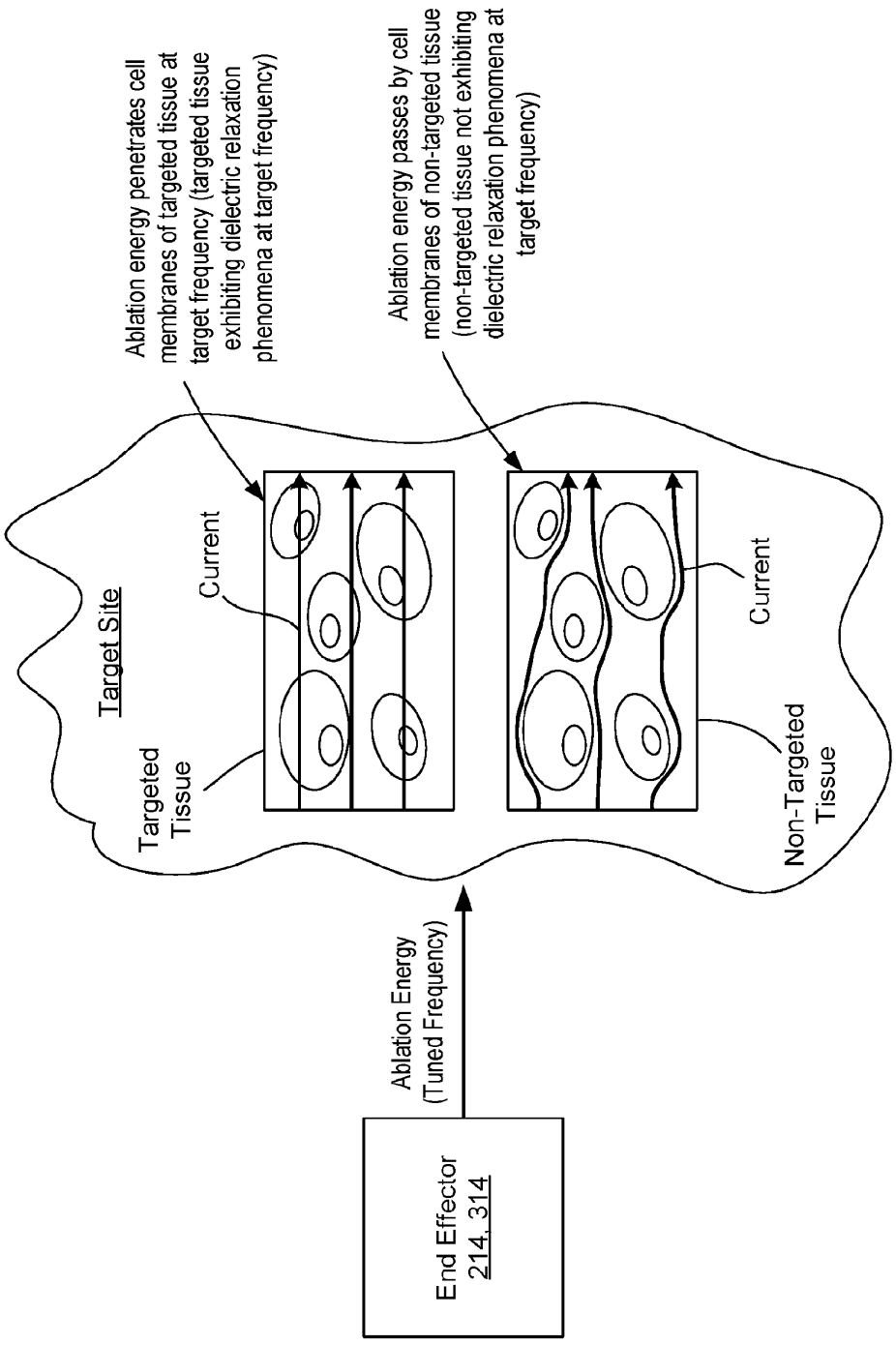


FIG. 10

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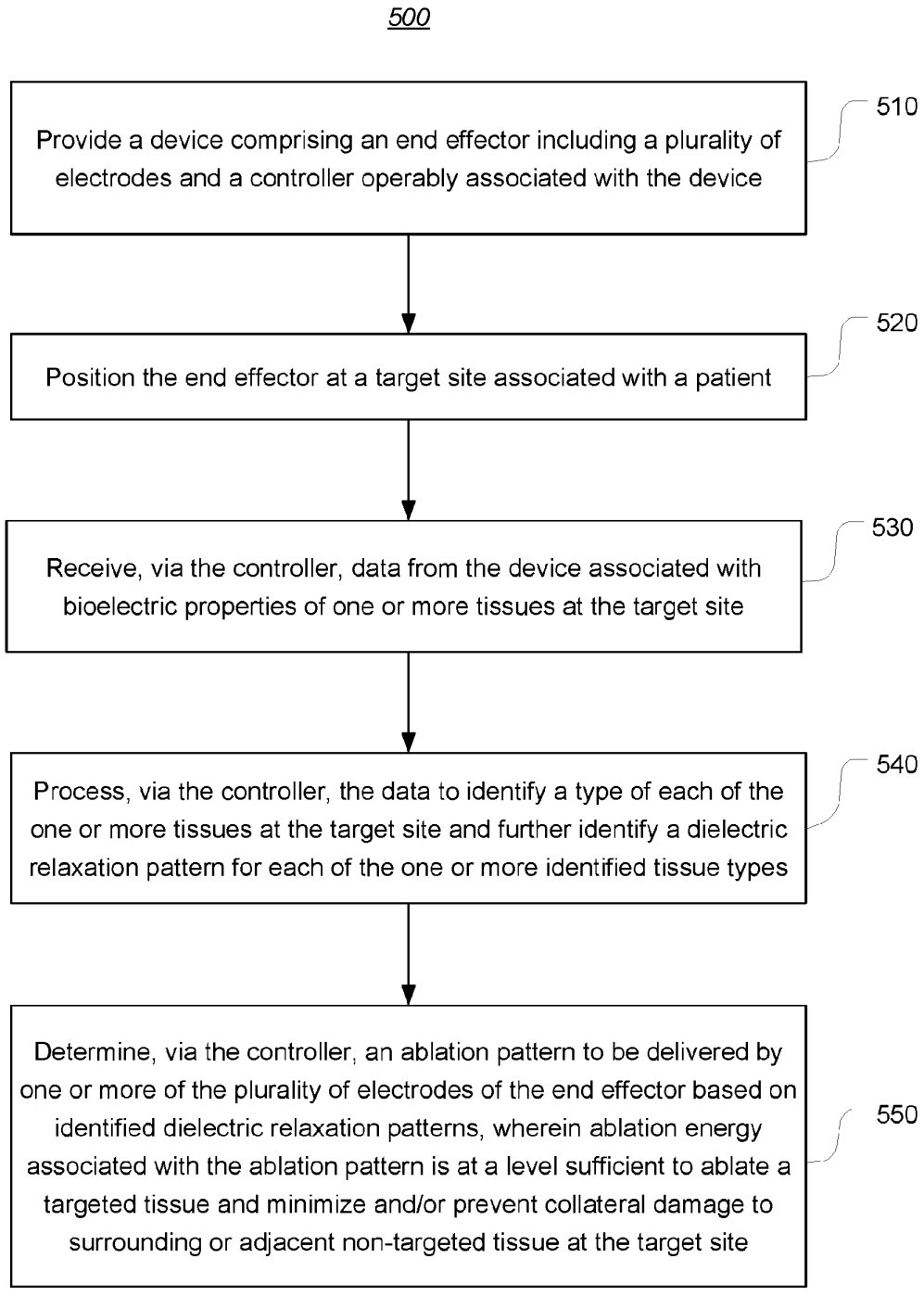


FIG. 11

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Aerin Medical Inc. v. Neurent Medical Ltd.
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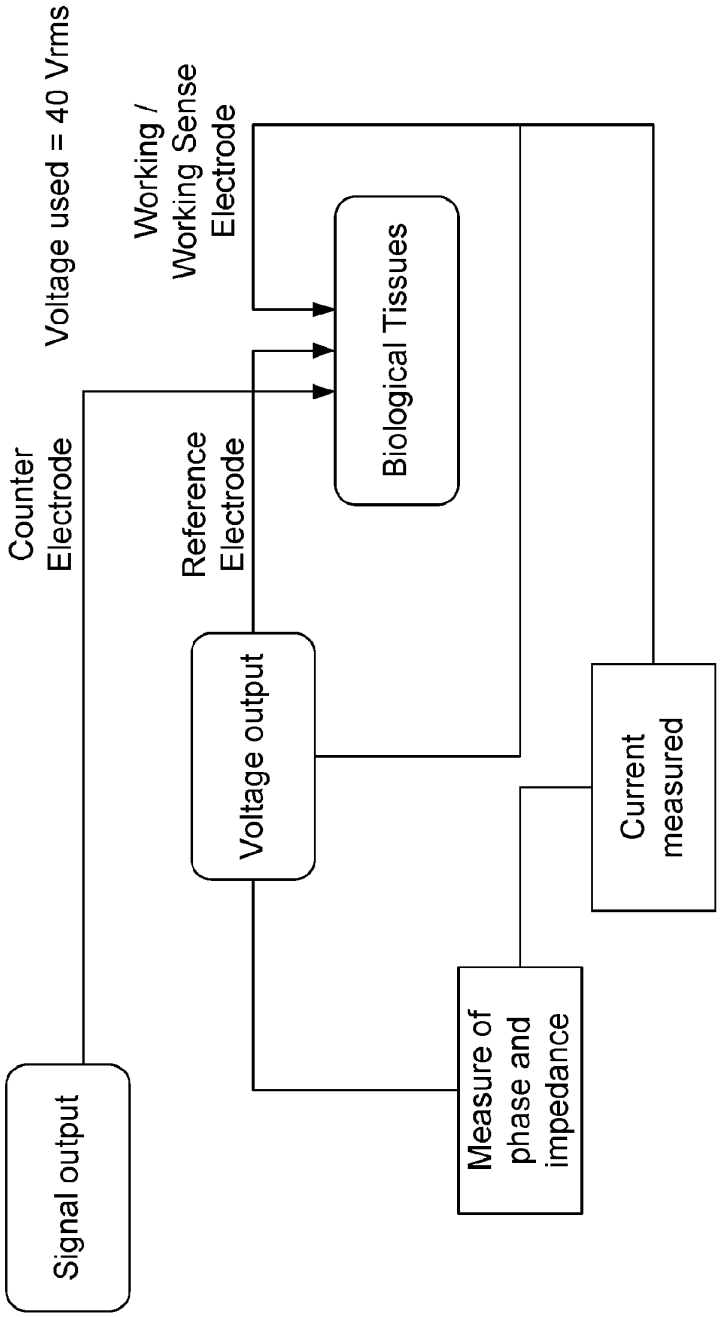


FIG. 12

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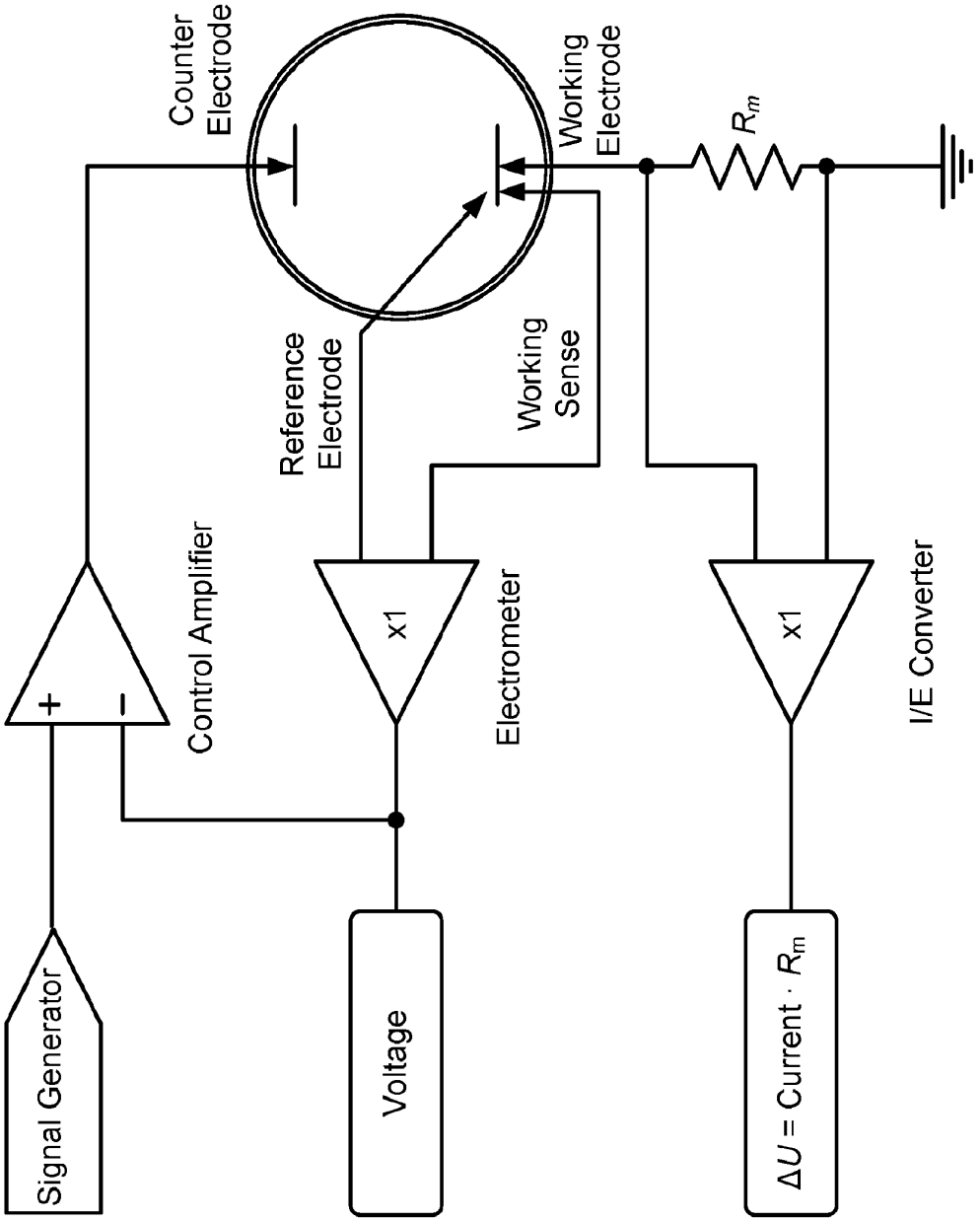


FIG. 12A

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IPR2025-01125

Dielectrical Properties: Spinal Cord Tissue vs. Muscle Tissue

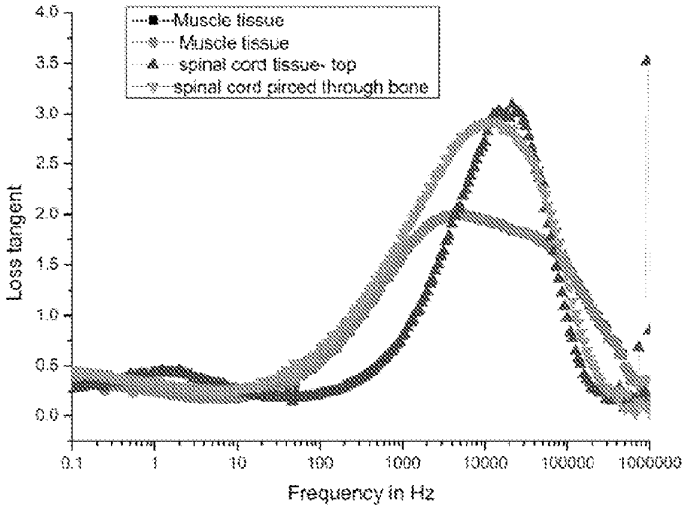


FIG. 13A

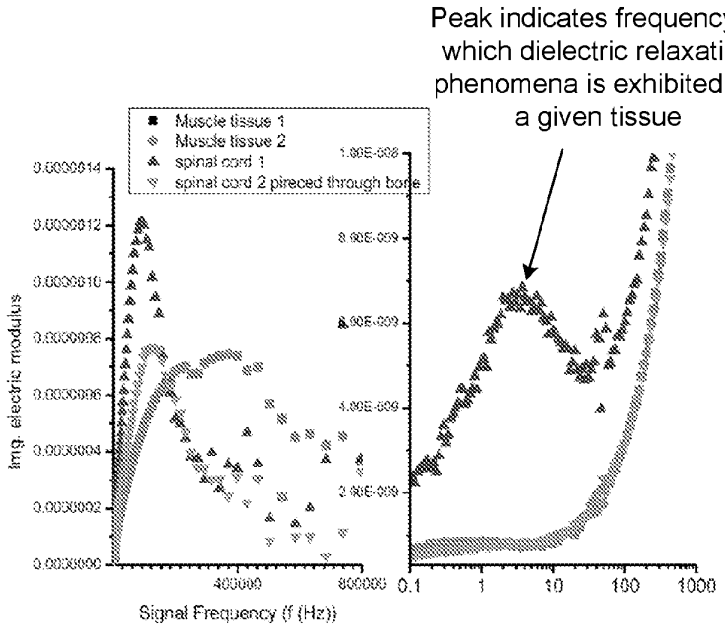


FIG. 13B

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HN Relaxation Phenomena: Upper Spinal Cord

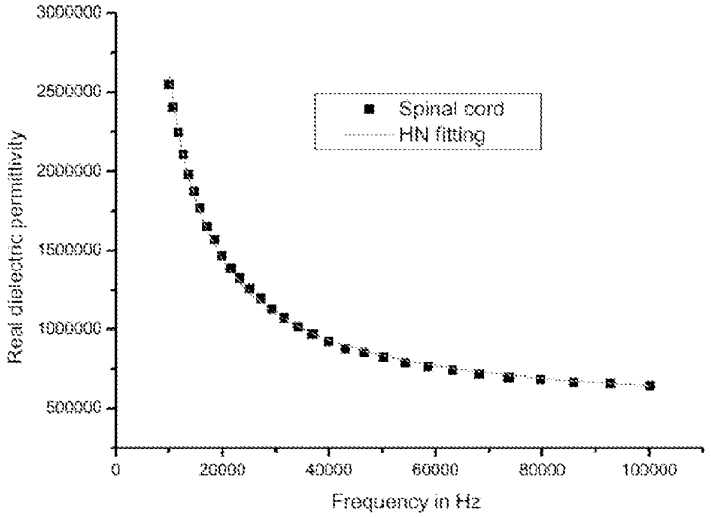


FIG. 14A

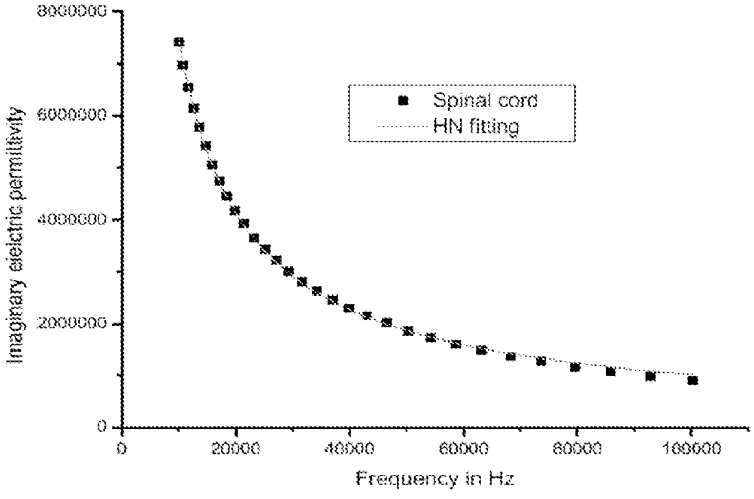


FIG. 14B

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IPR2025-01125

HN Relaxation Phenomena: Lower Spinal Cord

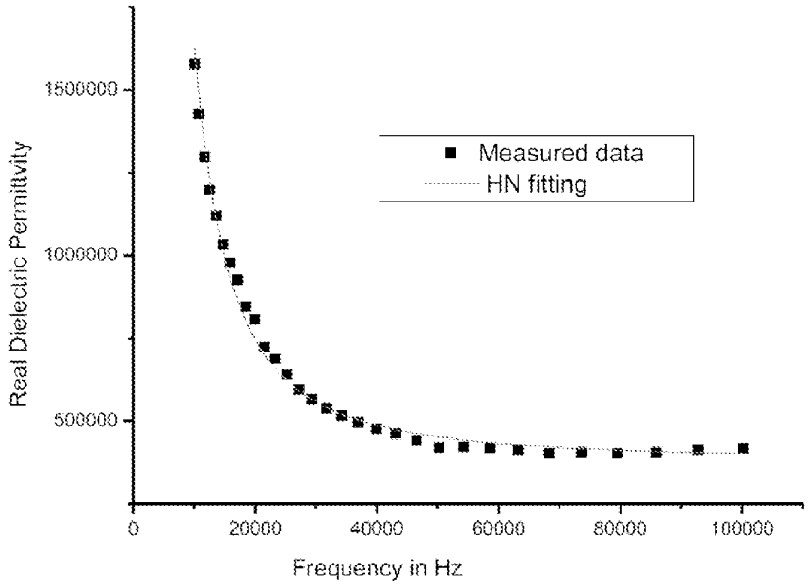


FIG. 14C

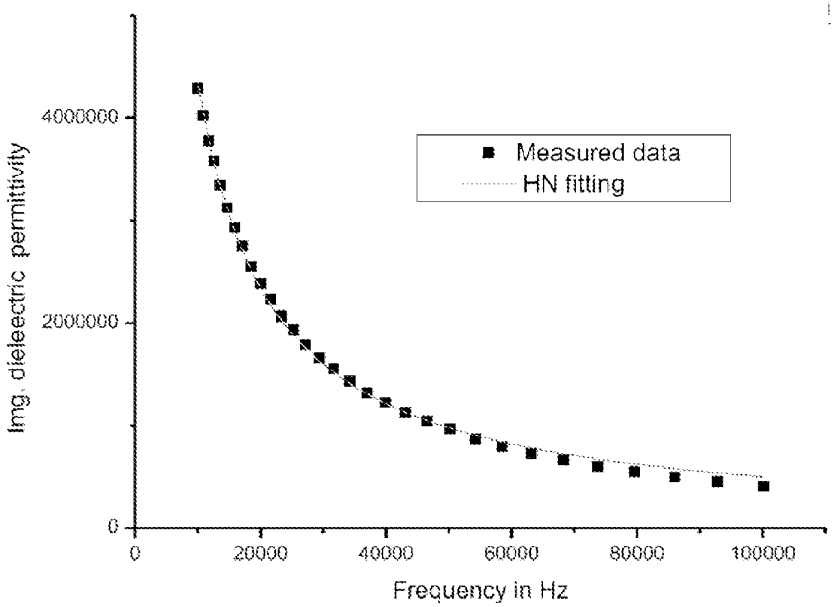


FIG. 14D

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

HN Relaxation Phenomena: Lower Back Muscle

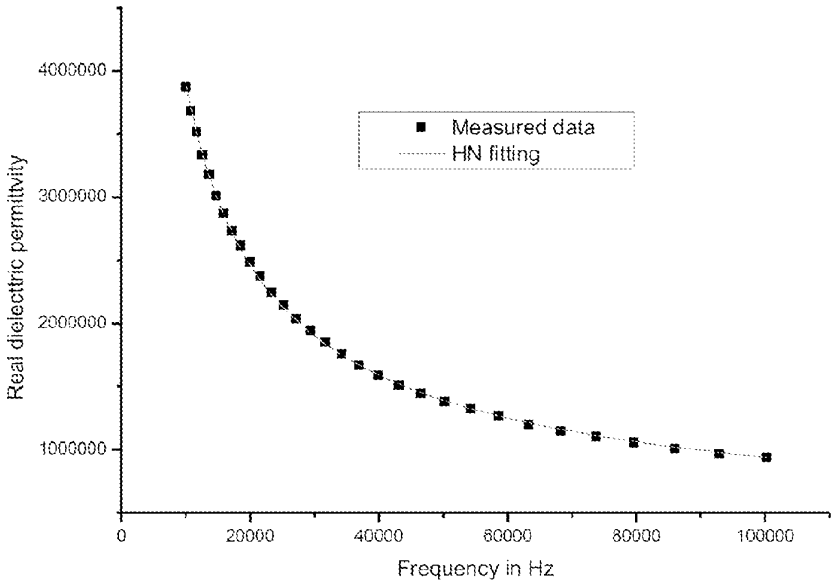


FIG. 14E

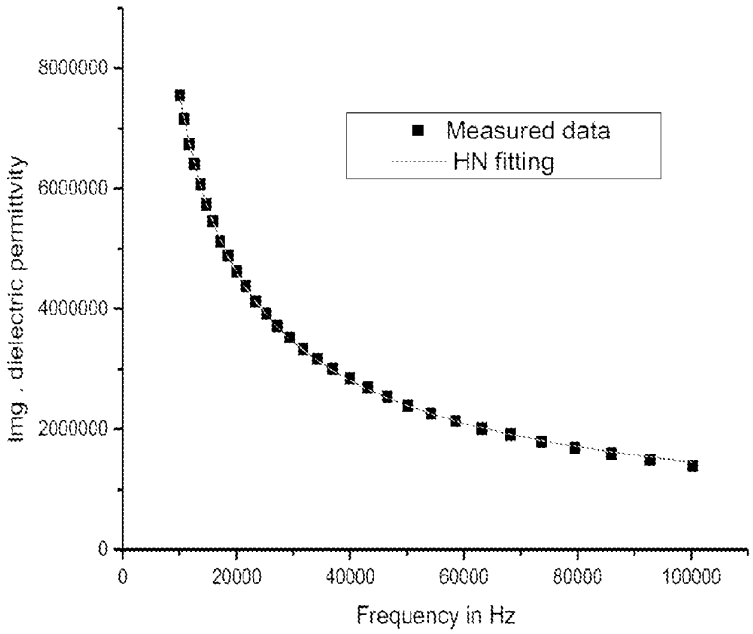


FIG. 14F

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IPR2025-01125

HN Relaxation Phenomena: Upper Back Muscle

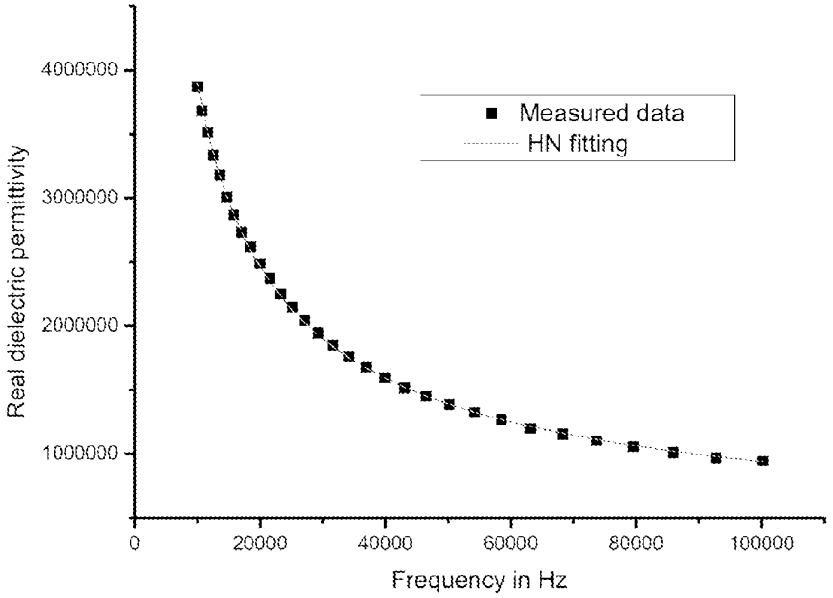


FIG. 14G

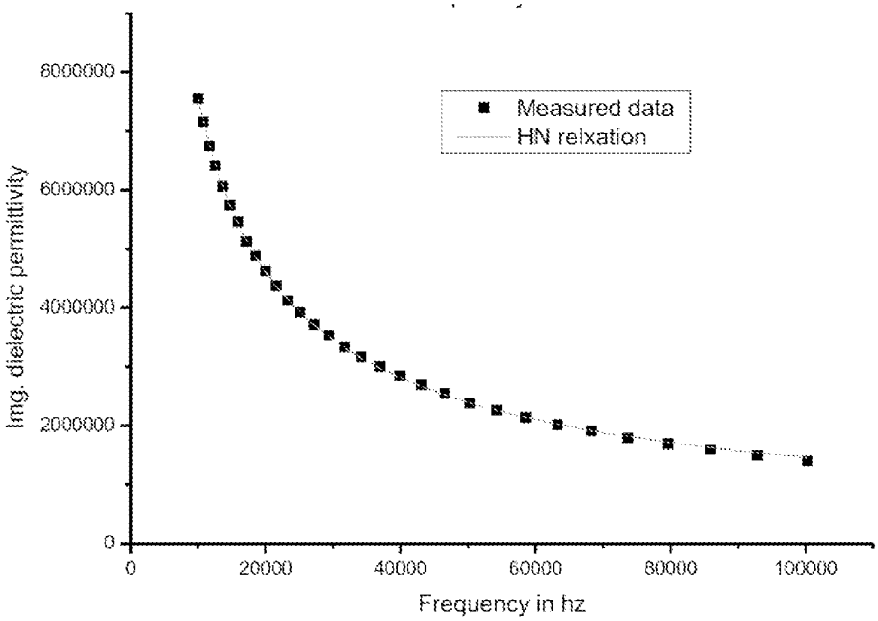


FIG. 14H

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Dielectrical Properties: Different Portions of Turbinate Tissue

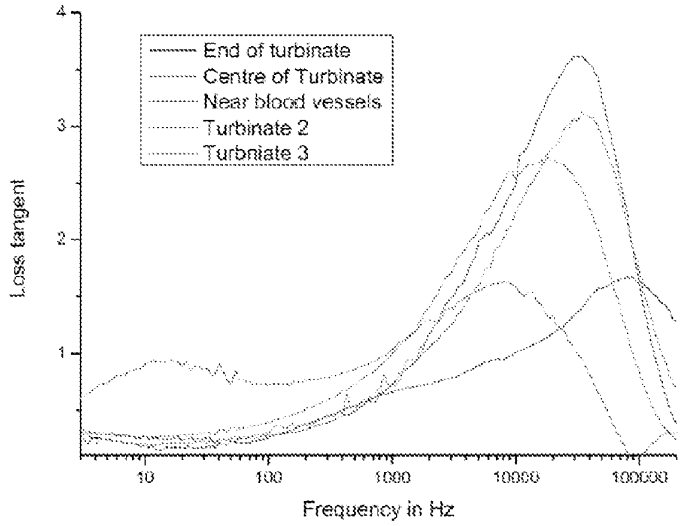


FIG. 15A

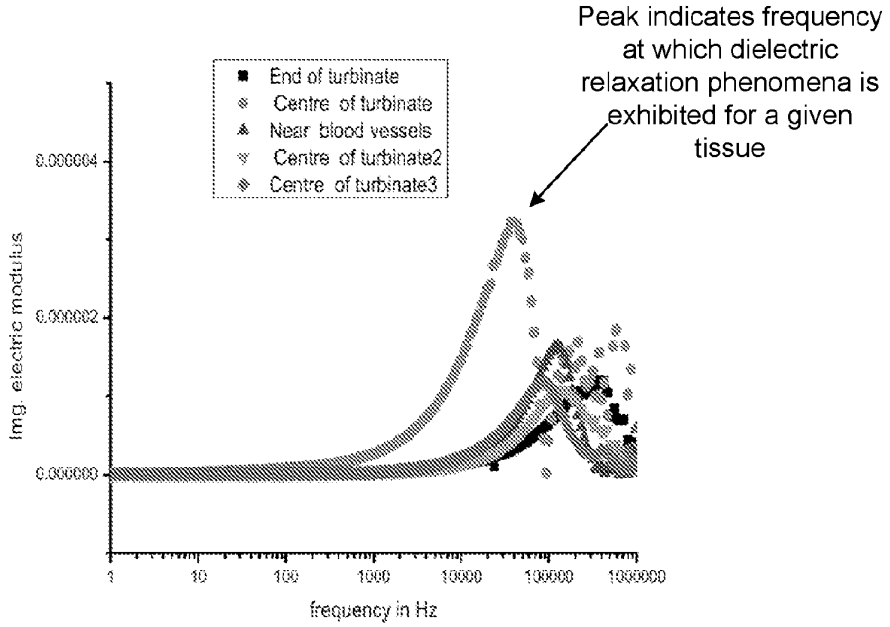


FIG. 15B

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IPR2025-01125

HN Relaxation Phenomena: End of Turbinate

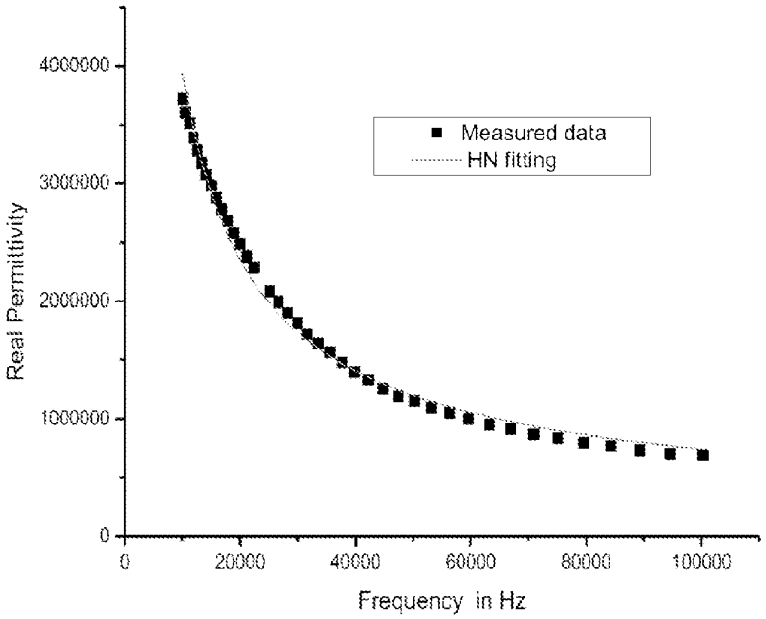


FIG. 16A

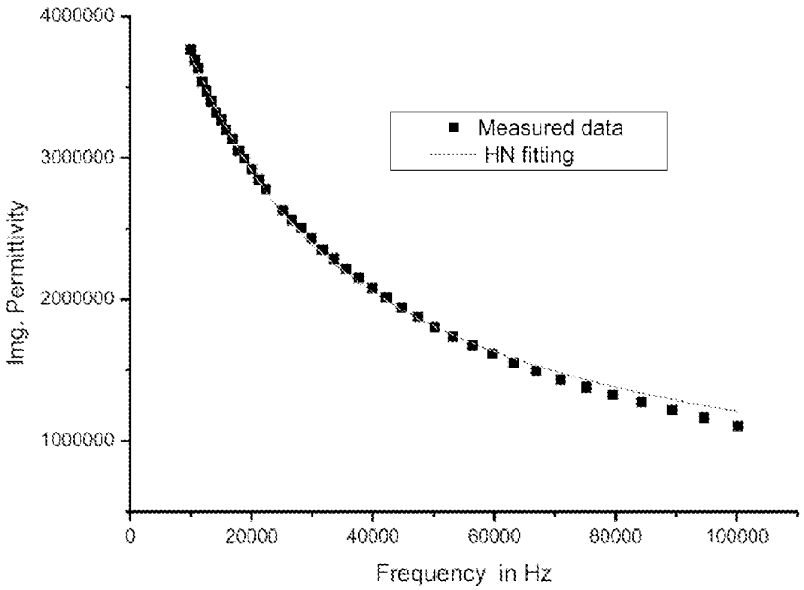


FIG. 16B

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HN Relaxation Phenomena: Center of Turbinate

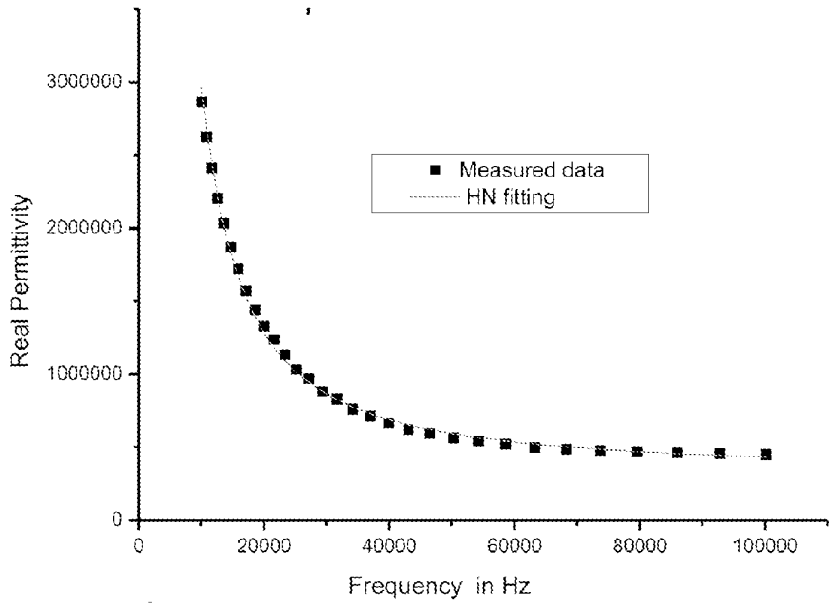


FIG. 16C

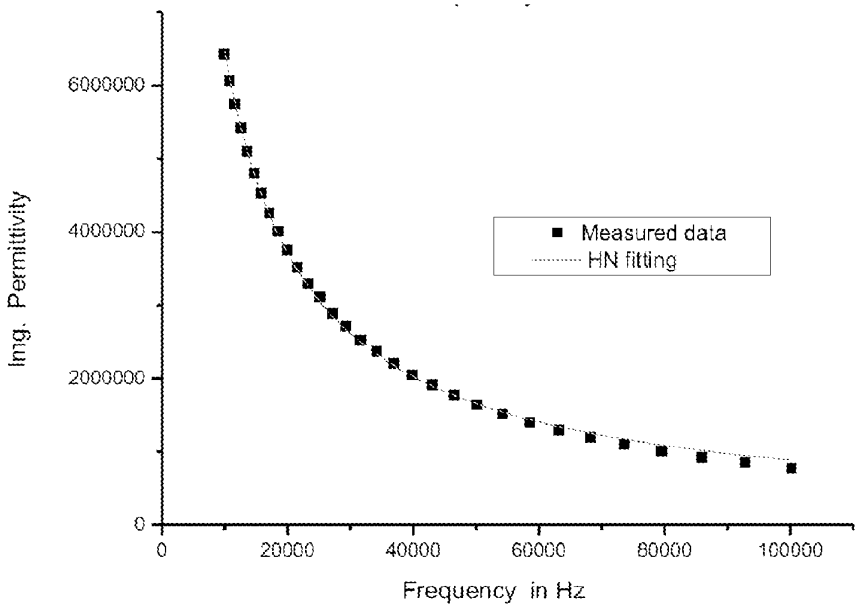


FIG. 16D

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IPR2025-01125

HN Relaxation Phenomena: Near Blood Vessels

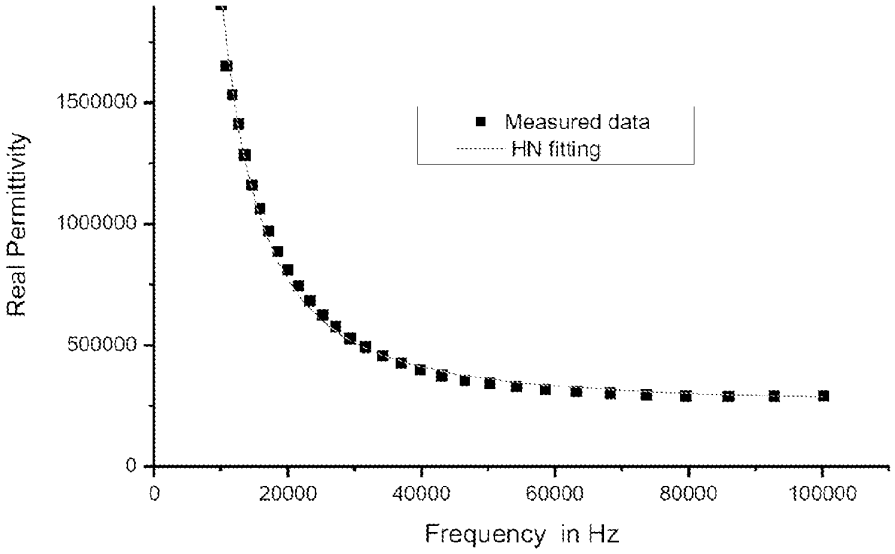


FIG. 16E

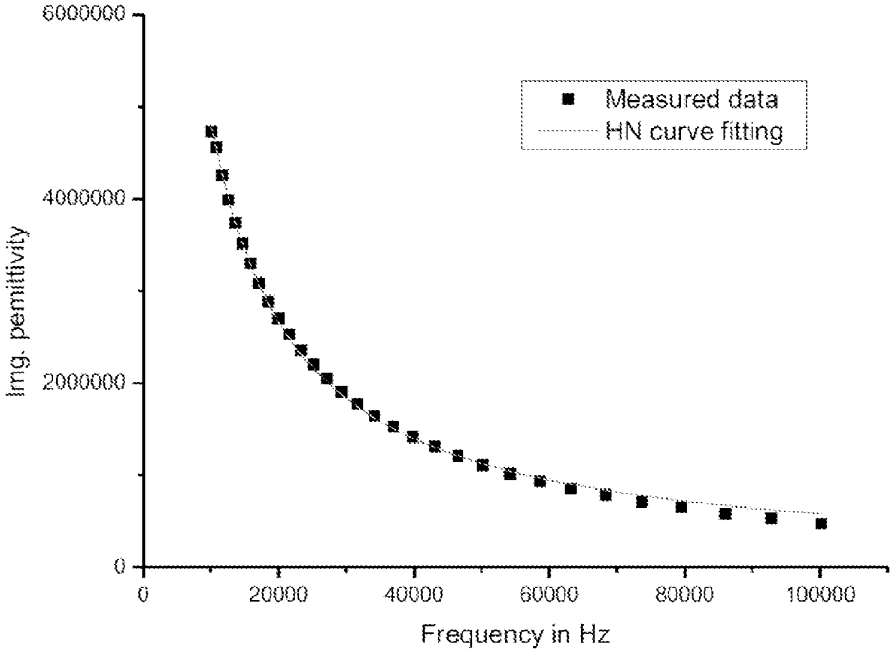


FIG. 16F

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IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000243

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/12
ADD. A61B18/00 A61B18/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, COMPENDEX, INSPEC, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17) cited in the application paragraphs [0002] - [0003], [0031], [0053] - [0055], [0071], [0119]; figure 3A	23-44

X	WO 2016/183337 A2 (NAT UNIV IRELAND GALWAY [IE]; QI ZHAN MICHELE [US]) 17 November 2016 (2016-11-17)	23-30, 34,35, 37-44
A	paragraphs [0002], [0038] - [0044], [0093] - [0096], [0111]; figure 2	31-33,36

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 August 2021	25/08/2021

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Aronsson, Fredrik

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000243

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-22
because they relate to subject matter not required to be searched by this Authority, namely:

The subject-matter of claims 1-22 refers to a surgical and therapeutic treatment.According to the PCT neither search (Rule 39.1(iv) PCT) nor examination (Rule 67.1(iv) PCT) is required for such subject-matter.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000243

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2018133460 A1	17-05-2018	AU 2017357869 A1	06-06-2019
		CA 3041440 A1	17-05-2018
		CN 110191674 A	30-08-2019
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		US 2020086112 A1	19-03-2020
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		US 2019239956 A1	08-08-2019
		US 2019239957 A1	08-08-2019
		US 2020100838 A1	02-04-2020
		US 2020107882 A1	09-04-2020
		WO 2016183337 A2	17-11-2016

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 December 2021 (30.12.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/260435 A1

(51) International Patent Classification:
A61B 18/12 (2006.01) *A61N 1/00* (2006.01)
A61B 18/14 (2006.01) *G06N 20/00* (2019.01)
A61B 34/35 (2016.01)

(21) International Application Number:
PCT/IB2021/000441

(22) International Filing Date:
25 June 2021 (25.06.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/044,904 26 June 2020 (26.06.2020) US

(71) Applicant: **NEURENT MEDICAL LIMITED** [IE/IE]; No. 1 Oran Point, Main Street, Oranmore, Galway (IE).

(72) Inventor: **TOWNLEY, David**; Latoon North, Newmarket-on-Fergus, County Clare (IE).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

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(54) **Title:** SYSTEMS AND METHODS FOR TARGETED TISSUE TREATMENT

(57) **Abstract:** The invention generally relates to systems and methods for providing detection, identification, and precision targeting of specific tissue of interest to undergo a therapeutic treatment while minimizing or avoiding collateral damage to surrounding or adjacent non- targeted tissue.

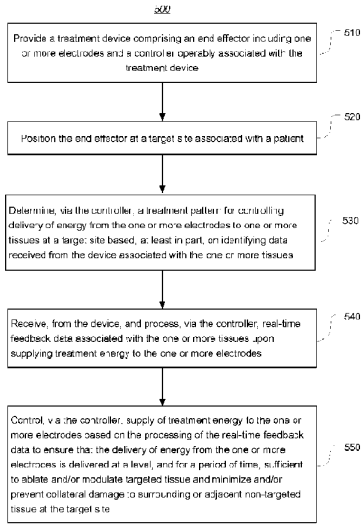


FIG. 10

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SYSTEMS AND METHODS FOR TARGETED TISSUE TREATMENT

Cross-reference to Related Applications

This application claims the benefit of, and priority to, U.S. Provisional Patent Application No. 63/044,904, filed June 26, 2020, the contents of which are incorporated by reference.

Field of the Invention

The invention generally relates to systems and methods for providing detection, identification, and precision targeting of specific tissue(s) of interest to undergo a therapeutic treatment while minimizing or avoiding collateral damage to surrounding or adjacent non-targeted tissue.

Background

Certain surgical procedures, such as ablation therapy, require a surgeon to apply precise treatment to the intended target site (i.e., tissue intended to receive treatment) at appropriate levels so as to avoid collateral damage to surrounding tissue, which can lead to further complications and even death. For example, certain procedures require increased precision due to the nature tissue to be treated and the location of such tissue in relation to any nearby or underlying tissue that may be highly sensitive and/or is critical to keep intact and free of unintended damage (i.e., blood vessels, nerves, etc.).

For example, many neuromodulation procedures require such precision. Neuromodulation refers to the alteration, or modulation, of nerve activity by delivering electrical (or sometimes pharmaceutical) agents directly to a target area. The delivery of electrical stimulation can result in partial or complete incapacitation, or other effective disruption, of neural activity. Therapeutic neuromodulation, for example, can include partially or completely inhibiting, reducing, and/or blocking neural communication along neural fibers for the treatment of certain conditions and disorders, specifically for pain relief and/or restoration of function. Some conditions and disorders that may be treated via neuromodulation include, but are not limited to, epilepsy, migraine headaches, spinal cord injuries, Parkinson's disease, and urinary incontinence, to name a few. Neuromodulation can also be used to treat certain conditions associated with the nose, such as rhinosinusitis, including, but not limited to, allergic rhinitis,

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non-allergic rhinitis, chronic rhinitis, acute rhinitis, recurrent rhinitis, chronic sinusitis, acute sinusitis, recurrent sinusitis, and medical resistant rhinitis and/or sinusitis, in addition to combinations of one or more of the preceding conditions.

Neuromodulation treatment procedures may generally involve the application of electrodes to the brain, the spinal cord, or peripheral nerves for subsequent treatment of conditions or disorders associated therewith. The electrodes are coupled, via an extension cable, to a pulse generator and power source, which generates the necessary electrical stimulation. An electrical current passes from the generator to the nerve, and can either inhibit pain signals or stimulate neural impulses where they were previously absent. Importantly, electrodes must be precisely placed and the level of electrical stimulation must be controlled so as to avoid or minimize creating collateral damage to surrounding or adjacent non-neural structures, such as bone and blood vessels, as well as non-targeted neural tissue.

Peripheral nerve stimulation is a commonly used approach to treat peripheral neurological conditions and conditions, including chronic pain. In order to establish accurate placement of electrodes and level of electrical stimulation to the targeted peripheral nerve, peripheral nerve stimulation treatment typically requires an initial testing or trial period. For example, a small electrical device (a wire-like electrode) is surgically implanted and placed next to one of the peripheral nerves. The electrode delivers rapid electrical pulses during the initial testing period (trial) to determine whether the electrical pulses result in the desired effect. Once the desired effect is established (via repositioning and/or adjusting of electrical stimulation levels) a more permanent electrode may be implanted into a patient's body. Accordingly, a drawback to current neuromodulation procedures, notably neuromodulation of peripheral nerves, is that such procedures cannot precisely target neural tissue, thereby presenting risk of causing significant collateral damage to surrounding non-neural tissue (such as blood vessels), and/or other non-targeted neural tissue.

Another exemplary procedure requiring precision includes interventional cardiac electrophysiology (EP) procedures, for example. In such a procedure, it is often necessary for the surgeon to determine the condition of cardiac tissue at a target ablation site in or near the heart. During some EP procedures, the surgeon may deliver a mapping catheter through a main vein or artery into an interior region of the heart to be treated. Using the mapping catheter, the surgeon may then determine the source of a cardiac rhythm disturbance or abnormality by

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placing a number of mapping elements carried by the catheter into contact with the adjacent cardiac tissue and then operating the catheter to generate an electrophysiology map of the interior region of the heart based on sensed electrical cardiac signals. Once a map of the heart is generated, the surgeon may then advance an ablation catheter into the heart, and position an ablation electrode carried by the catheter tip near the targeted cardiac tissue to ablate the tissue and form a lesion, thereby treating the cardiac rhythm disturbance or abnormality. In some techniques, the ablation catheter itself may include a number of mapping electrodes, allowing the same device to be used for both mapping and ablation.

Various ultrasound-based imaging catheters and probes have been developed for visualizing body tissue in applications such as interventional cardiology, interventional radiology, and electrophysiology. For interventional cardiac electrophysiology procedures, for example, ultrasound imaging devices have been developed that permit the visualization of anatomical structures of the heart directly and in real-time. While such imaging-based products allow some form of visualization of the targeted tissue, such procedures still lack the ability to precisely target and apply treatment to the tissue of interest while reducing or eliminating the risk of further treatment non-targeted, adjacent tissue.

Summary

The invention recognizes that knowing certain properties of tissue, both active and passive, at a given target site prior to and during electrotherapeutic treatment (i.e., neuromodulation, ablation, etc.) provides an ability to more precisely target a specific tissue of interest (i.e., targeted tissue) and minimize and/or prevent collateral damage to adjacent or surrounding non-targeted tissue.

For example, certain target sites intended to undergo treatment may consist of more than one type of tissue (i.e., nerves, muscles, bone, blood vessels, etc.). In particular, a tissue of interest (i.e., the specific tissue to undergo treatment) may be adjacent to one or more tissues that are not of interest (i.e., tissue that is not intended to undergo treatment). In one scenario, a surgeon may wish to provide electrotherapeutic stimulation to a nerve tissue, while avoiding providing any such stimulation to an adjacent blood vessel, for example, as unintended collateral damage may result in damage to the blood vessel and cause further complications. In such a scenario, the specific type of targeted tissue may generally dictate the level of electrical

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stimulation required to elicit a desired effect. Furthermore, physical properties of the targeted tissue, including the specific location and depth of the targeted tissue, in relation to the non-targeted tissue, further impacts the level of electrical stimulation necessary to result in effective therapeutic treatment.

The invention provides systems and methods with an ability to characterize, prior to an electrotherapeutic treatment, the type of tissue at a target site by sensing at least bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present at the target site. For example, different tissue types include different physiological and histological characteristics. As a result of the different characteristics, different tissue types have different associated bioelectrical properties and thus exhibit different behavior in response to application of energy applied thereto.

By knowing such properties of a given tissue, the systems and methods are configured to determine a specific treatment pattern for controlling delivery of energy at a specific level for a specific period of time to the tissue of interest (i.e., the targeted tissue) sufficient to ensure successful ablation/modulation of the targeted tissue while minimizing and/or preventing collateral damage to surrounding or adjacent non-targeted tissue at the target site. In particular, a given treatment pattern may include, for example, a predetermined treatment time, a precise level of energy to be delivered, and a predetermined impedance threshold for that particular tissue.

The systems and methods are further configured to receive and process real-time feedback data associated with the targeted tissue undergoing treatment to further ensure that energy delivered is maintained within the scope of the treatment pattern. More specifically, the systems and methods are configured to automatically control delivery of energy to the targeted tissue based on the processing of the real-time feedback data, wherein such data includes at least impedance measurement data associated with the targeted tissue collected during delivery of energy to the targeted tissue. The controller is configured to process impedance measurement data to detect a slope change event (e.g., an asymptotic rise) within an impedance profile associated with the treatment, wherein, with reference to the predetermined impedance threshold, the slope change event is indicative of whether the ablation/modulation of the targeted tissue is successful. In turn, the controller is configured to automatically control the delivery of energy to the targeted tissue based on real-time monitoring of feedback data, most notably impedance data, to ensure the desired ablation/modulation is achieved.

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As a result, the systems and methods are able to ensure that optimal energy is delivered in order to delay the onset of impedance roll-off, until the target ablation/modulation depth is achieved, while maintaining clinically relevant treatment time. Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types.

One aspect of the present invention provides a system for treating a condition. The system includes a treatment device including an end effector comprising one or more electrodes and a controller operably associated with the treatment device. The controller is configured to determine a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues. The controller is further configured to receive and process real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes. The controller is configured to then control supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

The identifying data is associated with one or more properties of the one or more tissues, wherein the one or more properties may include, but are not limited to, a type of tissue, a depth of the one or more tissues, and a location of the one or more tissues. For example, a subset of the one or more electrodes may be configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense at least bioelectric properties of the one or more tissues at the target site. The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

The controller is configured to process the identifying data to determine the treatment pattern. The processing of identifying data, via the controller, may include, for example comparing the identifying data received from the device with electric signature data associated

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with a plurality of known tissue types. The electric signature data, for example, may include at least bioelectric properties of known tissue types. The comparison may include correlating the identifying data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

The treatment pattern may include, for example, a predetermined treatment time, a level of energy to be delivered from the electrodes, and a predetermined impedance threshold. Accordingly, the feedback data may include at least impedance measurement data associated with the targeted tissue at the target site. The controller may be configured to process the impedance measurement data to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue. In particular, the controller may be configured to process the active impedance value using an algorithm to determine efficacy of ablation/modulation of the targeted tissue based on a comparison of the active impedance value with at least one of a predetermined minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value. In the event that the active impedance value is less than the predetermined minimum impedance value, the controller is configured to determine that ablation/modulation is unsuccessful and then further disables energy delivery from the one or more electrodes. In the event that the active impedance value is greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the controller is configured to calculate a slope change for the detection of a slope event. If a negative slope event is detected, the controller is configured to determine that ablation/modulation is successful and the controller disables energy delivery from the one or more electrodes upon detecting a negative slope event. If a negative slope event is not detected, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes. In the absence of detecting a slope event, the controller is configured to determine that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and the controller further disables energy delivery from the one or more electrodes.

The controller is further configured to transmit a signal resulting in an output, via an interactive interface, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue. The alert may include, for example, a visual alert including at least one of a color and text displayed on a graphical user interface (GUI) and

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indicating whether the ablation/modulation is successful or unsuccessful.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient. Additionally, or alternatively, the resulting local hypoxia may cause neuronal degeneration.

Another aspect of the invention provides a method for treating a condition. The method includes providing a treatment device comprising an end effector including one or more electrodes and a controller operably associated with the treatment device and positioning the end effector at a target site associated with a patient. The method further includes determining, via the controller, a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues. The method further includes receiving, from the device, and processing, via the controller, real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes. The method further includes controlling, via the controller, supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time,

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sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

The identifying data is associated with one or more properties of the one or more tissues, wherein the one or more properties may include, but are not limited to, a type of tissue, a depth of the one or more tissues, and a location of the one or more tissues. For example, a subset of the one or more electrodes may be configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense at least bioelectric properties of the one or more tissues at the target site. The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

The controller is configured to process the identifying data to determine the treatment pattern. The processing of identifying data, via the controller, may include, for example comparing the identifying data received from the device with electric signature data associated with a plurality of known tissue types. The electric signature data, for example, may include at least bioelectric properties of known tissue types. The comparison may include correlating the identifying data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

The treatment pattern may include, for example, a predetermined treatment time, a level of energy to be delivered from the electrodes, and a predetermined impedance threshold. Accordingly, the feedback data may include at least impedance measurement data associated with the targeted tissue at the target site. The controller may be configured to process the impedance measurement data to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue. In particular, the controller may be configured to process the active impedance value using an algorithm to determine efficacy of ablation/modulation of the targeted tissue based on a comparison of the active impedance value with at least one of a predetermined minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value. In the event that the active impedance value is less than the predetermined minimum impedance value, the controller is configured to determine that ablation/modulation is unsuccessful and then further disables energy delivery from the one or more electrodes. In the event that the active impedance value is

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greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the controller is configured to calculate a slope change for the detection of a slope event. If a negative slope event is detected, the controller is configured to determine that ablation/modulation is successful and the controller disables energy delivery from the one or more electrodes upon detecting a negative slope event. If a negative slope event is not detected, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes. In the absence of detecting a slope event, the controller is configured to determine that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and the controller further disables energy delivery from the one or more electrodes.

The controller is further configured to transmit a signal resulting in an output, via an interactive interface, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue. The alert may include, for example, a visual alert including at least one of a color and text displayed on a graphical user interface (GUI) and indicating whether the ablation/modulation is successful or unsuccessful.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase

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volumetric flow through a nasal passage of the patient. Additionally, or alternatively, the resulting local hypoxia may cause neuronal degeneration.

Brief Description of the Drawings

FIGS. 1A and 1B are diagrammatic illustrations of a system for treating a condition of a patient using a handheld device according to some embodiments of the present disclosure.

FIG. 2 is a diagrammatic illustration of the console coupled to the handheld device consistent with the present disclosure, further illustrating one embodiment of an end effector of the handheld device for delivering energy to tissue at one or more target sites.

FIG. 3 is a side view of one embodiment of a handheld device for providing therapeutic treatment consistent with the present disclosure.

FIG. 4 is an enlarged, perspective view of one embodiment of an end effector consistent with the present disclosure.

FIGS. 5A-5F are various views of the multi-segment end effector consistent with the present disclosure.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment and second (distal) segment. FIG. 5B is an exploded, perspective view of the multi-segment end effector. FIG. 5C is an enlarged, top view of the multi-segment end effector. FIG. 5D is an enlarged, side view of the multi-segment end effector. FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment of the multi-segment end effector. FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment of the multi-segment end effector.

FIG. 6 is a perspective view, partly in section, of a portion of a support element illustrating an exposed conductive wire serving as an energy delivery element or electrode element.

FIG. 7 is a cross-sectional view of a portion of the shaft of the handheld device taken along lines 7-7 of FIG. 3.

FIG. 8A is a side view of the handle of the handheld device.

FIG. 8B is a side view of the handle illustrating internal components enclosed within.

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FIG. 9A is a block diagram illustrating delivery of non-therapeutic energy from electrodes of the end effector at a frequency/waveform for sensing one or more properties associated with one or more tissues at a target site in response to the non-therapeutic energy.

FIG. 9B is a block diagram illustrating communication of sensor data from the handheld device to the controller and subsequent determination, via the controller, of a treatment pattern for controlling energy delivery based on the sensor data for precision targeting of tissue of interest and to be treated.

FIG. 9C is a block diagram illustrating delivery of energy to the target site based on the treatment pattern output from the controller, monitoring of real-time feedback data associated with the targeted tissue undergoing treatment, and subsequent control over the delivery of energy based on the processing of the feedback data.

FIG. 10 is a flow diagram illustrating one embodiment of a method for treating a condition.

FIGS. 11A and 11B are graphs illustrating impedance profiles of two different sets of electrodes delivering energy to respective portions of targeted tissue, wherein the graphs illustrate a slope change event (e.g., asymptotic rise) which is indicative of whether the ablation/modulation of the targeted tissue is successful.

FIG. 12A illustrates an exemplary embodiment of a handheld device with fully deployed end effector, including an RF generator with a GUI, consistent with the present disclosure.

FIG. 12B illustrates placement of a two stage end effector around the turbinates and in close proximity to the primary and accessory posterior nasal nerves.

FIG. 12C is a close up view of the leaflets of the two-stage end effector indicating ground and active electrode pairs shown with black and red colors, respectively.

FIG. 12D is a simplified model used for computational modeling and showing the electrode inter-pair (IP) spacing and electrode length (EL).

FIG. 12E is an experimental setup using liver tissue with one activated petal pointed by white arrow.

FIGS. 13A and 13B illustrate simulated ablation zones (black contour) of tissue depth and tissue surface, respectively, following RF ablation with different electrode lengths while maintaining the same power level.

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FIG. 13C is a graph illustrating transient impedance profiles for different electrode lengths.

FIG. 13D is a graph illustrating a computationally estimated ablation depth expressed as a percentage increase in depth with increase in EL.

FIGS. 14A and 14B illustrate simulated ablation zones (black contour) of tissue depth and tissue surface, respectively following RF ablation with different electrode lengths while maintaining same power level for all three models with different inter-IP spacing.

FIG. 14C is a graph illustrating transient impedance profiles for different IP spacing.

FIG. 14D is a graph illustrating a computationally estimated ablation depth expressed as a percentage increase in depth with increase in IP spacing.

FIGS. 15A and 15B illustrate simulated ablation zones (black contour) of tissue depth and tissue surface, respectively following RF ablation with two configurations for a base (short EL and IP spacing) and optimized (large EL and IP) at the same power level.

FIG. 15C is a graph illustrating transient impedance profiles for two configurations.

FIG. 15D is a graph illustrating a computationally estimated ablation depth expressed as a percentage increase in depth with respect to base configuration.

FIGS. 16A and 16B are graphs illustrating transient impedance profiles during RF ablation in ex vivo liver tissue, specifically showing experimentally measured impedance during ex vivo experiments (n=3) with triangular blue markers with an interval of 2 s while the simulated impedance from computational model is demonstrated by dashed black line.

FIG. 16C is a photo of showing ablation zones following RF ablation in ex vivo liver tissue.

FIG. 16D is a graph illustrating experimentally measured and computationally estimated ablation depths expressed as a percentage change relative to that of respective low-medium power level.

FIG. 17 shows a chart illustrating the impact of energy delivery strategy on ablation results, specifically showing simulation results following different energy delivery strategies including constant and duty cycle energy deliveries, including temperature maps of tissue depth are shown immediately following the treatment (after impedance role-off) for each heating protocol with contours of thermal damage.

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FIG. 18A is a graph illustrating transient impedance profiles for models with different blood perfusion rates while the power level was fixed for all models (P = 1 W). The black triangular markers and blue circular markers display the data related to model with high and low perfusion effects respectively, while the model with no perfusion effects is shown by red color, while the dashed black contours in temperature distribution maps represent the thermal damage. FIGS. 18B-18D illustrate ablation zones (black contour) of tissue depth and tissue surface, respectively following RF ablation.

Detailed Description

The invention recognizes that knowing certain properties of tissue, both active and passive, at a given target site prior to and during electrotherapeutic treatment (i.e., neuromodulation, ablation, etc.) provides an ability to more precisely target a specific tissue of interest (i.e., targeted tissue) and minimize and/or prevent collateral damage to adjacent or surrounding non-targeted tissue.

For example, certain target sites intended to undergo treatment may consist of more than one type of tissue (i.e., nerves, muscles, bone, blood vessels, etc.). In particular, a tissue of interest (i.e., the specific tissue to undergo treatment) may be adjacent to one or more tissues that are not of interest (i.e., tissue that is not intended to undergo treatment). In one scenario, a surgeon may wish to provide electrotherapeutic stimulation to a nerve tissue, while avoiding providing any such stimulation to an adjacent blood vessel, for example, as unintended collateral damage may result in damage to the blood vessel and cause further complications. In such a scenario, the specific type of targeted tissue may generally dictate the level of electrical stimulation required to elicit a desired effect. Furthermore, physical properties of the targeted tissue, including the specific location and depth of the targeted tissue, in relation to the non-targeted tissue, further impacts the level of electrical stimulation necessary to result in effective therapeutic treatment.

Neuromodulation, for example, is technology that acts directly upon nerves. It is the alteration, or modulation, of nerve activity by delivering electrical or pharmaceutical agents directly to a target area. Neuromodulation devices and treatments have been shown to be highly effective at treating a variety of conditions and disorders. The most common indication for neuromodulation is treatment of chronic pain. However, the number of neuromodulation

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applications over the years has increased to include more than just the treatment of chronic pain, such as deep brain stimulation (DBS) treatment for Parkinson's disease, sacral nerve stimulation for pelvic disorders and incontinence, and spinal cord stimulation for ischemic disorders (angina, peripheral vascular disease).

Neuromodulation is particularly useful in the treatment of peripheral neurological disorders. There are currently over 100 kinds of peripheral nerve disorders, which can affect one nerve or many nerves. Some are the result of other diseases, like diabetic nerve problems. Others, like Guillain-Barre syndrome, happen after a virus infection. Still others are from nerve compression, like carpal tunnel syndrome or thoracic outlet syndrome. In some cases, like complex regional pain syndrome and brachial plexus injuries, the problem begins after an injury. However, some people are born with peripheral neurological disorders.

Peripheral nerve stimulation has become established for very specific clinical indications, including certain complex regional pain syndromes, pain due to peripheral nerve injuries, and the like. Some of the common applications of peripheral nerve stimulation include treatment of back pain, occipital nerve stimulation for treatment of migraine headaches, and pudendal nerve stimulation that is being investigated for use in urinary bladder incontinence.

The invention provides systems and methods with an ability to characterize, prior to an electrotherapeutic treatment, the type of tissue at a target site by sensing at least bioelectric properties of tissue, wherein such characterization includes identifying specific types of tissue present. For example, different tissue types include different physiological and histological characteristics. As a result of the different characteristics, different tissue types have different associated bioelectrical properties and thus exhibit different behavior in response to application of energy and frequencies applied thereto.

By knowing such properties of a given tissue, the systems and methods are configured to determine a specific treatment pattern for controlling delivery of energy at a specific level for a specific period of time to the tissue of interest (i.e., the targeted tissue) sufficient to ensure successful ablation/modulation of the targeted tissue while minimizing and/or preventing collateral damage to surrounding or adjacent non-targeted tissue at the target site. In particular, a given treatment pattern may include, for example, a predetermined treatment time, a precise level of energy to be delivered, and a predetermined impedance threshold for that particular tissue.

The systems and methods are further configured to receive and process real-time

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feedback data associated with the targeted tissue undergoing treatment to further ensure that energy delivered is maintained within the scope of the treatment pattern. More specifically, the systems and methods are configured to automatically control delivery of energy to the targeted tissue based on the processing of the real-time feedback data, wherein such data includes at least impedance measurement data associated with the targeted tissue collected during delivery of energy to the targeted tissue. The controller is configured to process impedance measurement data to detect a slope change event (e.g., an asymptotic rise) within an impedance profile associated with the treatment, wherein, with reference to the predetermined impedance threshold, the slope change event is indicative of whether the ablation/modulation of the targeted tissue is successful. In turn, the controller is configured to automatically control the delivery of energy to the targeted tissue based on real-time monitoring of feedback data, most notably impedance data, to ensure the desired ablation/modulation is achieved.

As a result, the systems and methods are able to ensure that optimal energy is delivered in order to delay the onset of impedance roll-off, until the target ablation/modulation depth is achieved, while maintaining clinically relevant treatment time. Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types.

It should be noted that, although many of the embodiments are described with respect to devices, systems, and methods for therapeutically modulating nerves associated with the peripheral nervous system (PNS) and thus the treatment of peripheral neurological conditions or disorders, other applications and other embodiments in addition to those described herein are within the scope of the present disclosure. For example, at least some embodiments of the present disclosure may be useful for the treatment of other disorders, such as the treatment of disorders associated with the central nervous system.

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic system 100 for treating a condition of a patient using a handheld device 102 according to some embodiments of the present disclosure. The system 100 generally includes a device 102 and a console 104 to which the device 102 is to be connected. FIG. 2 is a diagrammatic illustrations of the console 104 coupled to the handheld device 102 illustrating an exemplary embodiment of an end effector 114 for delivering energy to tissue at the one or more target sites of a patient for the treatment of a

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neurological disorder. As illustrated, the device 102 is a handheld device, which includes end effector 114, a shaft 116 operably associated with the end effector 114, and a handle 118 operably associated with the shaft 116. The end effector 114 may be collapsible/retractable and expandable, thereby allowing for the end effector 114 to be minimally invasive (i.e., in a collapsed or retracted state) upon delivery to one or more target sites within a patient and then expanded once positioned at the target site. It should be noted that the terms "end effector" and "therapeutic assembly" may be used interchangeably throughout this disclosure.

For example, a surgeon or other medical professional performing a procedure can utilize the handle 118 to manipulate and advance the shaft 116 to a desired target site, wherein the shaft 116 is configured to locate at least a distal portion thereof intraluminally at a treatment or target site within a portion of the patient associated with tissue to undergo electrotherapeutic stimulation for subsequent treatment of an associated condition or disorder. In the event that the tissue to be treated is a nerve, such that electrotherapeutic stimulation thereof results in treatment of an associated neurological condition, the target site may generally be associated with peripheral nerve fibers. The target site may be a region, volume, or area in which the target nerves are located and may differ in size and shape depending upon the anatomy of the patient. Once positioned, the end effector 114 may be deployed and subsequently deliver energy to the one or more target sites. The energy delivered may be non-therapeutic stimulating energy at a frequency for locating neural tissue and further sensing one or more properties of the neural tissue. For example, the end effector 114 may include an electrode array, which includes at least a subset of electrodes configured to sense the presence of neural tissue at a respective position of each of the electrodes, as well as morphology of the neural tissue, wherein such data may be used for determining, via the console 104, the type of neural tissue, depth of neural tissue, and location of neural tissue.

Based on the identification of the neural tissue type, the console 104 is configured to determine a specific treatment pattern for controlling delivery of energy from the end effector 114 upon the target site at a specific level for a specific period of time to the tissue of interest (i.e., the targeted tissue) sufficient to ensure successful ablation/modulation of the targeted tissue while minimizing and/or preventing collateral damage to surrounding or adjacent non-targeted tissue at the target site. Accordingly, the end effector 114 is able to therapeutically modulating nerves of interest, particularly nerves associated with a peripheral neurological conditional or

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disorder so as to treat such condition or disorder, while minimizing and/or preventing collateral damage.

For example, the end effector 114 may include at least one energy delivery element, such as an electrode, configured to delivery energy to the target tissue which may be used for sensing presence and/or specific properties of tissue (such tissue including, but not limited to, muscle, nerves, blood vessels, bones, etc.) for therapeutically modulating tissues of interest, such as neural tissue. For example, one or more electrodes may be provided by one or more portions of the end effector 114, wherein the electrodes may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the end effector 114 may include other energy delivery elements configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power.

In some embodiments, the end effector 114 may include one or more sensors (not shown), such as one or more temperature sensors (e.g., thermocouples, thermistors, etc.), impedance sensors, and/or other sensors. The sensors and/or the electrodes may be connected to one or more wires extending through the shaft 116 and configured to transmit signals to and from the sensors and/or convey energy to the electrodes.

As shown, the device 102 is operatively coupled to the console 104 via a wired connection, such as cable 120. It should be noted, however, that the device 102 and console 104 may be operatively coupled to one another via a wireless connection. The console 104 is configured to provide various functions for the device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the device 102. For example, when the device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 may include an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy.

In some embodiments, the console 104 may include a controller 107 communicatively

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coupled to the device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via evaluation/feedback algorithms 110. For example, the evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the temperature of the tissue at the treatment site, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to monitor temperature at the treatment site during therapy and automatically shut off the energy delivery when the temperature reaches a predetermined maximum (e.g., when applying RF energy) or predetermined minimum (e.g., when applying cryotherapy). In other embodiments, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance rise of the targeted tissue (i.e., in comparison to a baseline

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impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a graphical user interface (GUI) 112 provided via a display on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104, such as a tablet or monitor. The GUI 112 may generally provide operational instructions for the procedure, such as indicating when the device 102 is primed and ready to perform the treatment, and further providing status of therapy during the procedure, including indicating when the treatment is complete.

For example, as previously described, the end effector 114 and/or other portions of the system 100 can be configured to detect various parameters of a tissue of interest at the target site to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate nerves and/or other structures, and allow for neural mapping. For example, the end effector 114 may be configured to detect impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural tissue or fibers in the target region, as described in greater detail herein.

As shown in FIG. 1A, the console 104 further includes a monitoring system 108 configured to receive data from the end effector 114 (i.e., detected electrical and/or thermal measurements of tissue at the target site), specifically sensed by appropriate sensors (e.g., temperature sensors and/or impedance sensors, or the like), and process this information to identify the presence of nerves, the location of nerves, neural activity at *the* target site, and/or other properties of the neural tissue, such a physiological properties (e.g., depth), bioelectric properties, and thermal properties. The nerve monitoring system 108 can be operably coupled to the electrodes and/or other features of the end effector 114 via signal wires (e.g., copper wires) that extend through the cable 120 and through the length of the shaft 116. In other embodiments, the end effector 114 can be communicatively coupled to the nerve monitoring system 108 using other suitable communication means.

The nerve monitoring system 108 can determine neural locations and activity before therapeutic neuromodulation to determine precise treatment regions corresponding to the positions of the desired nerves. The nerve monitoring system 108 can further be used during treatment to determine the effect of the therapeutic neuromodulation, and/or after treatment to

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evaluate whether the therapeutic neuromodulation treated the target nerves to a desired degree. This information can be used to make various determinations related to the nerves proximate to the target site, such as whether the target site is suitable for neuromodulation. In addition, the nerve monitoring system 108 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site. For example, the nerve monitoring system 108 can further determine electroneurogram (ENG) signals based on recordings of electrical activity of neurons taken by the end effector 114 before and after therapeutic neuromodulation. Statistically meaningful (e.g., measurable or noticeable) decreases in the ENG signal(s) taken after neuromodulation can serve as an indicator that the nerves were sufficiently ablated. Additional features and functions of the nerve monitoring system 108, as well as other functions of the various components of the console 104, including the evaluation/feedback algorithms 110 for providing real-time feedback capabilities for ensuring optimal therapy for a given treatment is administered, are described in at least U.S. Publication No. 2016/0331459 and U.S. Publication No. 2018/0133460, the contents of each of which are incorporated by reference herein in their entireties.

The device 102 provides access to target sites associated with peripheral nerves for the subsequent neuromodulation of such nerves and treatment of a corresponding peripheral neurological condition or disorder. The peripheral nervous system is one of two components that make up the nervous system of bilateral animals, with the other part being the central nervous system (CNS). The PNS consists of the nerves and ganglia outside the brain and spinal cord. The main function of the PNS is to connect the CNS to the limbs and organs, essentially serving as a relay between the brain and spinal cord and the rest of the body. The peripheral nervous system is divided into the somatic nervous system and the autonomic nervous system. In the somatic nervous system, the cranial nerves are part of the PNS with the exception of the optic nerve (cranial nerve II), along with the retina. The second cranial nerve is not a true peripheral nerve but a tract of the diencephalon. Cranial nerve ganglia originated in the CNS. However, the remaining ten cranial nerve axons extend beyond the brain and are therefore considered part of the PNS. The autonomic nervous system exerts involuntary control over smooth muscle and glands. The connection between CNS and organs allows the system to be in two different

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functional states: sympathetic and parasympathetic. Accordingly, the devices, systems, and methods of the present invention are useful in detecting, identifying, and precision targeting nerves associated with the peripheral nervous system for treatment of corresponding peripheral neurological conditions or disorders.

The peripheral neurological conditions or disorders may include, but are not limited to, chronic pain, movement disorders, epilepsy, psychiatric disorders, cardiovascular disorders, gastrointestinal disorders, genitourinary disorders, to name a few. For example, chronic pain may include headaches, complex regional pain syndrome, neuropathy, peripheral neuralgia, ischemic pain, failed back surgery syndrome, and trigeminal neuralgia. The movement disorders may include spasticity, Parkinson's disease, tremor, dystonia, Tourette syndrome, camptocormia, hemifacial spasm, and Meige syndrome. The psychiatric disorders may include depression, obsessive compulsive disorder, drug addiction, and anorexia/eating disorders. The functional restoration may include restoration of certain functions post traumatic brain injury, hearing impairment, and blindness. The cardiovascular disorders may include angina, heart failure, hypertension, peripheral vascular disorders, and stroke. The gastrointestinal disorders may include dysmotility and obesity. The genitourinary disorders may include painful bladder syndrome, interstitial cystitis, and voiding dysfunction.

For example, the system 100 may be used for the treatment of a cardiovascular disorder, such as arrhythmias or heart rhythm disorders, including, but not limited to, atrial fibrillation (AF or A-fib). Atrial fibrillation is an irregular and often rapid heart rate that can increase one's risk of stroke, heart failure, and other heart-related complications. Atrial fibrillation occurs when regions of cardiac tissue abnormally conduct electric signals to adjacent tissue, thereby disrupting the normal cardiac cycle and causing asynchronous rhythm. Atrial fibrillation symptoms often include heart palpitations, shortness of breath, and weakness. While episodes of atrial fibrillation can come and go, a person may develop atrial fibrillation that doesn't go away and thus will require treatment. Although atrial fibrillation itself usually isn't life-threatening, it is a serious medical condition that sometimes requires emergency treatment, as it may lead to complications. For example, atrial fibrillation is associated with an increased risk of heart failure, dementia, and stroke.

The normal electrical conduction system of the heart allows the impulse that is generated by the sinoatrial node (SA node) of the heart to be propagated to and stimulate the myocardium

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(muscular layer of the heart). When the myocardium is stimulated, it contracts. It is the ordered stimulation of the myocardium that allows efficient contraction of the heart, thereby allowing blood to be pumped to the body. In AF, the normal regular electrical impulses generated by the sinoatrial node in the right atrium of the heart are overwhelmed by disorganized electrical impulses usually originating in the roots of the pulmonary veins. This leads to irregular conduction of ventricular impulses that generate the heartbeat. In particular, during AF, the heart's two upper chambers (the atria) beat chaotically and irregularly, out of coordination with the two lower chambers (the ventricles) of the heart.

During atrial fibrillation, the regular impulses produced by the sinus node for a normal heartbeat are overwhelmed by rapid electrical discharges produced in the atria and adjacent parts of the pulmonary veins. Sources of these disturbances are either automatic foci, often localized at one of the pulmonary veins, or a small number of localized sources in the form of either a re-entrant leading circle, or electrical spiral waves (rotors). These localized sources may be found in the left atrium near the pulmonary veins or in a variety of other locations through both the left or right atrium. There are three fundamental components that favor the establishment of a leading circle or a rotor: 1) slow conduction velocity of cardiac action potential; 2) short refractory period; and 3) small wavelength. Wavelength is the product of velocity and refractory period. If the action potential has fast conduction, with a long refractory period and/or conduction pathway shorter than the wavelength, an AF focus would not be established. In multiple wavelet theory, a wavefront will break into smaller daughter wavelets when encountering an obstacle, through a process called vortex shedding; but under proper conditions, such wavelets can reform and spin around a center, forming an AF focus.

The system 100 provides for the treatment of AF, in which the device 102 may provide access to and provide treatment of one or more target sites associated with nerves that correspond to, or are otherwise associated with, treating AF. For example, the device 102, in conjunction with the console 104, may detect, identify, and precision target cardiac tissue and subsequently deliver energy at a level or frequency sufficient to therapeutically modulate nerves associated with such cardiac tissue. The therapeutic modulation of such nerves is sufficient to disrupt the origin of the signals causing the AF and/or disrupt the conducting pathway for such signals.

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Similar to the conduction system of the heart, a neural network exists which surrounds the heart and plays an important role in formation of the substrate of AF and when a trigger is originated, usually from pulmonary vein sleeves, AF occurs. This neural network includes ganglionated plexi (GP) located adjacent to pulmonary vein ostia which are under control of higher centers in normal people. For example, the heart is richly innervated by the autonomic nerves. The ganglion cells of the autonomic nerves are located either outside the heart (extrinsic) or inside the heart (intrinsic). Both extrinsic and intrinsic nervous systems are important for cardiac function and arrhythmogenesis. The vagal nerves include axons that come from various nuclei in the medulla. The extrinsic sympathetic nerves come from the paravertebral ganglia, including the superior cervical ganglion, middle cervical ganglion, the cervicothoracic (stellate) ganglion and the thoracic ganglia. The intrinsic cardiac nerves are found mostly in the atria, and are intimately involved in atrial arrhythmogenesis cardiovascular disorder, such as arrhythmias or heart rhythm disorders, including, but not limited to, atrial fibrillation. When GP become hyperactive owing to loss of inhibition from higher centers (e.g., in elderly), AF can occur.

The system 100 can be used to control hyperactive GP either by stimulating higher centers and their connections, such as vagus nerve stimulation, or simply by ablating GP. Accordingly, the device 102, in conjunction with the console 104, may detect and identify ganglionated plexus (GP) and further determine an energy level sufficient to therapeutically modulate or treat (i.e., ablate) the GP for the treatment of AF (i.e., surgically disrupting the origin of the signals causing the AF and disrupting the conducting pathway for such signals) while minimizing and/or preventing collateral damage to surrounding or adjacent non-neural tissue including bloods vessels and bone and non-targeted neural tissue. It should be noted that other nerves and/or cardiac tissue, or other structures, known to have an impact on or cause AF, may be targeted by the system 100, including, but not limited to, pulmonary veins (e.g., pulmonary vein isolation upon creation of lesions around PV ostia to prevent triggers from reaching atrial substrate).

In addition to treating arrhythmias, the system 100 may also be used for the treatment of other cardiovascular-related conditions, particularly those involving the kidney. The kidneys play a significant role in the progression of CHF, as well as in Chronic Renal Failure (CRF), End-Stage Renal Disease (ESRD), hypertension (pathologically high blood pressure), and other cardio-renal diseases.

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The functions of the kidney can be summarized under three broad categories: filtering blood and excreting waste products generated by the body's metabolism; regulating salt, water, electrolyte and acid-base balance; and secreting hormones to maintain vital organ blood flow. Without properly functioning kidneys, a patient will suffer water retention, reduced urine flow and an accumulation of waste toxins in the blood and body. These conditions resulting from reduced renal function or renal failure (kidney failure) are believed to increase the workload of the heart.

For example, in a CHF patient, renal failure will cause the heart to further deteriorate as the water build-up and blood toxins accumulate due to the poorly functioning kidneys and, in turn, cause the heart further harm. CHF is a condition that occurs when the heart becomes damaged and reduces blood flow to the organs of the body. If blood flow decreases sufficiently, kidney function becomes impaired and results in fluid retention, abnormal hormone secretions and increased constriction of blood vessels. These results increase the workload of the heart and further decrease the capacity of the heart to pump blood through the kidney and circulatory system. This reduced capacity further reduces blood flow to the kidney. It is believed that progressively decreasing perfusion of the kidney is a principal non-cardiac cause perpetuating the downward spiral of CHF. Moreover, the fluid overload and associated clinical symptoms resulting from these physiologic changes are predominant causes for excessive hospital admissions, reduced quality of life, and overwhelming costs to the health care system due to CHF.

End-stage renal disease is another condition at least partially controlled by renal neural activity. There has been a dramatic increase in patients with ESRD due to diabetic nephropathy, chronic glomerulonephritis and uncontrolled hypertension. Chronic renal failure (CRF) slowly progresses to ESRD. CRF represents a critical period in the evolution of ESRD. The signs and symptoms of CRF are initially minor, but over the course of 2-5 years, become progressive and irreversible. While some progress has been made in combating the progression to, and complications of, ESRD, the clinical benefits of existing interventions remain limited.

Arterial hypertension is a major health problem worldwide. Treatment-resistant hypertension is defined as the failure to achieve target blood pressure despite the concomitant use of maximally tolerated doses of three different antihypertensive medications, including a diuretic. Treatment-resistant hypertension is associated with considerable morbidity and

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mortality. Patients with treatment-resistant hypertension have markedly increased cardiovascular morbidity and mortality, facing an increase in the risk of myocardial infarction (MI), stroke, and death compared to patients whose hypertension is adequately controlled.

The autonomic nervous system is recognized as an important pathway for control signals that are responsible for the regulation of body functions critical for maintaining vascular fluid balance and blood pressure. The autonomic nervous system conducts information in the form of signals from the body's biologic sensors such as baroreceptors (responding to pressure and volume of blood) and chemoreceptors (responding to chemical composition of blood) to the central nervous system via its sensory fibers. It also conducts command signals from the central nervous system that control the various innervated components of the vascular system via its motor fibers.

It is known from clinical experience and research that an increase in renal sympathetic nerve activity leads to vasoconstriction of blood vessels supplying the kidney, decreased renal blood flow, decreased removal of water and sodium from the body, and increased renin secretion. It is also known that reduction of sympathetic renal nerve activity, e.g., via denervation, may reverse these processes.

The renal sympathetic nervous system plays a critical influence in the pathophysiology of hypertension. The adventitia of the renal arteries has efferent and afferent sympathetic nerves. Renal sympathetic activation via the efferent nerves initiates a cascade resulting in elevated blood pressure. Efferent sympathetic outflow leads to vasoconstriction with a subsequent reduction in glomerular blood flow, a lowering of the glomerular filtration rate, release of renin by the juxtaglomerular cells, and the subsequent activation of the renin-angiotensin-aldosterone axis leading to increased tubular reabsorption of sodium and water. Decreased glomerular filtration rate also prompts additional systemic sympathetic release of catecholamines. As a consequence, blood pressure increases by a rise in total blood volume and increased peripheral vascular resistance.

The system 100 can be used for the treatment of cardio-renal diseases, including hypertension, by providing renal neuromodulation and/or denervation. For example, the device 102 may be placed at one or more target sites associated with renal nerves other neural fibers that contribute to renal neural function, or other neural features. For example, the device 102, in conjunction with the console 104, may detect, identify, and precision target renal nerve tissue

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and subsequently deliver energy at a level or frequency sufficient to therapeutically modulate nerves associated with such renal tissue. The therapeutic modulation of such renal nerves and/or renal tissue is sufficient to completely block or denervate the target neural structures and/or disrupt renal nervous activity, while minimizing and/or preventing collateral damage to surrounding or adjacent non-neural tissue including bloods vessels and bone and non-targeted neural tissue.

It should further be noted that the system 100 can be used to determine disease progression. In particular, the present system 100 can obtain measurements at one or more target sites associated with a given disease, disorder, or the like. Such measurements may be based on the active neural parameters (i.e., neuronal firing and active voltage monitoring) and may be used to identify neurons. The active neural parameters (and thus behavior) change with disease progression, thereby allowing the present system to identify such changes and determine a progression of the underlying disease or disorder. Such capabilities are possible based, at least in part, on the fact that the present system 100 is configured to monitor passive electric phenomena (i.e., the present system 100 determines the ohmic conductivity frequency, which remains consistent, while conductivity will be different based on disease or disorder progression).

FIG. 3 is a side view of one embodiment of a handheld device for providing therapeutic neuromodulation consistent with the present disclosure. As previously described, the device 102 includes an end effector (not shown) transformable between a collapsed/retracted configuration and an expanded deployed configuration, a shaft 116 operably associated with the end effector, and a handle 118 operably associated with the shaft 116. The handle 118 includes at least a first mechanism 126 for deployment of the end effector from collapsed/retracted configuration to the expanded, deployed configuration, and a second mechanism 128, separate from the first mechanism 124, for control of energy output by the end effector, specifically electrodes or other energy elements provided by the end effector. The handheld device 102 may further include an auxiliary line 121, which may provide a fluid connection between a fluid source, for example, and the shaft 116 such that fluid may be provided to a target site via the distal end of the shaft 116. In some embodiments, the auxiliary line 121 may provide a connection between a vacuum source and the shaft 116, such that the device 102 may include suction capabilities (via the distal end of the shaft 116).

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FIG. 4 is an enlarged, perspective view of one embodiment of an end effector 214 consistent with the present disclosure. As shown, the end effector 214 is generally positioned at a distal portion 116b of the shaft 116. The end effector 214 is transformable between a low-profile delivery state to facilitate intraluminal delivery of the end effector 214 to a treatment site and an expanded state, as shown. The end effector 214 includes a plurality of struts 240 that are spaced apart from each other to form a frame or basket 242 when the end effector 214 is in the expanded state. The struts 240 can carry one or more energy delivery elements, such as a plurality of electrodes 244. In the expanded state, the struts 240 can position at least two of the electrodes 244 against tissue at a target site within a particular region. The electrodes 244 can apply bipolar or multi-polar RF energy to the target site to therapeutically modulate nerves associated with a peripheral neurological condition or disorder. In various embodiments, the electrodes 244 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

In the embodiment illustrated in FIG. 4, the basket 242 includes eight branches 246 spaced radially apart from each other to form at least a generally spherical structure, and each of the branches 246 includes two struts 240 positioned adjacent to each other. In other embodiments, however, the basket 242 can include fewer than eight branches 246 (e.g., two, three, four, five, six, or seven branches) or more than eight branches 246. In further embodiments, each branch 246 of the basket 242 can include a single strut 240, more than two struts 240, and/or the number of struts 240 per branch can vary. In still further embodiments, the branches 246 and struts 240 can form baskets or frames having other suitable shapes for placing the electrodes 244 in contact with tissue at the target site. For example, when in the expanded state, the struts 240 can form an ovoid shape, a hemispherical shape, a cylindrical structure, a pyramid structure, and/or other suitable shapes.

The end effector 214 can further include an internal or interior support member 248 that extends distally from the distal portion 116b of the shaft 116. A distal end portion 250 of the support member 248 can support the distal end portions of the struts 240 to form the desired basket shape. For example, the struts 240 can extend distally from the distal potion 116b of the shaft 116 and the distal end portions of the struts 240 can attach to the distal end portion 250 of the support member 248. In certain embodiments, the support member 248 can include an internal channel (not shown) through which electrical connectors (e.g., wires) coupled to the

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electrodes 244 and/or other electrical features of the end effector 214 can run. In various embodiments, the internal support member 248 can also carry an electrode (not shown) at the distal end portion 250 and/or along the length of the support member 248.

The basket 242 can transform from the low-profile delivery state to the expanded state (shown in FIG. 4) by either manually manipulating a handle of the device 102, interacting with the first mechanism 126 for deployment of the end effector 214 from collapsed/retracted configuration to the expanded, deployed configuration, and/or other feature at the proximal portion of the shaft 116 and operably coupled to the basket 242. For example, to move the basket 242 from the expanded state to the delivery state, an operator can push the support member 248 distally to bring the struts 240 inward toward the support member 248. An introducer or guide sheath (not shown) can be positioned over the low-profile end effector 214 to facilitate intraluminal delivery or removal of the end effector 214 from or to the target site. In other embodiments, the end effector 214 is transformed between the delivery state and the expanded state using other suitable means, such as the first mechanism 126, as will be described in greater detail herein.

The individual struts 240 can be made from a resilient material, such as a shape-memory material (e.g., Nitinol) that allows the struts 240 to self-expand into the desired shape of the basket 242 when in the expanded state. In other embodiments, the struts 240 can be made from other suitable materials and/or the end effector 214 can be mechanically expanded via a balloon or by proximal movement of the support member 248. The basket 242 and the associated struts 240 can have sufficient rigidity to support the electrodes 244 and position or press the electrodes 244 against tissue at the target site. In addition, the expanded basket 242 can press against surrounding anatomical structures proximate to the target site and the individual struts 240 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 214 at the treatment site during energy delivery. In addition, the expansion and conformability of the struts 240 can facilitate placing the electrodes 244 in contact with the surrounding tissue at the target site.

At least one electrode 244 is disposed on individual struts 240. In the illustrated embodiment, two electrodes 244 are positioned along the length of each strut 240. In other embodiments, the number of electrodes 244 on individual struts 240 be only one, more than two, zero, and/or the number of electrodes 244 on the different struts 240 can vary. The electrodes

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244 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene ("PEDOT"), titanium, titanium nitride, carbon, carbon nanotubes, platinum grey, Drawn Filled Tubing ("DFT") with a silver core made by Fort Wayne Metals of Fort Wayne, Ind., and/or other suitable materials for delivery RF energy to target tissue.

In certain embodiments, each electrode 444 can be operated independently of the other electrodes 244. For example, each electrode can be individually activated and the waveform, polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 of FIG. 1A). Various embodiments of such independently controlled electrodes 244 are described in greater detail herein. The selective independent control of the electrodes 244 allows the end effector 214 to deliver RF energy to highly customized regions and to further create multiple micro-lesions to selectively modulate a target neural structure by effectively causing multi-point interruption of a neural signal due to the multiple micro-lesions. For example, a select portion of the electrodes 244 can be activated to target neural fibers in a specific region while the other electrodes 244 remain inactive. In certain embodiments, for example, electrodes 244 may be activated across the portion of the basket 242 that is adjacent to tissue at the target site, and the electrodes 244 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves along a portion of a target site without applying energy to structures in other portions of the target site.

The electrodes 244 can be electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1A) via wires (not shown) that extend from the electrodes 244, through the shaft 116, and to the RF generator. When each of the electrodes 244 is independently controlled, each electrode 244 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 244 can be controlled together and, therefore, multiple electrodes 244 can be electrically coupled to the same wire extending through the shaft 116. The RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 244. For example, the RF generator can deliver RF power at about 200-300 W to the electrodes 244, and do so while activating the electrodes 244 in a predetermined pattern selected based on the position of the end effector 214 relative to the treatment site and/or the identified locations of the target nerves. In other

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embodiments, the RF generator delivers power at lower levels (e.g., less than 1 W, 2-5W, 5-15 W, 15-50 W, 50-150 W, etc.) and/or higher power levels.

The end effector 214 can further include one or more sensors 252 (e.g., temperature sensors, impedance sensors, etc.) disposed on the struts 240 and/or other portions of the end effector 214 and configured to sense/detect one or more properties associated with tissue at a target site. For example, temperature sensors are configured to detect the temperature adjacent thereto. The sensors 252 can be electrically coupled to a console (e.g., the console 104 of FIG. 1A) via wires (not shown) that extend through the shaft 116. In various embodiments, the sensors 252 can be positioned proximate to the electrodes 244 to detect various properties of targeted tissue and/or the treatment associated therewith. As will be described in greater detail herein, the sensed data can be provided to the console 104, wherein such data is generally related to at least bioelectric properties of tissue at the target site. In turn, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such data and determine to identify a type of each of the one or more tissues at the target site. The console (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is further configured to determine a treatment pattern (also referred to herein as "ablation pattern") to be delivered by one or more of the plurality of electrodes of the end effector based on the tissue type, as well as tissue location and/or depth. The ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site. In particular, a given treatment pattern may include, for example, a predetermined treatment time, a precise level of energy to be delivered, and a predetermined impedance threshold for that particular tissue.

The device 102 is further be configured to provide the console 104 with sensed data in the form of feedback data, in real-, or near-real, time. The real-time feedback data is associated with the effect of the therapeutic stimulation on the targeted tissue. For example, feedback data may be associated with efficacy of ablation upon targeted tissue (e.g., neural tissue) during and/or after delivery of initial energy from one or more of the plurality of electrodes. Accordingly, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such real-time feedback data to determine if certain properties of the targeted tissue undergoing treatment (e.g., tissue

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temperature, tissue impedance, etc.) reach predetermined thresholds for irreversible tissue damage.

More specifically, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to automatically control delivery of energy to the targeted tissue based on the processing of the real-time feedback data, wherein such data includes at least impedance measurement data associated with the targeted tissue collected during delivery of energy to the targeted tissue. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process impedance measurement data to detect a slope change event (e.g., an asymptotic rise) within an impedance profile associated with the treatment, wherein, with reference to the predetermined impedance threshold, the slope change event is indicative of whether the ablation/modulation of the targeted tissue is successful. In turn, the controller 107 can automatically tune energy output individually for the one or more electrodes after an initial level of energy has been delivered based, at least in part, on monitoring and processing of the real-time feedback data, most notably impedance data, to ensure the desired ablation/modulation is achieved. For example, once a slope change event (e.g., an asymptotic rise) within an impedance profile is detected, with reference to the predetermined impedance threshold of the targeted tissue (which is known via the treatment pattern), the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and to further prevent and/or minimize collateral damage to surrounding or adjacent non-targeted tissue. For example, in certain embodiments, the energy delivery can automatically be tuned based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 110 of FIG. 1A) stored on a console (e.g., the console 104 of FIG. 1A) operably coupled to the end effector 214.

FIGS. 5A-5F are various views of another embodiment of an end effector 314 consistent with the present disclosure. As generally illustrated, the end effector 314 is a multi-segmented end effector, which includes at least a first segment 322 and a second segment 324 spaced apart from one another. The first segment 322 is generally positioned closer to a distal portion of the shaft 116, and is thus sometimes referred to herein as the proximal segment 322, while the second segment 324 is generally positioned further from the distal portion of the shaft 116 and is thus sometimes referred to herein as the distal segment 324. Each of the first and second segments 322 and 324 is transformable between a retracted configuration, which includes a low-

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profile delivery state and a deployed configuration, which includes an expanded state, as shown in the figures. The end effector 314 is generally designed to be positioned within a nasal region of the patient for the treatment of a rhinosinusitis condition while minimizing or avoiding collateral damage to surrounding tissue, such as blood vessels or bone. In particular, the end effector 314 is configured to be advanced within the nasal cavity and be positioned at one or more target sites generally associated with postganglionic parasympathetic fibers that innervate the nasal mucosa. In turn, the end effector 314 is configured to therapeutically modulate the postganglionic parasympathetic nerves.

It should be noted, however, that an end effector consistent with the present disclosure may be multi-segmented in a similar fashion as end effector 314 and may be used to provide treatment in other regions of the patient outside of the nasal cavity and thus is not limited to the particular design/configuration as the end effector 314 nor the intended treatment site (e.g., nasal cavity). Rather, other multi-segmented designs are contemplated for use in particular regions of a patient, particularly regions in which the use of multiple and distinct segments would be advantageous, as is the case with the end effector 314 design due to the anatomy of the nasal cavity.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment 322 and second (distal) segment 324. FIG. 5B is an exploded, perspective view of the multi-segment end effector 314. FIG. 5C is an enlarged, top view of the multi-segment end effector 314. FIG. 5D is an enlarged, side view of the multi-segment end effector 314. FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment 322 of the multi-segment end effector 314 and FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment 324 of the multi-segment end effector 314.

As illustrated, the first segment 322 includes at least a first set of flexible support elements, generally in the form of wires, arranged in a first configuration, and the second segment 324 includes a second set of flexible support elements, also in the form of wires, arranged in a second configuration. The first and second sets of flexible support elements include composite wires having conductive and elastic properties. For example, in some embodiments, the composite wires include a shape memory material, such as Nitinol. The flexible support elements may further include a highly lubricious coating, which may allow for desirable electrical insulation properties as well as desirable low friction surface finish. Each of

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the first and second segments 322, 324 is transformable between a retracted configuration and an expanded deployed configuration such that the first and second sets of flexible support elements are configured to position one or more electrodes provided on the respective segments (see electrodes 336 in FIGS. 5E and 5F) into contact with one or more target sites when in the deployed configuration.

As shown, when in the expanded deployed configuration, the first set of support elements of the first segment 322 includes at least a first pair of struts 330a,330b, each comprising a loop (or leaflet) shape and extending in an upward direction and a second pair of struts 332a, 332b, each comprising a loop (or leaflet) shape and extending in a downward direction, generally in an opposite direction relative to at least the first pair of struts 330a, 330b. It should be noted that the terms upward and downward are used to describe the orientation of the first and second segments 322, 324 relative to one another. More specifically, the first pair of struts 330a, 330b generally extend in an outward inclination in a first direction relative to a longitudinal axis of the multi-segment end effector 314 and are spaced apart from one another. Similarly, the second pair of struts 332a, 332b extend in an outward inclination in a second direction substantially opposite the first direction relative to the longitudinal axis of the multi-segment end effector and spaced apart from one another.

The second set of support elements of the second segment 324, when in the expanded deployed configuration, includes a second set of struts 334(1), 334(2), 334(n) (approximately six struts), each comprising a loop shape extending outward to form an open-ended circumferential shape. As shown, the open-ended circumferential shape generally resembles a blooming flower, wherein each looped strut 334 may generally resemble a flower petal. It should be noted that the second set of struts 334 may include any number of individual struts and is not limited to six, as illustrated. For example, in some embodiments, the second segment 124 may include two, three, four, five, six, seven, eight, nine, ten, or more struts 334.

The first and second segments 322, 324, specifically struts 330, 332, and 334 include one or more energy delivery elements, such as a plurality of electrodes 336. It should be noted that any individual strut may include any number of electrodes 336 and is not limited to one electrode, as shown. In the expanded state, the struts 330, 332, and 334 can position any number of electrodes 336 against tissue at a target site within the nasal region (e.g., proximate to the palatine bone inferior to the SPF). The electrodes 336 can apply bipolar or multi-polar

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radiofrequency (RF) energy to the target site to therapeutically modulate postganglionic parasympathetic nerves that innervate the nasal mucosa proximate to the target site. In various embodiments, the electrodes 336 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

The first and second segments 322, 324 and the associated struts 330, 332, and 334 can have sufficient rigidity to support the electrodes 336 and position or press the electrodes 336 against tissue at the target site. In addition, each of the expanded first and second segments 322, 324 can press against surrounding anatomical structures proximate to the target site (e.g., the turbinates, the palatine bone, etc.) and the individual struts 330, 332, 334 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 314. In addition, the expansion and conformability of the struts 330, 332, 334 can facilitate placing the electrodes 336 in contact with the surrounding tissue at the target site. The electrodes 336 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene (PEDOT), titanium, titanium nitride, carbon, carbon nanotubes, platinum grey, Drawn Filled Tubing (DFT) with a silver core, and/or other suitable materials for delivery RF energy to target tissue. In some embodiments, such as illustrated in FIG. 6, a strut may include an outer jacket surrounding a conductive wire, wherein portions of the outer jacket are selectively absent along a length of the strut, thereby exposing the underlying conductive wire so as to act as an energy delivering element (i.e., an electrode) and/or sensing element, as described in greater detail herein.

In certain embodiments, each electrode 336 can be operated independently of the other electrodes 336. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein). The selective independent control of the electrodes 336 allows the end effector 314 to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 336 can be activated to target neural fibers in a specific region while the other electrodes 336 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 324 that is adjacent to tissue at the target site, and the electrodes 336 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations

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facilitate selective therapeutic modulation of nerves on the lateral nasal wall within one nostril without applying energy to structures in other portions of the nasal cavity.

The electrodes 336 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1A) via wires (not shown) that extend from the electrodes 336, through the shaft 116, and to the RF generator. When each of the electrodes 336 is independently controlled, each electrode 336 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 336 can be controlled together and, therefore, multiple electrodes 336 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 336. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 336, and do so while activating the electrodes 336 in a predetermined pattern selected based on the position of the end effector 314 relative to the treatment site and/or the identified locations of the target tissues. It should further be noted that the electrodes 336 may be individually activated and controlled (i.e., controlled level of energy output and delivery) based, at least in part, on feedback data. The RF generator is able to provide bipolar low power (10 watts with maximum setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

Once deployed, the first and second segments 322, 324 contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments 322, 324 become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes 336, precise and focused application of RF thermal energy or non-thermal energy to the one or more target sites to thereby therapeutically modulate associated neural tissue. More specifically, the first and second segments 322, 324 have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments 322, 324, and thus one or more electrodes associated therewith 336, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

For example, the first set of flexible support elements of the first segment 322 conforms to and complements a shape of a first anatomical structure at the first location when the first

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segment 322 is in the deployed configuration and the second set of flexible support elements of the second segment 124 conforms to and complements a shape of a second anatomical structure at the second location when the second segment is in the deployed configuration. The first and second anatomical structures may include, but are not limited to, inferior turbinate, middle turbinate, superior turbinate, inferior meatus, middle meatus, superior meatus, pterygopalatine region, pterygopalatine fossa, sphenopalatine foramen, accessory sphenopalatine foramen(ae), and sphenopalatine micro-foramen(ae).

In some embodiments, the first segment 322 of the multi-segment end effector 314 is configured in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to the middle turbinate and the second segment 324 of the multi-segment end effector is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the middle turbinate.

For example, the first set of flexible support elements of the first segment (i.e., struts 330 and 332) conforms to and complements a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 322 is in the deployed configuration and the second set of flexible support elements (i.e., struts 334) of the second segment 324 contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of middle turbinate when the second segment 324 is in the deployed configuration. Accordingly, when in the deployed configuration, the first and second segments 322, 324 are configured to position one or more associated electrodes 336 at one or more target sites relative to either of the middle turbinate and the plurality of tissue locations in the cavity behind the middle turbinate. In turn, electrodes 336 are configured to deliver RF energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

As illustrated in FIG. 5E, the first segment 322 comprises a bilateral geometry. In particular, the first segment 322 includes two identical sides, including a first side formed of struts 330a, 332a and a second side formed of struts 330b, 332b. This bilateral geometry allows at least one of the two sides to conform to and accommodate an anatomical structure within the nasal cavity when the first segment 322 is in an expanded state. For example, when in the expanded state, the plurality of struts 330a, 332a contact multiple locations along multiple portions of the anatomical structure and electrodes provided by the struts are configured to emit

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energy at a level sufficient to create multiple micro-lesions in tissue of the anatomical structure that interrupt neural signals to mucus producing and/or mucosal engorgement elements. In particular, struts 330a, 332a conform to and complement a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 322 is in the deployed configuration, thereby allowing for both sides of the anatomical structure to receive energy from the electrodes. By having this independence between first and second side (i.e., right and left side) configurations, the first segment 322 is a true bilateral device. By providing a bilateral geometry, the multi-segment end effector 314 does not require a repeat use configuration to treat the other side of the anatomical structure, as both sides of the structure are accounted at the same time due to the bilateral geometry. The resultant micro-lesion pattern can be repeatable and is predictable in both macro element (depth, volume, shape parameter, surface area) and can be controlled to establish low to high effects of each, as well as micro elements (the thresholding of effects within the range of the macro envelope can be controlled), as well be described in greater detail herein. The systems of the present invention are further able to establish gradients within allowing for control over neural effects without having widespread effect to other cellular bodies, as will be described in greater detail herein.

FIG. 7 is a cross-sectional view of a portion of the shaft 116 of the handheld device taken along lines 7-7 of FIG. 3. As illustrated, the shaft 116 may be constructed from multiple components so as to have the ability to constrain the end effector in the retracted configuration (i.e., the low-profile delivery state) when the end effector is retracted within the shaft 116, and to further provide an atraumatic, low profile and durable means to deliver the end effector to the target site. The shaft 116 includes coaxial tubes which travel from the handle 118 to a distal end of the shaft 116. The shaft 116 assembly is low profile to ensure adequate delivery of therapy in areas requiring low-profile access. The shaft 116 includes an outer sheath 138, surrounding a hypotube 140, which is further assembled over electrode wires 129 which surround an inner lumen 142. The outer sheath 138 serves as the interface between the anatomy and the device 102. The outer sheath 138 may generally include a low friction PTFE liner to minimize friction between the outer sheath 138 and the hypotube 140 during deployment and retraction. In particular the outer sheath 138 may generally include an encapsulated braid along a length of the shaft 116 to provide flexibility while retaining kink resistance and further retaining column

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and/or tensile strength. For example, the outer sheath 138 may include a soft Pebax material, which is atraumatic and enables smooth delivery through a passageway.

The hypotube 140 is assembled over the electrode wires starting within the handle 118 and travelling to the proximal end of the end effector. The hypotube 140 generally acts to protect the wires during delivery and is malleable to enable flexibility without kinking to thereby improve trackability. The hypotube 140 provides stiffness and enables torqueability of the device 102 to ensure accurate placement of the end effector 314. The hypotube 140 also provides a low friction exterior surface which enables low forces when the outer sheath 138 moves relative to the hypotube 140 during deployment and retraction or constraint. The shaft 116 may be pre-shaped in such a manner so as to complement a given anatomy (e.g., nasal cavity). For example, the hypotube 140 may be annealed to create a bent shaft 116 with a pre-set curve. The hypotube 140 may include a stainless-steel tubing, for example, which interfaces with a liner in the outer sheath 138 for low friction movement.

The inner lumen 142 may generally provide a channel for fluid extraction during a treatment procedure. For example, the inner lumen 142 extends from the distal end of the shaft 116 through the hypotube 140 and to atmosphere via a fluid line (line 121 of FIG. 3). The inner lumen 142 materials are chosen to resist forces of external components acting thereon during a procedure.

FIG. 8A is a side view of the handle of the handheld 118 and FIG. 8B is a side view of the handle 118 illustrating internal components enclosed within. The handle 118 generally includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. For example, the handle 118 may include specific contours, including recesses 144, 146, and 148 which are designed to naturally receive one or more of an operator's fingers in either of an overhand grip or underhand grip style and provide a comfortable feel for the operator. For example, in an underhand grip, recess 144 may naturally receive an operator's index finger, recess 146 may naturally receive an operator's middle finger, and recess 148 may naturally receive an operator's ring and little (pinkie or pinky) fingers which wrap around the proximal protrusion 150 and the operator's thumb naturally rests on a top portion of the handle 118 in a location adjacent to the first mechanism 126. In an overhand grip, the operator's index finger may naturally rest on the

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top portion of the handle 118, adjacent to the first mechanism 126, while recess 144 may naturally receive the operator's middle finger, recess 146 may naturally receive a portion of the operator's middle and/or ring fingers, and recess 148 may naturally receive and rest within the space (sometimes referred to as the purlicue) between the operator's thumb and index finger.

As previously described, the handle includes multiple user-operated mechanisms, including at least a first mechanism 126 for deployment of the end effector from the collapsed/retracted configuration to the expanded deployed configuration and a second mechanism 128 for controlling of energy output by the end effector, notably energy delivery from one or more electrodes. As shown, the user inputs for the first and second mechanisms 126, 128 are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. For example, user input for the first mechanism 126 is positioned on a top portion of the handle 118 adjacent the grip portion and user input for the second mechanism 128 is positioned on side portions of the handle 118 adjacent the grip portion. As such, in an underhand grip style, the operator's thumb rests on the top portion of the handle adjacent to the first mechanism 126 and at least their middle finger is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. In an overhand grip system, the operator's index finger rests on the top portion of the handle adjacent to the first mechanism 126 and at least their thumb is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

Referring to FIG. 8B, the various components provided within the handle 118 are illustrated. As shown, the first mechanism 126 may generally include a rack and pinion assembly providing movement of end effector between the retracted and deployed configurations in response to input from a user-operated controller. The rack and pinion assembly generally includes a set of gears 152 for receiving input from the user-operated controller and converting the input to linear motion of a rack member 154 operably associated with at least one of the shaft 116 and the end effector. The rack and pinion assembly comprises a gearing ratio sufficient to balance a stroke length and retraction and deployment forces, thereby improving control over the deployment of the end effector. As shown, the rack member 154 may be coupled to a portion of

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the shaft 116, for example, such that movement of the rack member 154 in a direction towards a proximal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector remains stationary, thereby exposing the end effector and allowing the end effector to transition from the constrained, retracted configuration to the expanded, deployed configuration. Similarly, movement of the rack member 154 in a direction towards a distal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector remains stationary, and thereby encloses the end effector within the shaft 116. It should be noted that, in other embodiments, the rack member 154 may be directly coupled to a portion of the end effector such that movement of the rack member 154 results in corresponding movement of the end effector while the shaft 116 remains stationary, thereby transitioning the end effector between the retracted and deployed configurations.

The user-operated controller associated with the first mechanism 126 may include a slider mechanism operably associated with the rack and pinion rail assembly. Movement of the slider mechanism in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and movement of the slider mechanism in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration. In other embodiment, the user-operated controller associated with the first mechanism 126 may include a scroll wheel mechanism operably associated with the rack and pinion rail assembly. Rotation of the wheel in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and rotation of the wheel in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration.

FIGS. 9A, 9B, and 9C are block diagrams illustrating the process of sensing, via an end effector, data associated with one or more tissues at a target site, notably bioelectric properties of one more tissues at the target site, and the subsequent processing of such data (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) to determine the type of tissue(s) at the target site, determining a treatment pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified tissue types (as well as tissue location and/or depth), and subsequent receipt and processing of real-time feedback data associated with the targeted tissue undergoing treatment. The ablation energy associated with

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the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

It should be noted that, while the block diagrams of FIGS. 9A, 9B, and 9C include reference to end effector 214, other end effector embodiments, including end effector 314, are similarly configured with respect to sensing data associated with at least the presence of neural tissue and other properties of the neural tissue, including neural tissue depth. Accordingly, the following process is not limited to end effector 214.

FIG. 9A is a block diagram illustrating delivery of non-therapeutic energy from electrodes 244 of the end effector at a frequency for sensing one or more properties associated with tissue at a target site in response to the non-therapeutic energy.

As previously described, the handheld treatment device includes an end effector comprising a micro-electrode array arranged about a plurality of struts. For example, end effector 214 includes a plurality of struts 240 that are spaced apart from each other to form a frame or basket 242 when the end effector 214 is in the expanded state. The struts 240 include a plurality of energy delivery elements, such as a plurality of electrodes 244. In the expanded state, each of the plurality of struts is able to conform to and accommodate an anatomical structure at a target site. When positioned, the struts may contact multiple locations along multiple portions of a target site and thereby position one or more electrodes 244 against tissue at a target site. At least a subset of electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense the bioelectric properties of the one or more tissues at the target site, and further convey such data to the console 104. In addition to bioelectric properties, the data may also include at least one of physiological properties and thermal properties of tissue at the target site.

For example, upon delivering non-therapeutic stimulating energy (via one or more electrodes 244) to respective positions, various properties of the tissue at the one or more target sites can be detected. This information can then be transmitted to the console 104, particularly the controller 107, monitoring system 108, and evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate a tissue of interest (targeted tissue to receive electric therapeutic stimulation), such as neural tissue, differentiate between different types of neural tissue, and map the anatomical and/or neural structure at the target site. For example, the end effector 214 can be

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used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in the target region. In certain embodiments, the end effector 214, together with the console 104 components, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. For example, the evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes 244).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-50Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures, including the firing of neural tissue, differences between neural tissue and other anatomical structures (e.g., blood vessels), and even different types of neural tissue. This information can be analyzed by the evaluation/feedback algorithms 110 and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural tissue and other anatomy at the treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode 244 can be operated independently of the other electrodes 244. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes 244 allows the end effector 214 to detect information (i.e., the presence of neural tissue, depth of neural tissue, and other physiological and bioelectrical properties) and subsequently deliver RF energy to highly customized regions. For example, a select portion of the electrodes 244 can be activated to target specific neural fibers in a specific region while the other electrodes 244 remain inactive. In addition, the electrodes 244 can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

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As previously described, the system 100 can identify tissue type of one or more tissues at a target site prior to therapy such that the therapeutic stimulation can be applied to precise regions including targeted tissue, while avoiding negative effects on non-targeted tissue and structures (e.g., blood vessels). For example, the system 100 can detect various bioelectrical parameters in an interest zone to determine the location and morphology of various tissue types (e.g., different types of neural tissue, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony regions, etc.). The system 100 is further configured to measure bioelectric potential.

To do so, one or more of the electrodes 244 is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies, and/or alternating (sine, square, triangle, sawtooth, etc.) wave or direct constant current/power/voltage source at one or more frequencies) are applied to the tissue by one or more electrodes 244 at or near the treatment site, and the voltage and/or current differences based on the wave applied at various different frequencies between various pairs of electrodes 244 of the end effector 214 may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural tissue, and/or other types of tissue) in the region of interest. For example, a fixed current (i.e., direct or alternating current) can be applied to a pair of electrodes 244 adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes 244 are measured. Conversely, a fixed voltage (i.e. mono or bi-phasic) can be applied to a pair of electrodes 244 adjacent to each other and the resultant current between other pairs of adjacent electrodes 244 are measured. It will be appreciated that the current injection electrodes 244 and measurement electrodes 244 need not be adjacent, and that modifying the spacing between the two current injection electrodes 244 can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes 244 provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes 244 that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric potential

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measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector 114), and this information can be used to map the neural and anatomical structures by the use of frequency differentiation reconstruction. In particular, current-voltage data may be observed with the difference in dielectric and conductive properties of tissue type when different levels of current frequencies are applied. Applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters. At high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of the neural tissue do not impede current flow, and the current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes of the cells or cell spacing. The stimulation frequencies can be in the megahertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

Further, the inherent morphology and composition of the anatomical structures within a given region or zone of a patient's body react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural tissue, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy.

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In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes 244 at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, passive bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes 244 and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes 244 are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural tissue that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural tissue that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the

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selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate neural fibers associated with certain neurological conditions or disorders to be treated. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

FIG. 9B is a block diagram illustrating communication of sensor data from the handheld device 102 to the controller and subsequent determination, via the controller, of a treatment pattern for controlling delivery of energy at a specific level for a specific period of time to the tissue of interest (i.e., the targeted tissue) sufficient to ensure successful ablation/modulation of the targeted tissue while minimizing and/or preventing collateral damage to surrounding or adjacent non-targeted tissue at the target site. As shown, the end effector 214 communicates the tissue data (i.e., bioelectric properties of tissue at the target site) to the console 104. The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, induced electromotive force, and combinations thereof. The dielectric properties may include, for example, at least a complex relative dielectric permittivity.

In turn, console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process such data and determine a type of tissue at the target site. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is further configured to determine a treatment pattern to be delivered by one or more of the plurality of electrodes of the end effector based, at least in part, on identified tissues. The treatment pattern (also referred to herein as "ablation pattern"), may include various parameters associated with the delivery of energy, including, for example, a predetermined treatment time, a precise level of energy to be delivered, and a predetermined

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impedance threshold for that particular tissue. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to tune energy output (i.e., delivery of electrical therapeutic stimulation) based on the treatment pattern of a tissue of interest such that the energy delivered is at a specific frequency for a predetermined period of time and up to a predetermined impedance threshold, such that energy delivery is targeted the tissue of interest while avoiding the non-targeted tissue.

It should be noted that, in some embodiments, the system 100 may include a database 400 containing a plurality of profiles 402(1)-402(n) of identified and known tissue types, wherein each profile may include electric signature data for the associated tissue type. The electric signature data may generally include previously identified bioelectric properties of the tissue type, including impedance profiles with known impedance threshold values associated with successful and unsuccessful ablation and/or modulation treatment of that particular tissue. Accordingly, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process data received from the end effector 114 (i.e., bioelectric properties of one or more tissues at the target site) and determine a type of tissue at the target site, and a treatment pattern for each of the one or more identified tissue types based on a comparison of the data with the electric signature data stored in each of the profiles 402. Upon a positive correlation between data sets, the console 104 is configured to identify a matching profile and thus determine the one or more tissue types at the target site and the respective treatment patterns of each.

FIG. 9C is a block diagram illustrating delivery of energy to the target site based on the treatment pattern output from the controller, monitoring of real-time feedback data associated with the targeted tissue undergoing treatment, and subsequent control over the delivery of energy based on the processing of the feedback data. Upon delivery energy from the electrodes to the targeted tissue (based on the treatment pattern), the device 102, via the electrodes/sensors (244, 252) is further configured to provide the console 104 with sensed data in the form of feedback data, in real-, or near-real, time. The real-time feedback data is associated with the effect of the therapeutic stimulation on the targeted tissue. For example, feedback data may be associated with efficacy of ablation upon targeted tissue (e.g., neural tissue) during and/or after delivery of initial energy from one or more of the plurality of electrodes. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process

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such real-time feedback data to determine if certain properties of the targeted tissue undergoing treatment (e.g., tissue temperature, tissue impedance, etc.) reach predetermined thresholds for irreversible tissue damage.

More specifically, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to automatically control delivery of energy to the targeted tissue based on the processing of the real-time feedback data, wherein such data includes at least impedance measurement data associated with the targeted tissue collected during delivery of energy to the targeted tissue. The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process impedance measurement data to detect a slope change event (e.g., an asymptotic rise) within an impedance profile associated with the treatment, wherein, with reference to the predetermined impedance threshold, the slope change event is indicative of whether the ablation/modulation of the targeted tissue is successful. In turn, the controller 107 can automatically tune energy output individually for the one or more electrodes after an initial level of energy has been delivered based, at least in part, on monitoring and processing of the real-time feedback data, most notably impedance data, to ensure the desired ablation/modulation is achieved. For example, once a slope change event (e.g., an asymptotic rise) within an impedance profile is detected, with reference to the predetermined impedance threshold of the targeted tissue (which is known via the treatment pattern), the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and to further prevent and/or minimize collateral damage to surrounding or adjacent non-targeted tissue. For example, in certain embodiments, the energy delivery can automatically be tuned based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 110 of FIG. 1A) stored on a console (e.g., the console 104 of FIG. 1A) operably coupled to the end effector 214.

For example, in one embodiment, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is configured to process the impedance measurement data (received as part of the real-time feedback data) to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue. In particular, the console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) may be configured to process the active impedance value using an algorithm to determine efficacy of ablation/modulation of the targeted tissue based on a

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comparison of the active impedance value with at least one of a predetermined minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value. For example, the impedance values (i.e., predetermined minimum impedance value, predetermined low terminal impedance value, and predetermined high terminal impedance value) may range between approximately 100 ohms and 1 kohms. In the event that the active impedance value is less than the predetermined minimum impedance value, the console 104 is configured to determine that ablation/modulation is unsuccessful and then further disables energy delivery from the one or more electrodes. In the event that the active impedance value is greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the console 104 is configured to calculate a slope change for the detection of a slope event. If a negative slope event is detected, the console 104 is configured to determine that ablation/modulation is successful and the controller disables energy delivery from the one or more electrodes upon detecting a negative slope event. If a negative slope event is not detected, the console 104 determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes. In the absence of detecting a slope event, the console 104 is configured to determine that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and the controller further disables energy delivery from the one or more electrodes.

The electrodes 244 are configured to be independently controlled and activated by the controller 107 (in conjunction with the evaluation/feedback algorithms 110) to thereby deliver energy independent of one another. Accordingly, the controller 107 can tune energy output individually for the one or more electrodes 244 after an initial level of energy has been delivered based, at least in part, on feedback data. For example, once the threshold is reached, the application of therapeutic stimulation energy can be terminated to allow the tissue to remain intact. In other embodiments, if the threshold has not been reached, the controller can maintain, reduce, or increase energy output to a given electrode 244 until such threshold is reached. Accordingly, the energy delivery of any given electrode 244 can automatically be tuned based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 110 of FIG. 1A) stored on a console (e.g., the console 104 of FIG. 1A) operably coupled to the end effector 214. For example, at least some of the electrodes 244 may have different levels of energy to be

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delivered at respective positions sufficient to ablate neural tissue at the respective positions based on the feedback data received for the respective locations.

The console 104 (via the controller 107, monitoring system 108, and evaluation/feedback algorithms 110) is further configured to transmit a signal resulting in an output, via interactive interface 112, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue. The alert may include, for example, a visual alert including at least one of a color and text displayed on a graphical user interface (GUI) and indicating whether the ablation/modulation is successful or unsuccessful, particularly with respect to respective sets of electrodes.

FIG. 10 is a flow diagram illustrating one embodiment of a method 500 for treating a condition. The condition may include, for example, a peripheral neurological condition of a patient. The method 500 includes providing a treatment device comprising an end effector including one or more electrodes and a controller operably associated with the treatment device (operation 510). The method 500 further includes positioning the end effector at a target site associated with a patient (operation 520) and determining, via the controller, a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues (operation 530).

The identifying data is associated with one or more properties of the one or more tissues, wherein the one or more properties may include, but are not limited to, a type of tissue, a depth of the one or more tissues, and a location of the one or more tissues. For example, a subset of the one or more electrodes may be configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense at least bioelectric properties of the one or more tissues at the target site. The bioelectric properties may include, but are not limited to, complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

The controller is generally configured to process the identifying data to determine the

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treatment pattern. The processing of identifying data, via the controller, may include, for example comparing the identifying data received from the device with electric signature data associated with a plurality of known tissue types. The electric signature data, for example, may include at least bioelectric properties of known tissue types. The comparison may include correlating the identifying data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network

The processing of the data may include, for example: a) comparing the data received from the device with electric signature data associated with a plurality of known tissue types; and (b) use of (i) a supervised and/or (ii) an unsupervised trained neural network. For example, the controller may be configured to compare the tissue data (i.e., data received from the treatment device associated with tissue at the target site) with profiles of known tissue types stored in a database, for example. Each profile may generally include electric signature data that generally characterizes a known tissue type, including previously identified physiological, histological, and bioelectric properties of a known tissue type, including impedance profiles with known impedance threshold values associated with successful and unsuccessful ablation and/or modulation treatment of that particular tissue.

The method 500 further includes receiving, from the device, and processing, via the controller, real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes (operation 540). The method 500 further includes controlling, via the controller, supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site (operation 550).

The treatment pattern may include, for example, a predetermined treatment time, a level of energy to be delivered from the electrodes, and a predetermined impedance threshold. Accordingly, the feedback data may include at least impedance measurement data associated with the targeted tissue at the target site. The controller may be configured to process the impedance measurement data to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue. In particular, the controller may be configured to process the active impedance value using an algorithm to determine efficacy of

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ablation/modulation of the targeted tissue based on a comparison of the active impedance value with at least one of a predetermined minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value. In the event that the active impedance value is less than the predetermined minimum impedance value, the controller is configured to determine that ablation/modulation is unsuccessful and then further disables energy delivery from the one or more electrodes. In the event that the active impedance value is greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the controller is configured to calculate a slope change for the detection of a slope event. If a negative slope event is detected, the controller is configured to determine that ablation/modulation is successful and the controller disables energy delivery from the one or more electrodes upon detecting a negative slope event. If a negative slope event is not detected, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes. In the absence of detecting a slope event, the controller is configured to determine that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and the controller further disables energy delivery from the one or more electrodes.

The controller is further configured to transmit a signal resulting in an output, via an interactive interface, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue. The alert may include, for example, a visual alert including at least one of a color and text displayed on a graphical user interface (GUI) and indicating whether the ablation/modulation is successful or unsuccessful.

In some embodiments, the condition includes a peripheral neurological condition. The peripheral neurological condition may be associated with a nasal condition or a non-nasal condition of the patient. For example, the non-nasal condition may include atrial fibrillation (AF). In some embodiments, the nasal condition may include rhinosinusitis. Accordingly, in some embodiments, the target site is within a sino-nasal cavity of the patient. The delivery of the ablation energy may result in disruption of multiple neural signals to, and/or result in local hypoxia of, mucus producing and/or mucosal engorgement elements within the sino-nasal cavity of the patient. The targeted tissue is proximate or inferior to a sphenopalatine foramen. Yet still, delivery of the ablation energy may result in therapeutic modulation of postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine

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bone of the patient. In particular, delivery of the ablation energy causes multiple points of interruption of neural branches extending through foramina and microforamina of palatine bone. Yet still, in some embodiments, delivery of the ablation energy may cause thrombus formation within one or more blood vessels associated with mucus producing and/or mucosal engorgement elements within the nose. The resulting local hypoxia of the mucus producing and/or mucosal engorgement elements may result in decreased mucosal engorgement to thereby increase volumetric flow through a nasal passage of the patient. Additionally, or alternatively, the resulting local hypoxia may cause neuronal degeneration.

FIGS. 11A and 11B are graphs illustrating impedance profiles of two different sets of electrodes delivering energy to respective portions of targeted tissue, wherein the graphs illustrate a slope change event (e.g., asymptotic rise) which is indicative of whether the ablation/modulation of the targeted tissue is successful.

As previously described, systems and methods are further configured to receive and process real-time feedback data associated with the targeted tissue undergoing treatment to further ensure that energy delivered is maintained within the scope of the treatment pattern. More specifically, the systems and methods are configured to automatically control delivery of energy to the targeted tissue based on the processing of the real-time feedback data, wherein such data includes at least impedance measurement data associated with the targeted tissue collected during delivery of energy to the targeted tissue. The controller is configured to process impedance measurement data to detect a slope change event (e.g., an asymptotic rise) within an impedance profile associated with the treatment, wherein, with reference to the predetermined impedance threshold, the slope change event is indicative of whether the ablation/modulation of the targeted tissue is successful. In turn, the controller is configured to automatically control the delivery of energy to the targeted tissue based on real-time monitoring of feedback data, most notably impedance data, to ensure the desired ablation/modulation is achieved.

As a result, the systems and methods are able to ensure that optimal energy is delivered in order to delay the onset of impedance roll-off, until the target ablation/modulation depth is achieved, while maintaining clinically relevant treatment time. Accordingly, the invention solves the problem of causing unnecessary collateral damage to non-targeted tissue during a procedure involving the application of electrotherapeutic stimulation at a target site composed of a variety of tissue types.

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The following provides a detailed description of the various capabilities of systems and methods of the present invention, including, but not limited to, neuromodulation monitoring, feedback, and mapping capabilities, which, in turn, allowing for detection of anatomical structures and function, neural identification and mapping, and anatomical mapping, for example.

Neuromodulation Monitoring, Feedback, and Mapping Capabilities

As previously described, the system 100 includes a console 104 to which the device 102 is to be connected. The console 104 is configured to provide various functions for the device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the device 102. The console 104 can further be configured to generate a selected form and/or magnitude of energy for delivery to tissue or nerves at the target site via the end effector (214, 314), and therefore the console 104 may have different configurations depending on the treatment modality of the device 102. For example, when device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 includes an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy. When the device 102 is configured for cryotherapeutic treatment, the console 104 can include a refrigerant reservoir (not shown), and can be configured to supply the device 102 with refrigerant. Similarly, when the device 102 is configured for chemical-based treatment (e.g., drug infusion), the console 104 can include a chemical reservoir (not shown) and can be configured to supply the device 102 with one or more chemicals.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector (214, 314) directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or

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to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, perform nerve mapping, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via mapping/evaluation/feedback algorithms 110. For example, the mapping/evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the location of other anatomical structures (e.g., vessels) at the treatment site, the temperature at the treatment site during monitoring and modulation, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the mapping/evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107 and the end effector (214, 314), can be configured to monitor neural activity and/or temperature at the treatment site during therapy and automatically shut off the energy delivery when the neural activity and/or temperature reaches a predetermined threshold (e.g., a threshold reduction in neural activity, a threshold maximum temperature when applying RF energy, or a threshold minimum temperature when applying cryotherapy). In other embodiments, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance or resistance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic

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function. This and other information associated with the operation of the system 100 can be communicated to the operator via a display 112 (e.g., a monitor, touchscreen, user interface, etc.) on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104.

In various embodiments, the end effector (214, 314) and/or other portions of the system 100 can be configured to detect various bioelectric-parameters of the tissue at the target site, and this information can be used by the mapping/evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate neural tissue, differentiate between different types of neural tissue, map the anatomical and/or neural structure at the target site, and/or identify neuromodulation patterns of the end effector (214, 314) with respect to the patient's anatomy. For example, the end effector (214, 314) can be used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in the target region. In certain embodiments, the end effector (214, 314), together with the mapping/evaluation/feedback algorithms 110, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. The mapping/evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes (244, 336)).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-2000Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures and events, including the firing of neural tissue, differences between neural tissue and other anatomical structures (e.g., blood vessels), and event different types of neural tissue. This information can be analyzed by the mapping/evaluation/feedback algorithms and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural tissue and other anatomy at the treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode (244, 336) can be

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operated independently of the other electrodes (244, 336). For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes (244, 336) allows the end effector (214, 314) to detect information and deliver RF energy to highly customized regions. For example, a select portion of the electrodes (244, 336) can be activated to target specific neural fibers in a specific region while the other electrodes (244, 336) remain inactive. In certain embodiments, for example, electrodes (244, 336) may be activated across the portion of a strut that is adjacent to tissue at the target site, and the electrodes (244, 336) that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. In addition, the electrodes (244, 336) can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

The electrodes (244, 336) can be electrically coupled to the energy generator 106 via wires (not shown) that extend from the electrodes (244, 336), through the shaft 116, and to the energy generator 106. When each of the electrodes (244, 336) is independently controlled, each electrode (244, 336) couples to a corresponding wire that extends through the shaft 116. This allows each electrode (244, 336) to be independently activated for stimulation or neuromodulation to provide precise ablation patterns and/or individually detected via the console 104 to provide information specific to each electrode (244, 336) for neural or anatomical detection and mapping. In other embodiments, multiple electrodes (244, 336) can be controlled together and, therefore, multiple electrodes (244, 336) can be electrically coupled to the same wire extending through the shaft 116. The energy generator 16 and/or components (e.g., a control module) operably coupled thereto can include custom algorithms to control the activation of the electrodes (244, 336). For example, the RF generator can deliver RF power at about 200-100 W to the electrodes (244, 336), and do so while activating the electrodes (244, 336) in a predetermined pattern selected based on the position of the end effector (214, 314) relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the energy generator 106 delivers power at lower levels (e.g., less than 1 W, 1-5 W, 5-15 W, 15-50 W, 50-150 W, etc.) for stimulation and/or higher power levels. For example, the energy generator 106 can be configured to delivery stimulating energy pulses of 1-3 W via the

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electrodes (244, 336) to stimulate specific targets in the tissue.

As previously described, the end effector (214, 314) can further include one or more temperature sensors disposed on the struts and/or other portions of the end effector (214, 314) and electrically coupled to the console 104 via wires (not shown) that extend through the shaft 116. In various embodiments, the temperature sensors can be positioned proximate to the electrodes (244, 336) to detect the temperature at the interface between tissue at the target site and the electrodes (244, 336). In other embodiments, the temperature sensors can penetrate the tissue at the target site (e.g., a penetrating thermocouple) to detect the temperature at a depth within the tissue. The temperature measurements can provide the operator or the system with feedback regarding the effect of the therapeutic neuromodulation on the tissue. For example, in certain embodiments the operator may wish to prevent or reduce damage to the tissue at the treatment site, and therefore the temperature sensors can be used to determine if the tissue temperature reaches a predetermined threshold for irreversible tissue damage. Once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and avoid significant tissue sloughing during wound healing. In certain embodiments, the energy delivery can automatically terminate based on the mapping/evaluation/feedback algorithm 110 stored on the console 104 operably coupled to the temperature sensors.

In certain embodiments, the system 100 can determine the locations and/or morphology of neural tissue and/or other anatomical structures before therapy such that the therapeutic neuromodulation can be applied to precise regions including target neural tissue, while avoiding negative effects on non-target structures, such as blood vessels. As described in further detail below, the system 100 can detect various bioelectrical parameters in an interest zone to determine the location and morphology of various neural tissue (e.g., different types of neural tissue, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony regions, etc.). In some embodiments, the system 100 is configured to measure bioelectric potential. To do so, one or more of the electrodes (244, 336) is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies) are applied to the tissue by one or more electrodes (244, 336) at or near the treatment site, and the voltage and/or current differences at various different frequencies between various pairs of electrodes (244, 336) of the end effector (214,

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314) may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural tissue, and/or other types of tissue) in the region of interest. For example, current (i.e., direct or alternating current) can be applied to a pair of electrodes (244, 336) adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes (244, 336) are measured. It will be appreciated that the current injection electrodes (244, 336) and measurement electrodes (244, 336) need not be adjacent, and that modifying the spacing between the two current injection electrodes (244, 336) can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes (244, 336) provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes (244, 336) that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector (214, 314)), and this information can be used to map the neural and anatomical structures by the use of frequency differentiation reconstruction. Applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters. At high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of the neural tissue do not impede current flow, and the current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids, ions, proteins and polysaccharides. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes and morphologies of the cells or cell densities or cell spacing. The stimulation frequencies can be in the megabertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

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Further, the inherent morphology and composition of the anatomical structures in a given region or zone of the patient react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural tissue, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy. In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes (244, 336) at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or

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more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes (244, 336) and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes (244, 336) are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural tissue that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural tissue that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate the postganglionic parasympathetic neural fibers that innervate the mucosa at numerous neural entrance points within a given zone or region of a patient. Further, because there are not any clear anatomical markers denoting the location of the SPF, accessory foramen, and microforamina, the neural mapping allows the operator to identify and therapeutically modulate nerves that would otherwise be unidentifiable without intricate dissection of the mucosa. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the mapping/evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

In various embodiments, the system 100 can also be configured to map the expected therapeutic modulation patterns of the electrodes (244, 336) at specific temperatures and, in certain embodiments, take into account tissue properties based on the anatomical mapping of the

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target site. For example, the system 100 can be configured to map the ablation pattern of a specific electrode ablation pattern at the 45° C. isotherm, the 55° C. isotherm, the 65° C. isotherm, and/or other temperature/ranges (e.g., temperatures ranging from 45° C. to 70° C. or higher) depending on the target site and/or structure.

The system 100 may provide, via the display 112, three-dimensional views of such projected ablation patterns of the electrodes (244, 336) of the end effector (214, 314). The ablation pattern mapping may define a region of influence that each electrode (244, 336) has on the surrounding tissue. The region of influence may correspond to the region of tissue that would be exposed to therapeutically modulating energy based on a defined electrode activation pattern (i.e., one, two, three, four, or more electrodes on any given strut). In other words, the ablation pattern mapping can be used to illustrate the ablation pattern of any number of electrodes (244, 336), any geometry of the electrode layout, and/or any ablation activation protocol (e.g., pulsed activation, multi-polar/sequential activation, etc.).

In some embodiments, the ablation pattern may be configured such that each electrode (244, 336) has a region of influence surrounding only the individual electrode (244, 336) (i.e., a "dot" pattern). In other embodiments, the ablation pattern may be such that two or more electrodes (244, 336) may link together to form a sub-grouped regions of influence that define peanut-like or linear shapes between two or more electrodes (244, 336). In further embodiments, the ablation pattern can result in a more expansive or contiguous pattern in which the region of influence extends along multiple electrodes (244, 336) (e.g., along each strut). In still further embodiments, the ablation pattern may result in different regions of influence depending upon the electrode activation pattern, phase angle, target temperature, pulse duration, device structure, and/or other treatment parameters. The three-dimensional views of the ablation patterns can be output to the display 112 and/or other user interfaces to allow the clinician to visualize the changing regions of influence based on different durations of energy application, different electrode activation sequences (e.g., multiplexing), different pulse sequences, different temperature isotherms, and/or other treatment parameters. This information can be used to determine the appropriate ablation algorithm for a patient's specific anatomy. In other embodiments, the three-dimensional visualization of the regions of influence can be used to illustrate the regions from which the electrodes (244, 336) detect data when measuring bioelectrical properties for anatomical mapping. In this embodiment, the three dimensional

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visualization can be used to determine which electrode activation pattern should be used to determine the desired properties (e.g., impedance, resistance, etc.) in the desired area. In certain embodiments, it may be better to use dot assessments, whereas in other embodiments it may be more appropriate to detect information from linear or larger contiguous regions.

In some embodiments, the mapped ablation pattern is superimposed on the anatomical mapping to identify what structures (e.g., neural tissue, vessels, etc.) will be therapeutically modulated or otherwise affected by the therapy. An image may be provided to the surgeon which includes a digital illustration of a predicted or planned neuromodulation zone in relation to previously identified anatomical structures in a zone of interest. For example, the illustration may show numerous neural tissue and, based on the predicted neuromodulation zone, identifies which neural tissue are expected to be therapeutically modulated. The expected therapeutically modulated neural tissue may be shaded to differentiate them from the non-affected neural tissue. In other embodiments, the expected therapeutically modulated neural tissue can be differentiated from the non-affected neural tissue using different colors and/or other indicators. In further embodiments, the predicted neuromodulation zone and surrounding anatomy (based on anatomical mapping) can be shown in a three dimensional view (and/or include different visualization features (e.g., color-coding to identify certain anatomical structures, bioelectric properties of the target tissue, etc.). The combined predicted ablation pattern and anatomical mapping can be output to the display 112 and/or other user interfaces to allow the clinician to select the appropriate ablation algorithm for a patient's specific anatomy.

The imaging provided by the system 100 allows the clinician to visualize the ablation pattern before therapy and adjust the ablation pattern to target specific anatomical structures while avoiding others to prevent collateral effects. For example, the clinician can select a treatment pattern to avoid blood vessels, thereby reducing exposure of the vessel to the therapeutic neuromodulation energy. This reduces the risk of damaging or rupturing vessels and, therefore, prevents immediate or latent bleeding. Further, the selective energy application provided by the neural mapping reduces collateral effects of the therapeutic neuromodulation, such as tissue sloughing off during wound healing (e.g., 1-3 weeks post ablation), thereby reducing the aspiration risk associated with the neuromodulation procedure.

The system 100 can be further configured to apply neuromodulation energy (via the electrodes (244, 336)) at specific frequencies attuned to the target neural structure and, therefore,

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specifically target desired neural tissue over non-target structures. For example, the specific neuromodulation frequencies can correspond to the frequencies identified as corresponding to the target structure during neural mapping. As described above, the inherent morphology and composition of the anatomical structures react differently to different frequencies. Thus, frequency-tuned neuromodulation energy tailored to a target structure does not have the same modulating effects on non-target structures. More specifically, applying the neuromodulation energy at the target-specific frequency causes ionic agitation in the target neural structure, leading to differentials in osmotic potentials of the targeted neural tissue and dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure). This causes degeneration, possibly resulting in vacuolar degeneration and, eventually, necrosis at the target neural structure, but is not expected to functionally affect at least some non-target structures (e.g., blood vessels). Accordingly, the system 100 can use the neural-structure specific frequencies to both (1) identify the locations of target neural tissue to plan electrode ablation configurations (e.g., electrode geometry and/or activation pattern) that specifically focus the neuromodulation on the target neural structure; and (2) apply the neuromodulation energy at the characteristic neural frequencies to selectively ablate the neural tissue responsive to the characteristic neural frequencies. For example, the end effector (214, 314) of the system 100 may selectively stimulate and/or modulate parasympathetic fibers, sympathetic fibers, sensory fibers, alpha/beta/delta fibers, C-fibers, anoxic terminals of one or more of the foregoing, insulated over non-insulated fibers (regions with fibers), and/or other neural tissue. In some embodiments, the system 100 may also selectively target specific cells or cellular regions during anatomical mapping and/or therapeutic modulation, such as smooth muscle cells, sub-mucosal glands, goblet cells, and stratified cellular regions within a given tissue type. Therefore, the system 100 provides highly selective neuromodulation therapy specific to targeted neural tissue, and reduces the collateral effects of neuromodulation therapy to non-target structures (e.g., blood vessels).

The present disclosure provides a method of anatomical mapping and therapeutic neuromodulation. The method includes expanding an end effector (i.e., end effector (214, 314)) at a zone of interest ("interest zone"). For example, the end effector (214, 314) can be expanded such that at least some of the electrodes (244, 336) are placed in contact with tissue at the interest zone. The expanded device can then take bioelectric measurements via the electrodes (244, 336)

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and/or other sensors to ensure that the desired electrodes are in proper contact with the tissue at the interest zone. In some embodiments, for example, the system 100 detects the impedance and/or resistance across pairs of the electrodes (244, 336) to confirm that the desired electrodes have appropriate surface contact with the tissue and that all of the electrodes are (244, 336) functioning properly.

The method continues by optionally applying an electrical stimulus to the tissue, and detecting bioelectric properties of the tissue to establish baseline norms of the tissue. For example, the method can include measuring resistance, complex impedance, current, voltage, nerve firing rate, neuromagnetic field, muscular activation, and/or other parameters that are indicative of the location and/or function of neural tissue and/or other anatomical structures (e.g., glandular structures, blood vessels, etc.). In some embodiments, the electrodes (244, 336) send one or more stimulation signals (e.g., pulsed signals or constant signals) to the interest zone to stimulate neural activity and initiate action potentials. The stimulation signal can have a frequency attuned to a specific target structure (e.g., a specific neural structure, a glandular structure, a vessel) that allows for identification of the location of the specific target structure. The specific frequency of the stimulation signal is a function of the host permeability and, therefore, applying the unique frequency alters the tissue attenuation and the depth into the tissue the RF energy will penetrate. For example, lower frequencies typically penetrate deeper into the tissue than higher frequencies.

Pairs of the non-stimulating electrodes (244, 336) of the end effector (214, 314) can then detect one or more bioelectric properties of the tissue that occur in response to the stimulus, such as impedance or resistance. For example, an array of electrodes (e.g., the electrodes (244, 336)) can be selectively paired together in a desired pattern (e.g., multiplexing the electrodes (244, 336)) to detect the bioelectric properties at desired depths and/or across desired regions to provide a high level of spatial awareness at the interest zone. In certain embodiments, the electrodes (244, 336) can be paired together in a time-sequenced manner according to an algorithm (e.g., provided by the mapping/evaluation/feedback algorithms 110). In various embodiments, stimuli can be injected into the tissue at two or more different frequencies, and the resultant bioelectric responses (e.g., action potentials) in response to each of the injected frequencies can be detected via various pairs of the electrodes (244, 336). For example, an anatomical or neural mapping algorithm can cause the end effector (214, 314) to deliver pulsed

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RF energy at specific frequencies between different pairs of the electrodes (244, 336) and the resultant bioelectric response can be recorded in a time sequenced rotation until the desired interest zone is adequately mapped (i.e., "multiplexing"). For example, the end effector (214, 314) can deliver stimulation energy at a first frequency via adjacent pairs of the electrodes (244, 336) for a predetermined time period (e.g., 1-50 milliseconds), and the resultant bioelectric activity (e.g., resistance) can be detected via one or more other pairs of electrodes (244, 336) (e.g., spaced apart from each other to reach varying depths within the tissue). The end effector (214, 314) can then apply stimulation energy at a second frequency different from the first frequency, and the resultant bioelectric activity can be detected via the other electrodes. This can continue when the interest zone has been adequately mapped at the desired frequencies. As described in further detail below, in some embodiments the baseline tissue bioelectric properties (e.g., nerve firing rate) are detected using static detection methods (without the injection of a stimulation signal).

After detecting the baseline bioelectric properties, the information can be used to map anatomical structures and/or functions at the interest zone. For example, the bioelectric properties detected by the electrodes (244, 336) can be amazed via the mapping/evaluation/feedback algorithms 110, and an anatomical map can be output to a user via the display 112. In some embodiments, complex impedance, dielectric, or resistance measurements can be used to map parasympathetic nerves and, optionally, identify neural tissue in a diseased state of hyperactivity. The bioelectric properties can also be used to map other non-target structures and the general anatomy, such as blood vessels, bone, and/or glandular structures. The anatomical locations can be provided to a user (e.g., on the display 112) as a two-dimensional map (e.g., illustrating relative intensities, illustrating specific sites of potential target structures) and/or as a three-dimensional image. This information can be used to differentiate structures on a submicron, cellular level and identify very specific target structures (e.g., hyperactive parasympathetic nerves). The method can also predict the ablation patterns of the end effector (214, 314) based on different electrode neuromodulation protocol and, optionally, superimpose the predicted neuromodulation patterns onto the mapped anatomy to indicate to the user which anatomical structures will be affected by a specific neuromodulation protocol. For example, when the predicted neuromodulation pattern is displayed in relation to the mapped anatomy, a clinician can determine whether target structures will be appropriately

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ablated and whether non-target structures (e.g., blood vessels) will be undesirably exposed to the therapeutic neuromodulation energy. Thus, the method can be used for planning neuromodulation therapy to locate very specific target structures, avoid non-target structures, and select electrode neuromodulation protocols.

Once the target structure is located and a desired electrode neuromodulation protocol has been selected, the method continues by applying therapeutic neuromodulation to the target structure. The neuromodulation energy can be applied to the tissue in a highly targeted manner that forms micro-lesions to selectively modulate the target structure, while avoiding non-targeted blood vessels and allowing the surrounding tissue structure to remain healthy for effective wound healing. In some embodiments, the neuromodulation energy can be applied in a pulsed manner, allowing the tissue to cool between modulation pulses to ensure appropriate modulation without undesirably affecting non-target tissue. In some embodiments, the neuromodulation algorithm can deliver pulsed RF energy between different pairs of the electrodes (244, 336) in a time sequenced rotation until neuromodulation is predicted to be complete (i.e., "multiplexing"). For example, the end effector (214, 314) can deliver neuromodulation energy (e.g., having a power of 5-10 W (e.g., 7 W, 8 W, 9 W) and a current of about 50-100 mA) via adjacent pairs of the electrodes (244, 336) until at least one of the following conditions is met: (a) load resistance reaches a predefined maximum resistance (e.g., 350Ω); (b) a thermocouple temperature associated with the electrode pair reaches a predefined maximum temperature (e.g., 80° C.); or (c) a predetermined time period has elapsed (e.g., 10 seconds). After the predetermined conditions are met, the end effector (214, 314) can move to the next pair of electrodes in the sequence, and the neuromodulation algorithm can terminate when all of the load resistances of the individual pairs of electrodes is at or above a predetermined threshold (e.g., 100Ω). In various embodiments, the RF energy can be applied at a predetermined frequency (e.g., 450-500 kHz) and is expected to initiate ionic agitation of the specific target structure, while avoiding functional disruption of non-target structures.

During and/or after neuromodulation therapy, the method continues by detecting and, optionally, mapping the post-therapy bioelectric properties of the target site. This can be performed in a similar manner as described above. The post-therapy evaluation can indicate if the target structures (e.g., hyperactive parasympathetic nerves) were adequately modulated or ablated. If the target structures are not adequately modulated (i.e., if neural activity is still

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detected in the target structure and/or the neural activity has not decreased), the method can continue by again applying therapeutic neuromodulation to the target. If the target structures were adequately ablated, the neuromodulation procedure can be completed.

Detection of Anatomical Structures and Function

Various embodiments of the present technology can include features that measure bio-electric, dielectric, and/or other properties of tissue at target sites to determine the presence, location, and/or activity of neural tissue and other anatomical structures and, optionally, map the locations of the detected neural tissue and/or other anatomical structures. For example, the present technology can be used to detect glandular structures and, optionally, their mucoserous functions and/or other functions. The present technology can also be configured to detect vascular structures (e.g., arteries) and, optionally, their arterial functions, volumetric pressures, and/or other functions. The mapping features discussed below can be incorporated into any the system 100 and/or any other devices disclosed herein to provide an accurate depiction of nerves at the target site.

Neural and/or anatomical detection can occur (a) before the application of a therapeutic neuromodulation energy to determine the presence or location of neural tissue and other anatomical structures (e.g., blood vessels, glands, etc.) at the target site and/or record baseline levels of neural activity; (b) during therapeutic neuromodulation to determine the real-time effect of the energy application on the neural fibers at the treatment site; and/or (c) after therapeutic neuromodulation to confirm the efficacy of the treatment on the targeted structures (e.g., nerves glands, etc.). This allows for the identification of very specific anatomical structures (even to the micro-scale or cellular level) and, therefore, provides for highly targeted neuromodulation. This enhances the efficacy and efficiency of the neuromodulation therapy. In addition, the anatomical mapping reduces the collateral effects of neuromodulation therapy to non-target sites. Accordingly, the targeted neuromodulation inhibits damage or rupture of blood vessels (i.e., inhibits undesired bleeding) and collateral damage to tissue that may be of concern during wound healing (e.g., when damaged tissue sloughs off).

In certain embodiments, the systems disclosed herein can use bioelectric measurements, such as impedance, resistance, voltage, current density, and/or other parameters (e.g., temperature) to determine the anatomy, in particular the neural, glandular, and vascular anatomy,

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at the target site. The bioelectric properties can be detected after the transmission of a stimulus (e.g., an electrical stimulus, such as RF energy delivered via the electrodes (244, 336); i.e., "dynamic" detection) and/or without the transmission of a stimulus (i.e., "static" detection).

Dynamic measurements include various embodiments to excite and/or detect primary or secondary effects of neural activation and/or propagation. Such dynamic embodiments involve the heightened states of neural activation and propagation and use this dynamic measurement for nerve location and functional identification relative to the neighboring tissue types. For example, a method of dynamic detection can include: (1) delivering stimulation energy to a treatment site via a treatment device (e.g., the end effector) to excite parasympathetic nerves at the treatment site; (2) measuring one or more physiological parameters (e.g., resistance, impedance, etc.) at the treatment site via a measuring/sensing array of the treatment device (e.g., the electrodes (244, 336)); (4) based on the measurements, identifying the relative presence and position of parasympathetic nerves at the treatment site; and (5) delivering ablation energy to the identified parasympathetic nerves to block the detected para-sympathetic nerves.

Static measurements include various embodiments associated with specific native properties of the stratified or cellular composition at or near the treatment site. The static embodiments are directed to inherent biologic and electrical properties of tissue types at or near the treatment site, the stratified or cellular compositions at or near the treatment site, and contrasting both foregoing measurements with tissue types adjacent the treatment site (and that are not targeted for neuromodulation). This information can be used to localize specific targets (e.g., parasympathetic fibers) and non-targets (e.g., vessels, sensory nerves, etc.). For example, a method of static detection can include: (1) before ablation, utilizing a measuring/sensing array of a treatment device (e.g., the electrodes (244, 336)) to determine one or more baseline physiological parameters; (2) geometrically identifying inherent tissue properties within a region of interest based on the measured physiological parameters (e.g., resistance, impedance, etc.); (3) delivering ablation energy to one or more nerves within the region of via treatment device interest; (4) during the delivery of the ablation energy, determining one or more mid-procedure physiological parameters via the measuring/sensing array; and (5) after the delivery of ablation energy, determining one or more post-procedure physiological parameters via the measurement/sensing array to determine the effectiveness of the delivery of the ablation energy on blocking the nerves that received the ablation energy.

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After the initial static and/or dynamic detection of bioelectric properties, the location of anatomical features can be used to determine where the treatment site(s) should be with respect to various anatomical structures for therapeutically effective neuromodulation of the targeted nerves. The bioelectric and other physiological properties described herein can be detected via electrodes (e.g., the electrodes (244, 336) of the end effector (214, 314)), and the electrode pairings on a device (e.g., end effector (214, 314)) can be selected to obtain the bioelectric data at specific zones or regions and at specific depths of the targeted regions. The specific properties detected at or surrounding target neuromodulation sites and associated methods for obtaining these properties are described below. These specific detection and mapping methods discussed below are described with reference to the system 100 , although the methods can be implemented on other suitable systems and devices that provide for anatomical identification, anatomical mapping and/or neuromodulation therapy.

Neural Identification and Mapping

In many neuromodulation procedures, it is beneficial to identify the portions of the nerves that fall within a zone and/or region of influence (referred to as the "interest zone") of the energy delivered by a device 102, as well as the relative three-dimensional position of the neural tissue relative to the device 102. Characterizing the portions of the neural tissue within the interest zone and/or determining the relative positions of the neural tissue within the interest zone enables the clinician to (1) selectively activate target neural tissue over non-target structures (e.g., blood vessels), and (2) sub-select specific targeted neural tissue (e.g., parasympathetic nerves) over non-target neural tissue (e.g., sensory nerves, subgroups of neural tissue, neural tissue having certain compositions or morphologies) The target structures (e.g., parasympathetic nerves) and non-target structures (e.g., blood vessels, sensory nerves, etc.) can be identified based on the inherent signatures of specific structures, which are defined by the unique morphological compositions of the structures and the bioelectrical properties associated with these morphological compositions. For example, unique, discrete frequencies can be associated with morphological compositions and, therefore, be used to identify certain structures. The target and non-target structures can also be identified based on relative bioelectrical activation of the structures to sub-select specific neural structures. Further, target and non-target structures can be identified by the differing detected responses of the structures to a tailored

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injected stimuli. For example, the systems described herein can detect the magnitude of response of structures and the difference in the responses of anatomical structures with respect to differing stimuli (e.g., stimuli injected at different frequencies).

At least for purposes of this disclosure, a nerve can include the following portions that are defined based on their respective orientations relative to the interest zone: terminating neural tissue (e.g., terminating axonal structures), branching neural tissue (e.g., branching axonal structures), and travelling neural tissue (e.g., travelling axonal structures). For example, terminating neural tissue enter the zone but do not exit. As such, terminating neural tissue are terminal points for neuronal signaling and activation. Branching neural tissue are nerves that enter the interest zone and increase number of nerves exiting the interest zone. Branching neural tissue are typically associated with a reduction in relative geometry of nerve bundle. Travelling neural tissue are nerves that enter the interest zone and exit the zone with no substantially no change in geometry or numerical value.

The system 100 can be used to detect voltage, current, complex impedance, resistance, permittivity, and/or conductivity, which are tied to the compound action potentials of nerves, to determine and/or map the relative positions and proportionalities of nerves in the interest zone. Neuronal cross-sectional area ("CSA") is expected to be due to the increase in axonic structures. Each axon is a standard size. Larger nerves (in cross-sectional dimension) have a larger number of axons than nerves having smaller cross-sectional dimensions. The compound action responses from the larger nerves, in both static and dynamic assessments, are greater than smaller nerves. This is at least in part because the compound action potential is the cumulative action response from each of the axons. When using static analysis, for example, the system 100 can directly measure and map impedance or resistance of nerves and, based on the determined impedance or resistance, determine the location of nerves and/or relative size of the nerves. In dynamic analysis, the system 100 can be used to apply a stimulus to the interest zone and detect the dynamic response of the neural tissue to the stimulus. Using this information, the system 100 can determine and/or map impedance or resistance in the interest zone to provide information related to the neural positions or relative nerve sizes. Neural impedance mapping can be illustrated by showing the varying complex impedance levels at a specific location at differing cross-sectional depths. In other embodiments, neural impedance or resistance can be mapped in a three-dimensional display.

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Identifying the portions and/or relative positions of the nerves within the interest zone can inform and/or guide selection of one or more treatment parameters (e.g., electrode ablation patterns, electrode activation plans, etc.) of the system 100 for improving treatment efficiency and efficacy. For example, during neural monitoring and mapping, the system 100 can identify the directionality of the nerves based at least in part on the length of the neural structure extending along the interest zone, relative sizing of the neural tissue, and/or the direction of the action potentials. This information can then be used by the system 100 or the clinician to automatically or manually adjust treatment parameters (e.g., selective electrode activation, bipolar and/or multipolar activation, and/or electrode positioning) to target specific nerves or regions of nerves. For example, the system 100 can selectively activate specific electrodes (244, 336), electrode combinations (e.g., asymmetric or symmetric), and/or adjust the bi-polar or multi-polar electrode configuration. In some embodiments, the system 100 can adjust or select the waveform, phase angle, and/or other energy delivery parameters based on the nerve portion/position mapping and/or the nerve proportionality mapping. In some embodiments, structure and/or properties of the electrodes (244, 336) themselves (e.g., material, surface roughening, coatings, cross-sectional area, perimeter, penetrating, penetration depth, surface-mounted, etc.) may be selected based on the nerve portion and proportionality mapping.

In various embodiments, treatment parameters and/or energy delivery parameters can be adjusted to target on-axis or near axis travelling neural tissue and/or avoid the activation of traveling neural tissue that are at least generally perpendicular to the end effector (214, 314). Greater portions of the on-axis or near axis travelling neural tissue are exposed and susceptible to the neuromodulation energy provided by the end effector (214, 314) than a perpendicular travelling neural structure, which may only be exposed to therapeutic energy at a discrete cross-section. Therefore, the end effector (214, 314) is more likely to have a greater effect on the on-axis or near axis travelling neural tissue. The identification of the neural structure positions (e.g., via complex impedance or resistance mapping) can also allow targeted energy delivery to travelling neural tissue rather than branching neural tissue (typically downstream of the travelling neural tissue) because the travelling neural tissue are closer to the nerve origin and, therefore, more of the nerve is affected by therapeutic neuromodulation, thereby resulting in a more efficient treatment and/or a higher efficacy of treatment. Similarly, the identification of neural structure positions can be used to target travelling and branching neural tissue over

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terminal neural tissue. In some embodiments, the treatment parameters can be adjusted based on the detected neural positions to provide a selective regional effect. For example, a clinician can target downstream portions of the neural tissue if only wanting to influence partial effects on very specific anatomical structures or positions.

In various embodiments, neural locations and/or relative positions of nerves can be determined by detecting the nerve-firing voltage and/or current over time. An array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone, and the electrodes (244, 336) can measure the voltage and/or current associated with nerve-firing. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves in a hyper state (i.e., excessive parasympathetic tone). Rhinitis is at least in part the result of over-firing nerves because this hyper state drives the hyper-mucosal production and hyper-mucosal secretion. Therefore, detection of nerve firing rate via voltage and current measurements can be used to locate the portions of the interest region that include hyper-parasympathetic neural function (i.e., nerves in the diseased state). This allows the clinician to locate specific nerves (i.e., nerves with excessive parasympathetic tone) before neuromodulation therapy, rather than simply targeting all parasympathetic nerves (including non-diseased state parasympathetic nerves) to ensure that the correct tissue is treated during neuromodulation therapy. Further, nerve firing rate can be detected during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy. For example, recording decreases or elimination of nerve firing rate after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In various embodiments, the system 100 can detect neural activity using dynamic activation by injecting a stimulus signal (i.e., a signal that temporarily activates nerves) via one or more of the electrodes (244, 336) to induce an action potential, and other pairs of electrodes (244, 336) can detect bioelectric properties of the neural response. Detecting neural tissue using dynamic activation involves detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The ability to numerically measure, profile, map, and/or image fast neuronal depolarization for generating an accurate index of activity is a factor in measuring the rate of discharge in neurons and their processes. The action potential causes a rapid increase in the voltage across nerve fiber and the electrical impulse then spreads along the fiber. As an action potential occurs, the conductance of

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a neural cell membrane changes, becoming about 40 times larger than it is when the cell is at rest. During the action potential or neuronal depolarization, the membrane resistance diminishes by about 80 times, thereby allowing an applied current to enter the intracellular space as well. Over a population of neurons, this leads to a net decrease in the resistance during coherent neuronal activity, such as chronic para-sympathetic responses, as the intracellular space will provide additional conductive ions. The magnitude of such fast changes has been estimated to have local resistivity changes with recording near DC is 2.8-3.7% for peripheral nerve bundles.

Detecting neural tissue using dynamic activation includes detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The basis of each this discharge is the action potential, during which there is a depolarization of the neuronal membrane of up to 110 mV or more, lasting approximately 2 milliseconds, and due to the transfer of micromolar quantities of ions (e.g., sodium and potassium) across the cellular membrane. The complex impedance or resistance change due to the neuronal membrane falls from 1000 to 25 Ωcm. The introduction of a stimulus and subsequent measurement of the neural response can attenuate noise and improve signal to noise ratios to precisely focus on the response region to improve neural detection, measurement, and mapping.

In some embodiments, the difference in measurements of physiological parameters (e.g., complex impedance, resistance, voltage) over time, which can reduce errors, can be used to create a neural profiles, spectrums, or maps. For example, the sensitivity of the system 100 can be improved because this process provides repeated averaging to a stimulus. As a result, the mapping function outputs can be a unit-less ratio between the reference and test collated data at a single frequency and/or multiple frequencies and/or multiple amplitudes. Additional considerations may include multiple frequency evaluation methods that consequently expand the parameter assessments, such as resistivity, admittivity, center frequency, or ratio of extra- to intracellular resistivity.

In some embodiments, the system 100 may also be configured to indirectly measure the electrical activity of neural tissue to quantify the metabolic recovery processes that accompany action potential activity and act to restore ionic gradients to normal. These are related to an accumulation of ions in the extracellular space. The indirect measurement of electrical activity can be approximately a thousand times larger (in the order of millimolar), and thus are easier to

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measure and can enhance the accuracy of the measured electrical properties used to generate the neural maps.

The system 100 can perform dynamic neural detection by detecting nerve-firing voltage and/or current and, optionally, nerve firing rate over time, in response to an external stimulation of the nerves. For example, an array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone, one or more of the electrodes (244, 336) can be activated to inject a signal into the tissue that stimulates the nerves, and other electrodes (244, 336) of the electrode array can measure the neural voltage and/or current due to nerve firing in response to the stimulus. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves and, in certain embodiments, identify parasympathetic nerves in a hyper state (e.g., indicative of Rhinitis or other diseased state). The dynamic detection of neural activity (voltage, current, firing rate, etc.) can be performed before neuromodulation therapy to detect target nerve locations to select the target site and treatment parameters to ensure that the correct tissue is treated during neuromodulation therapy. Further, dynamic detection of neural activity can be performed during or after neuromodulation therapy to allow the clinician to monitor changes in neural activity to validate treatment efficacy. For example, recording decreases or elimination of neural activity after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In some embodiments, a stimulating signal can be delivered to the vicinity of the targeted nerve via one or more penetrating electrodes (e.g., microneedles that penetrate tissue) associated with the end effector (214, 314) and/or a separate device. The stimulating signal generates an action potential, which causes smooth muscle cells or other cells to contract. The location and strength of this contraction can be detected via the penetrating electrode(s) and, thereby, indicate to the clinician the distance to the nerve and/or the location of the nerve relative to the stimulating needle electrode. In some embodiments, the stimulating electrical signal may have a voltage of typically 1-2 mA or greater and a pulse width of typically 100-200 microseconds or greater. Shorter pulses of stimulation result in better discrimination of the detected contraction, but may require more current. The greater the distance between the electrode and the targeted nerve, the more energy is required to stimulate. The stimulation and detection of contraction strength and/or location enables identification of how close or far the electrodes are from the nerve, and therefore can be used to localize the nerve spatially. In some embodiments, varying

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pulse widths may be used to measure the distance to the nerve. As the needle becomes closer to the nerve, the pulse duration required to elicit a response becomes less and less.

To localize nerves via muscle contraction detection, the system 100 can vary pulse-width or amplitude to vary the energy (Energy=pulse-width*amplitude) of the stimulus delivered to the tissue via the penetrating electrode(s). By varying the stimulus energy and monitoring muscle contraction via the penetrating electrodes and/or other type of sensor, the system 100 can estimate the distance to the nerve. If a large amount of energy is required to stimulate the nerve/contract the muscle, the stimulating/penetrating electrode is far from the nerve. As the stimulating/penetrating electrode, moves closer to the nerve, the amount of energy required to induce muscle contraction will drop. For example, an array of penetrating electrodes can be positioned in the tissue at the interest zone and one or more of the electrodes can be activated to apply stimulus at different energy levels until they induce muscle contraction. Using an iterative process, localize the nerve (e.g., via the mapping/evaluation/feedback algorithm 110).

In some embodiments, the system 100 can measure the muscular activation from the nerve stimulus (e.g., via the electrodes (244, 336)) to determine neural positioning for neural mapping, without the use of penetrating electrodes. In this embodiment, the treatment device targets the smooth muscle cells' varicosities surrounding the submucosal glands and the vascular supply, and then the compound muscle action potential. This can be used to summate voltage response from the individual muscle fiber action potentials. The shortest latency is the time from stimulus artifact to onset of the response. The corresponding amplitude is measured from baseline to negative peak and measured in millivolts (mV). Nerve latencies (mean±SD) in adults typically range about 2-6 milliseconds, and more typically from about 3.4±0.8 to about 4.0±0.5 milliseconds.

In some embodiments, the system 100 can record a neuromagnetic field outside of the nerves to determine the internal current of the nerves without physical disruption of the nerve membrane. Without being bound by theory, the contribution to the magnetic field from the current inside the membrane is two orders of magnitude larger than that from the external current, and that the contribution from current within the membrane is substantially negligible. Electrical stimulation of the nerve in tandem with measurements of the magnetic compound action fields ("CAFs") can yield sequential positions of the current dipoles such that the location of the conduction change can be estimated (e.g., via the least-squares method). Visual

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representation (e.g., via the display 112) using magnetic contour maps can show normal or non-normal neural characteristics (e.g., normal can be equated with a characteristic quadrupolar pattern propagating along the nerve), and therefore indicate which nerves are in a diseases, hyperactive state and suitable targets for neuromodulation.

During magnetic field detection, an array of the electrodes (244, 336) can be positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes (244, 336) can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire), and therefore changing magnetic fields are indicative of the nerve nerve-firing rate. The changing magnetic field caused by neural firing can induce a current detected by nearby sensor wire (e.g., the sensor 314) and/or wires associated with the nearby electrodes (244, 336). By measuring this current, the magnetic field strength can be determined. The magnetic fields can optionally be mapped (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. Further, the magnetic field information can be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In other embodiments, the neuromagnetic field is measured with a Hall Probe or other suitable device, which can be integrated into the end effector (214, 314) and/or part of a separate device delivered to the interest zone. Alternatively, rather than measuring the voltage in the second wire, the changing magnetic field can be measured in the original wire (i.e. the nerve) using a Hall probe. A current going through the Hall probe will be deflected in the semi-conductor. This will cause a voltage difference between the top and bottom portions, which can be measured. In some aspects of this embodiments, three orthogonal planes are utilized.

In some embodiments, the system 100 can be used to induce electromotive force ("EMF") in a wire (i.e., a frequency-selective circuit, such as a tunable/LC circuit) that is tunable to resonant frequency of a nerve. In this embodiment, the nerve can be considered to be a current carrying wire, and the firing action potential is a changing voltage. This causes a changing current which, in turn, causes a changing magnetic flux (i.e., the magnetic field that is perpendicular to the wire). Under Faraday's Law of Induction/Faraday's Principle, the changing

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magnetic flux induces EMF (including a changing voltage) in a nearby sensor wire (e.g., integrated into the end effector (214, 314), the sensor 314, and/or other structure), and the changing voltage can be measured via the system 100.

In further embodiments, the sensor wire (e.g., the sensor 314) is an inductor and, therefore, provides an increase of the magnetic linkage between the nerve (i.e., first wire) and the sensor wire (i.e., second wire), with more turns for increasing effect. (e.g., V2,rms=V1,rms (N2/N1)). Due to the changing magnetic field, a voltage is induced in the sensor wire, and this voltage can be measured and used to estimate current changes in the nerve. Certain materials can be selected to enhance the efficiency of the EMF detection. For example, the sensor wire can include a soft iron core or other high permeability material for the inductor.

During induced EMF detection, the end effector (214, 314) and/or other device including a sensor wire is positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes (244, 336) can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire) that induces a current in the sensor wire (e.g., the sensor 314). This information can be used to determine neural location and/or map the nerves (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. EMF information can also be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In some embodiments, the system 100 can detect magnetic fields and/or EMF generated at a selected frequency that corresponds to a particular type of nerve. The frequency and, by extension, the associated nerve type of the detected signal can be selected based on an external resonant circuit. Resonance occurs on the external circuit when it is matched to the frequency of the magnetic field of the particular nerve type and that nerve is firing. In manner, the system 100 can be used to locate a particular sub-group/type of nerves.

In some embodiments, the system 100 can include a variable capacitor frequency-selective circuit to identify the location and/or map specific nerves (e.g., parasympathetic nerve, sensory nerve, nerve fiber type, nerve subgroup, etc.). The variable capacitor frequency-selective circuit can be defined by the sensor 314 and/or other feature of the end effector (214,

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314). Nerves have different resonant frequencies based on their function and structure. Accordingly, the system 100 can include a tunable LC circuit with a variable capacitor (C) and/or variable inductor (L) that can be selectively tuned to the resonant frequency of desired nerve types. This allows for the detection of neural activity only associated with the selected nerve type and its associated resonant frequency. Tuning can be achieved by moving the core in and out of the inductor. For example, tunable LC circuits can tune the inductor by: (i) changing the number of coils around the core; (ii) changing the cross-sectional area of the coils around the core; (iii) changing the length of the coil, and/or (iv) changing the permeability of the core material (e.g., changing from air to a core material). Systems including such a tunable LC circuit provide a high degree of dissemination and differentiation not only as to the activation of a nerve signal, but also with respect to the nerve type that is activated and the frequency at which the nerve is firing.

Anatomical Mapping

In various embodiments, the system 100 is further configured to provide minimally-invasive anatomical mapping that uses focused energy current/voltage stimuli from a spatially localized source (e.g., the electrodes (244, 336)) to cause a change in the conductivity of the of the tissue at the interest zone and detect resultant biopotential and/or bioelectrical measurements (e.g., via the electrodes (244, 336)). The current density in the tissue changes in response to changes of voltage applied by the electrodes (244, 336), which creates a change in the electric current that can be measured with the end effector (214, 314) and/or other portions of the system 100. The results of the bioelectrical and/or biopotential measurements can be used to predict or estimate relative absorption profilometry to predict or estimate the tissue structures in the interest zone. More specifically, each cellular construct has unique conductivity and absorption profiles that can be indicative of a type of tissue or structure, such as bone, soft tissue, vessels, nerves, types of nerves, and/or certain neural tissue. For example, different frequencies decay differently through different types of tissue. Accordingly, by detecting the absorption current in a region, the system 100 can determine the underlying structure and, in some instances, to a sub-microscale, cellular level that allows for highly specialized target localization and mapping. This highly specific target identification and mapping enhances the efficacy and efficiency of

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neuromodulation therapy, while also enhancing the safety profile of the system 100 to reduce collateral effects on non-target structures.

To detect electrical and dielectric tissue properties (e.g., resistance, complex impedance, conductivity, and/or, permittivity as a function of frequency), the electrodes (244, 336) and/or another electrode array is placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli (current/voltage) to the tissue. The electrical properties of the tissue between the source and the receiver electrodes (244, 336) are measured, as well as the current and/or voltage at the individual receiver electrodes (244, 336). These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest and, in certain embodiments, the location of firing nerves. For example, the anatomical mapping can be provided as a color-coded or gray-scale three-dimensional or two-dimensional map showing differing intensities of certain bioelectric properties (e.g., resistance, impedance, etc.), or the information can be processed to map the actual anatomical structures for the clinician. This information can also be used during neuromodulation therapy to monitor treatment progression with respect to the anatomy, and after neuromodulation therapy to validate successful treatment. In addition, the anatomical mapping provided by the bioelectrical and/or biopotential measurements can be used to track the changes to non-target tissue (e.g., vessels) due to neuromodulation therapy to avoid negative collateral effects. For example, a clinician can identify when the therapy begins to ligate a vessel and/or damage tissue, and modify the therapy to avoid bleeding, detrimental tissue ablation, and/or other negative collateral effects.

Furthermore, the threshold frequency of electric current used to identify specific targets can subsequently be used when applying therapeutic neuromodulation energy. For example, the neuromodulation energy can be applied at the specific threshold frequencies of electric current that are target neuronal-specific and differentiated from other non-targets (e.g., blood vessels, non-target nerves, etc.). Applying ablation energy at the target-specific frequency results in an electric field that creates ionic agitation in the target neural structure, which leads to differentials in osmotic potentials of the targeted neural tissue. These osmotic potential differentials cause dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure) that lead to vacuolar degeneration of the targeted neural tissue and, eventually, necrosis. Using the highly targeted threshold neuromodulation

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energy to initiate the degeneration allows the system 100 to deliver therapeutic neuromodulation to the specific target, while surrounding blood vessels and other non-target structures are functionally maintained.

In some embodiments, the system 100 can further be configured to detect bioelectrical properties of tissue by non-invasively recording resistance changes during neuronal depolarization to map neural activity with electrical impedance, resistance, bio-impedance, conductivity, permittivity, and/or other bioelectrical measurements. Without being bound by theory, when a nerve depolarizes, the cell membrane resistance decreases (e.g., by approximately 80×) so that current will pass through open ion channels and into the intracellular space. Otherwise the current remains in the extracellular space. For non-invasive resistance measurements, tissue can be stimulated by applying a current of less than 100 Hz, such as applying a constant current square wave at 1 Hz with an amplitude less than 25% (e.g., 10%) of the threshold for stimulating neuronal activity, and thereby preventing or reducing the likelihood that the current does not cross into the intracellular space or stimulating at 2 Hz. In either case, the resistance and/or complex impedance is recorded by recording the voltage changes. A complex impedance or resistance map or profile of the area can then be generated.

For impedance/conductivity/permittivity detection, the electrodes (244, 336) and/or another electrode array are placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli to the tissue, and the current and/or voltage at the individual receiver electrodes (244, 336) is measured. The stimuli can be applied at different frequencies to isolate different types of nerves. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest. The neural mapping can also be used during neuromodulation therapy to select specific nerves for therapy, monitor treatment progression with respect to the nerves and other anatomy, and validate successful treatment.

In some embodiments of the neural and/or anatomical detection methods described above, the procedure can include comparing the mid-procedure physiological parameter(s) to the baseline physiological parameter(s) and/or other, previously-acquired mid-procedure physiological parameter(s) (within the same energy delivery phase). Such a comparison can be used to analyze state changes in the treated tissue. The mid-procedure physiological parameter(s) may also be compared to one or more predetermined thresholds, for example, to

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indicate when to stop delivering treatment energy. In some embodiments of the present technology, the measured baseline, mid-, and post-procedure parameters include a complex impedance. In some embodiments of the present technology, the post-procedure physiological parameters are measured after a pre-determined time period to allow the dissipation of the electric field effects (ionic agitation and/or thermal thresholds), thus facilitating accurate assessment of the treatment.

In some embodiments, the anatomical mapping methods described above can be used to differentiate the depth of soft tissues within the nasal mucosa. The depth of mucosa on the turbinates is relatively deep while the depth off the turbinate is relatively shallow and, therefore, identifying the tissue depth in the present technology also identifies positions within the nasal mucosa and where precisely to target. Further, by providing the micro-scale spatial impedance mapping of epithelial tissues as described above, the inherent unique signatures of stratified layers or cellular bodies can be used as identifying the region of interest. For example, different regions have larger or small populations of specific structures, such as submucosal glands, so target regions can be identified via the identification of these structures.

In some embodiments, the system 100 includes additional features that can be used to detect anatomical structures and map anatomical features. For example, the system 100 can include an ultrasound probe for identification of neural tissue and/or other anatomical structures. Higher frequency ultrasound provides higher resolution, but less depth of penetration. Accordingly, the frequency can be varied to achieve the appropriate depth and resolution for neural/anatomical localization. Functional identification may rely on the spatial pulse length ("SPL") (wavelength multiplied by number of cycles in a pulse). Axial resolution (SPL/2) may also be determined to locate nerves.

In some embodiments, the system 100 can further be configured to emit stimuli with selective parameters that suppress rather than fully stimulate neural activity. For example, in embodiments where the strength-duration relationship for extracellular neural stimulation is selected and controlled, a state exists where the extracellular current can hyperpolarize cells, resulting in suppression rather than stimulation spiking behavior (i.e., a full action potential is not achieved). Both models of ion channels, Hodgkin–Huxley (HH) and Retinol Ganglion Cell (RGC), suggest that it is possible to hyperpolarize cells with appropriately designed burst extracellular stimuli, rather than extending the stimuli. This phenomenon could be used to

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suppress, rather than stimulate, neural activity during any of the embodiments of neural detection and/or modulation described herein.

In various embodiments, the system 100 could apply the anatomical mapping techniques disclosed herein to locate or detect the targeted vasculature and surrounding anatomy before, during, and/or after treatment.

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes.

Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein. The subject matter herein contains important information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment. Thus, appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments.

The terms and expressions which have been employed herein are used as terms of description and not of limitation, and there is no intention, in the use of such terms and expressions, of excluding any equivalents of the features shown and described (or portions thereof), and it is recognized that various modifications are possible within the scope of the claims. Accordingly, the claims are intended to cover all such equivalents.

EXAMPLES

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The following description provides details and results of a study concerning the characterization and optimization of radiofrequency (RF) thermal ablations for the treatment of nasal conditions, namely rhinitis, in accordance with the systems and methods of the present invention.

I. Introduction:

Rhinitis (allergic or non-allergic or combination of both types) is an inflammation mediated disease of mucosal tissue lining the nasal cavity. Rhinitis can result in a variety of local conditions e.g., post-nasal drainage, nasal obstruction, rhinorrhea, sneezing, itching, and numerous other symptoms, adversely affecting quality of life. Rhinitis is one of the most common nasal disorders in the United States with an estimated prevalence of approximately 80 million.

Autonomic fibers innervate the submucosal glands and the vasculature of the nasal mucosa and sub-mucosa. An imbalance in the autonomic nervous function often leads to inflammation of the nasal mucosa, where an increase in parasympathetic input drives hyperactivity of the submucosal glands and engorgement of the venous sinusoids; resulting in glandular secretion and vasodilation. Recently, sphenopalatine nerve resection has been described as an effective surgical treatment that severs the post-ganglionic neural pathways within the nose, and can provide beneficial symptomatic relief.

The NEUROMARK System, designed and developed by Neurent Medical Ltd, as shown in Figure 1a and 1b, is a novel device with a multi-stage electrode array that treats rhinitis. The NEUROMARK™ System through local application of radio frequency (RF) in the nasal cavity targets the primary and accessory innervation pathways of the posterior nasal nerves providing lasting symptom relief for treatment of chronic rhinitis. NEUROMARK™ System creates multiple distinct focal lesions on the lateral wall of the nasal cavity targeting two high density nerve rich regions whilst simultaneously limiting surface damage and avoiding wider collateral tissue damage.

Typically, during RF ablation, ~500 kHz current is applied to the target tissue via a pair of electrodes that induces localized volumetric heating due to the Joule effect thus creating regions of high current density. Prior RF ablation studies have demonstrated the importance of selecting appropriate power delivery algorithms, as applied power level during ablative

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treatments greatly impacts the rate of heating and transient changes in impedance at the electrode – tissue interface, and consequently the size and shape of ablation zones. Generally, the target temperature using RF for ablating a nerve is considered to be at or above 45°C. RF ablation is a commonly used approach for *in situ* thermal ablation of tissue, and is in clinical use as a minimally invasive therapeutic method for volumetric reduction of gross tissue treating hypertrophied turbinates.

The objective of the present study was to perform single and multifactorial evaluation of significant electromechanical parameters of the NEUROMARK™ system; such as electrode geometry, electrode spacing, energy delivery strategy to assess both the individual impact and as a complex interactive set on treatment outputs such as ablation depth and volume, treatment-temperature isotherms, treatment time and tissue thermal damage. As tissue damage is a function of both temperature and time; this research evaluated relevant electromechanical parameters and determined an optimization set of the identified parameters to maximize the ablation depth; with specific interest on creating isothermic contours between 55-60°C – 85-90°C to ensure submucosal neurogenic pathways are ablated while minimizing collateral tissue damage whilst maintaining a clinically relevant treatment duration. Temperatures higher than 90°C often lead to irreversible changes in the tissue such as carbonization and desiccation of the tissue surrounding the active electrodes, limiting any further conduction of thermal energy and restricting the energy deposition and thus reducing the size of ablation volume (references).

We employed a combination of multi-physics computational modelling and *ex vivo* studies to carry out the optimization studies. Specifically, the effects of electrode geometry including the electrode length and inter-pair spacing on temperature isotherms, lesion depth as well as treatment time was evaluated individually as well as a combination with respect to different power levels. Multiple duty cycle energy delivery strategies were also investigated with respect to treatment times. Modeling results were validated with benchtop experiments using *excised* tissue. To estimate the anticipated performance *in vivo*, a second set of modelling study was also performed by incorporating the effects of tissue blood perfusion.

II. Methods:

A. Radiofrequency Ablation System for Rhinitis Treatment

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The NEUROMARK™ system consists of a handheld RF NEUROMARK™ device, incorporating a deployable electrode array and a NEUROMARK™ RF generator providing control of power delivery (see FIG. 12A). The device shaft is suitable for advancement into the nasal cavity alongside and under the guidance of nasal endoscope. Once advanced to the treatment site, the atraumatic super elastic electrode array is deployed to facilitate electrical contact with the nasal mucosa.

The end effector consists of two stages of 6 petals each, with every petal consisting of multiple bipolar electrode pairs (see FIGS. 12A and 12B). NEUROMARK™ RF generator contains a multiplexer unit that can independently power and control each petal. The RF generator provides power at 460 kHz in pulsed or continuous mode. Prior to, and during power delivery, the generator constantly monitors electrical impedance at the tissue interface for each petal.

B. NEUROMARK™ System: Rhinitis Treatment Objectives

The main objective of this treatment is to create distinct multi-point lesions along the lateral wall of the nasal cavity, with the depth of each respective lesion up to 4 mm to ablate the sub-mucosal tissue and submucosal neurogenic tone while minimizing surface mucosal and collateral tissue damage within and between each ablation lesion. Another objective of this treatment is to deliver optimum energy in order to delay the onset of impedance roll-off until the target ablation depth is achieved, while maintaining clinically relevant treatment time.

C. Model-Based Assessment and Optimization of Device Geometry and Energy-Delivery Settings

We employed computational Bio-heat transfer models to characterize the impact of NEUROMARK™ device electrode geometrical parameters and energy delivery strategies that play a dominant role on current density patterns within tissue, as these can be expected to considerably impact thermal ablation profiles. Device geometry parameters that affect current density patterns, include electrode diameter, electrode length, intra-pair and inter-pair electrode spacing, rendered in FIG. 12C. These parameters and their respective ranges were evaluated individually first and then subsequently as a combination with respect to various power levels. The critical parameters, and their optimum ranges were chosen based on: 1) percentage target

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ablation depth achieved and 2) maximal separation between thermal damage/isothermal contours ranging between 55-60°C – 85-90°C (or zone of impact) to ensure the submucosal neurogenic tone are ablated while minimizing unintended tissue damage by maintaining a clinically relevant treatment duration.

In the present study, electrode diameter and intra-pair spacing were kept constant. The range of electrode length investigated from a baseline and 20% and 40% higher than the baseline also referred to as short, medium and large respectively. Similarly, the range of electrode inter-pair spacing investigated was from a baseline and 30% and 60% higher than the baseline, also referred to as short, medium and large respectively. To fully comprehend the complex interplay of these parameters on ablation depth, zone of impact and treatment time, the combined effect of the optimum/critical parameters selected from single factor optimization was also evaluated. In addition; constant applied power and pulsed or duty cycled (DC) power delivery (100%, 70% and 50% of the constant power) was also investigated with respect to the ablation depth, isothermal contours as well as the treatment time.

Using COMSOL Multiphysics we performed two types of simulations: 1) *ex vivo* scenario to carry out the single and multifactorial parameter optimization and validation with bench testing data and 2) *in vivo* scenario incorporating the blood perfusion effect.

D. Modeling Strategy to Predict Thermal Ablation Characteristics *ex vivo*

The *ex vivo* scenario modeling was used to develop and validate the computational model using *ex vivo* data. This model was then used for all the optimization work. Liver tissue was used in this approach for various reasons including 1) widely researched modeling strategies for RFA in liver tissue; 2) readily available tissue to enable *ex vivo* testing and validation. Using this approach, as discussed in the previous section, we assessed the impacts of energy delivery strategy (i.e., continuous vs. duty cycle) and electrode configuration (EL and IP spacing). The simulations were carried out at room temperature as initial tissue temperature and was terminated either following the impedance roll-off or after a sufficiently long ablation time (see FIG. 17). To validate the model and confirm the simulated thermal lesion characteristics, *ex vivo* experiments were conducted on fresh bovine liver tissue at room temperature. Power level of low-medium and medium-high range were chosen for bench testing to achieve similar treatment times (time for impedance roll-off) as that of the computational modeling.

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As depicted in Table 1 below, Arrhenius thermal damage model was implemented to simulate thermal damage dependent changes in tissue electrical conductivity (*in vivo* and *ex vivo*) at 450 kHz. As previously reported [31], optimized values of model parameters were selected as: $\alpha = 1.26 \times 10^{-2}$ [°C^{-1}], $\beta = 1.25$, and $\gamma = 2.0 \times 10^{-15}$ [°C^{-8}].

Table 1 Biophysical properties implemented in the *ex vivo* model

Liver tissue	Unit	Value @ 25 °C	Temperature dependency
Thermal conductivity k [30]	$w.(m.k)^{-1}$	$K_0 = 0.498$	$k(T) = k_0 + 0.0008\ T$
Electrical conductivity σ [31], [32]	$S.m^{-1}$	$\sigma_0 = 0.228$	$\sigma(t,T) = \sigma_0[1 - \alpha(T-T_0) + \beta u(T) - \gamma(T-T_0)^8]$
Heat capacity c [33], [30]	$j.(kg.K)^{-1}$	$c_0 = 3800$	$c(T) = \begin{cases} c_0 \\ c_0 + 28.9\,(T - 63.5) \end{cases}$
Density ρ [30]	$kg.(m)^{-3}$	$\rho = 1060$	$\rho(T) = 1060$

E. Modeling Strategy to Predict Thermal Ablation Characteristics *in vivo*

Computational modeling was also performed to evaluate the *in vivo* scenario, i.e., incorporating blood perfusion effects starting at initial body temperature. Since the mucosal dielectric properties at the frequency of interest are not readily available in the literature, muscle tissue properties were used as muscle deemed comparable to that of the mucosal tissue. Recently, blood perfusion value of the mucosal tissue became available and was significantly different (~ 16-fold) than that of the muscle tissue. In order to consider and appreciate the effect of blood perfusion during RFA, muscle electro-thermal tissue properties were implemented in our model at 37°C (initial body temperature) with three cases using: 1) muscle blood perfusion value (or low blood perfusion case); 2) mucosal blood perfusion value (or high blood perfusion case); 3) no blood perfusion effect. All the tissue properties used for the *in vivo* simulations are listed in Table 2 below.

Table 2 Biophysical properties implemented in the *in vivo* model

Muscle tissue	Unit	Value @ 37 °C
Density ρ	$kg.(m)^{-3}$	$\rho_0 = 1090$

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Thermal conductivity k	$w.(m.k)^{-1}$	$K_0 = 0.49$
Electrical conductivity σ	$S.m^{-1}$	$\sigma_0 = 0.446$
Heat capacity c	$J.(kg.K)^{-1}$	$c_0 = 3421$

Tissue type	**Blood perfusion rate**
Muscle	37 $ml.(\text{min.kg})^{-1}$
Mucosal	594 $ml.(\text{min.kg})^{-1}$

F. Mathematical Modeling and Governing Equations

We employed finite element method (FEM) computational models to simulate RF ablation with the NEUROMARK™ micro-electrode array. A coupled electro-thermal model was implemented to compute the electric field density in tissue, electric power density profiles, and transient heat transfer. For modeling RF ablation at ~500 kHz, the quasi-static approximation was employed in our model. The Laplace's equation was solved for determining the voltage profile in the target tissue while the subsequent spatial distribution of tissue temperature was obtained by solving the Penne's bio-heat transfer equation. Tissue electrical and thermal properties vary considerably as a function of the time– temperature history during heating. Table 1 includes temperature dependent properties implemented in our model.

A simplified 3D computational model was implemented to emulate bipolar configuration of the RF ablation device (FIG. 12C). To simplify simulations, computational models of a universal set of two bipolar pairs were considered; the wires were implemented as straight conductors, rather than curved. Device domains in our computational model included electrodes as perfect conductors, and insulated coating as perfectly non-conducting insulator.

In these studies, the NEUROMARK™ RF generator was used in a constant power mode, i.e., the voltage at the electrode surface is adjusted to maintain a constant time-averaged power delivered to tissue. The voltage needs to be adjusted since the tissue conductivity changes during heating, and thus maintaining a constant voltage would yield variations in power delivered to tissue. Thus, we also sought to implement a constant power scheme within our simulations. This was done by implementing a closed loop binary control system that first estimated the total current delivered to tissue and then adjusted the voltage boundary condition at the electrode

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surface in order to maintain a constant power. Total electric current during simulation was used as an indicator for input voltage. The electric current in our model was calculated by summing the current density vectors normal to each surface of a test cuboid defined to surround the active electrodes, and the implicit control interface within COMSOL Multiphysics was used to define an upper and lower threshold for the total power with a tolerance of less than 5%.

G. Details of The Mesh

A total of 432,159 tetrahedral mesh elements were used to discretize the model geometry, with a minimum and maximum element size of 0.08 mm and 0.4 mm respectively in the target tissue. Finest mesh density was selected in electrode domains with maximum element size of 0.06 mm as the electro-thermal gradients tend to be steep in these regions. An initial source voltage ($V_0 \neq 0$) was applied to the boundaries of active electrodes. The corresponding electrodes were defined as electrical ground returns ($V = 0$). Initial modeling results indicating that when using the same applied voltage at the electrodes, as recovered from generator logs, the time to impedance roll off observed in simulations occurred considerably faster in simulation, consequently allowing insufficient time for the thermal ablation zone to grow. Thus, we decided to adjust the initial applied voltage (and thus the power level controlled) such that the time to roll-off in simulations agreed (within 0–5 s) with experimental observations.

Electrode and insulation domains were omitted from our model due to negligible resistive heating because the electrode and insulation domains are assumed to be perfect conductor and insulator respectively. To reasonably approximate free convective cooling in *ex vivo* tissue, a convective heat flux boundary condition was applied to the exterior surface of modeling domain. The convective heat transfer coefficient and external temperature were selected as 10 $[W.(m^2.K)^{-1}]$, and 25°C, respectively.

The outputs of the computational model were the extent of the thermal damage zone, and the transient impedance profile. The extent of the thermal damage zone was determined using the Arrhenius thermal damage model where values of frequency factor and activation energy were respectively defined as 5.51×10^{41} $[S^{-1}]$, and 2.769×10^5 [J $(mol)^{-1}$] for the liver tissue. Correspondingly, for the changes in the electrical conductivity of muscle tissue, the parameters were implemented as 2.94×10^{39} $[S^{-1}]$, 2.596×10^5 [J $(mol)^{-1}$]. Finally, boundaries of ablation zones were estimated based on a threshold of $\Omega(T, t) = 1$, corresponding to 63% of the thermal

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damage process being complete.

G. Benchtop Experimental Evaluation in *ex vivo* Tissue

To characterize thermal ablation profiles and validate computational models, initial experiments were conducted on the benchtop in fresh *ex vivo* bovine liver tissue with the NEUROMARK™ device (FIG. 12D). In these experiments, the impact of power levels on the size and shape of ablation zone was characterized, through the electrical profile logs from the generator and co-registered through dimensional assessments of ablation zones; assessed by the extent of opacification, i.e., visibly discolored tissue. We also considered variable input ranges within the applied power levels including constant power delivery and duty cycle power delivery and assessed the electrical profile logs in bench studies which were consistent with that in the simulations. Prior to ablation, liver tissue was preheated up to room temperature of 25°C in the water bath, then each heating protocol was conducted in 3 trials for repeatability purposes.

III. Results:

A. Effect of Electrode Length on Thermal Ablation Zones

Simulations were run with different electrode lengths (i.e., short, medium, and long electrodes) with same energy delivery strategy to investigate the effect on ablation outcomes while keeping the other geometrical parameters fixed. FIGS. 13A and 13B show that the zone of impact increased with increase in EL where the maximum separation between 55-60 °C to 85-90°C isothermal contours was also observed. With increase in EL, the ablation depth also increased significantly, over 200 percent, as shown in the Figure 2a, 2b, suggesting that the EL could be a critical factor in determining the ablation depth. However, FIG. 13C shows that increasing the EL delayed the impedance roll-off, resulting in a longer ablation time.

B. Effect of Electrode Inter-Pair Spacing on Thermal Ablation Zones

Simulations were run with different electrode IP spacing with the same energy delivery strategy to investigate the effects of IP spacing on ablation outcomes while keeping other geometrical parameters fixed.

FIGS. 14A and 14B show that with the short IP spacing, the lesions appeared to be

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merged between two electrode pairs and as the IP spacing increased, the distinct lesions were present with greater zone of impact. The lesion depth remained similar with only a slight increase in case of large IP spacing (FIGS. 14A and 14D). FIG. 14C shows that increasing the IP spacing prolonged the ablation time by delaying the impedance roll-off, leading to larger surface ablation.

C. Combined Effects of Electrode Length and Inter-pair Spacing on Thermal Ablation Zones

To evaluate the multifactorial/combined effects of EL and IP spacing on ablation outcomes, simulations were run to using base electrode configuration (short EL and short IP spacing) and optimized configuration (long EL and long IP spacing).

FIGS. 15A and 15B show that with the base configuration, the zone of impact is narrow and shallow which significantly increased with the optimized configuration. Most importantly, the separation between the isothermal zones 55-60°C and 85-90°C is much more pronounced with the optimized configuration. Consistent with the observations in the single factor simulations of various EL, the percentage increase in the ablation depth with the optimized configuration was over 200 when compared to that of base configuration. However, FIG. 15C shows that the optimized configuration prolonged the ablation time by delaying the impedance roll-off, leading to larger surface ablation.

D. *Ex vivo* Validation of Computational Modeling with Optimized Electrode Geometry Configuration

Ex vivo experiments on liver tissue were conducted using the device with optimum electrode configuration (i.e., long EL, and long IP spacing) to verify and validate the computational modeling outcomes. FIGS. 16A and 16B show that the power levels in the computational modeling was adjusted to match the treatment times closely with that of two ranges of power levels (low-medium and medium-high) in bench testing.

FIG. 16C shows the ablated liver tissue that appears as slightly paler and the depth of the ablated tissue was measured and compared between different power ranges. FIG. 16D shows that 1) the ablation depths predicted by computational modeling closely matched to that of the experiment at the respective power levels; and 2) increasing the power level does not necessarily increase the ablation depth. Also, these results demonstrate that the treatment time and power

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level are inter-dependent and plays a critical role in ablation outcomes.

E. Effect of Energy Delivery Strategy on Ablation Zones

FIG. 17 details the simulation results following different energy delivery strategies including constant and duty cycle energy deliveries. Temperature maps of tissue depth are shown immediately following the treatment (after impedance role-off) for each heating protocol with contours of thermal damage.

As demonstrated in FIG. 17, duty cycle mode delayed the impedance roll-off and resulted in longer ablation time compared to constant power delivery mode. Impedance roll-off occurred in 15 s, 29 s, and 120 s for constant power delivery, 70% duty cycle and 50% duty cycle, respectively. Ablation depth was however similar regardless of the energy delivery strategy, but the temperatures at which the thermal damage occurred varied with the % duty cycle compared to that of constant power. These results show that the similar ablation outcomes can be achieved with pulsed energy delivery strategy within a reasonable treatment time.

F. Effect of Blood Perfusion on Ablation Results

Models of muscle tissue with different blood perfusion effects (i.e., no blood perfusion, muscle blood perfusion (low perfusion scenario), and mucosal blood perfusion (high perfusion scenario) were considered to simulate the effect of blood flow on ablation results. Temperature maps and tissue impedance plots following RF ablation were simulated (FIG. 18).

Model with mucosal perfusion (high perfusion) effect impeded out slightly later than that of muscle perfusion (low perfusion) effect. Despite a prolonged ablation time when using mucosal blood perfusion that is significantly higher than that of muscle, all three models resulted in a similar zone of impact and ablation depth.

IV. Discussion:

In this study, we employed Multiphysics modeling and bench testing to comparatively assess the impact and subsequently optimize the NEUROMARK™ RF ablation device geometry and energy delivery parameters to achieve desired lesion characteristics, with application to treatment of chronic rhinitis. For safe and successful rhinitis treatment, sufficiently deep thermal

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ablation zones (up to 4 mm) should target posterior lateral nasal nerves to effectively decrease Rhinitis symptoms while minimizing tissue surface damage within the nasal cavity. Our *ex vivo* computational results illustrate that achieving deeper ablation zones may also increase tissue surface damage. Thus, RF delivery for rhinitis treatments should balance the trade-offs of achieving ablation zones at adequate depth, while minimizing wider tissue collateral damage.

Computational models predicted deeper and longer ablation zones when using longer electrodes indicating that the EL is a significant factor in determining the ablation depth. Impedance roll-off was significantly delayed (8x time period for long electrodes compared to for short electrodes) when using longer electrodes and was associated with longer ablation durations and consequently deeper and larger ablation zones. This may be attributed to the lower current density when using longer electrodes. Since the rate of RF heating is proportional to the current density, a lower current density leads to more gradual heating, delaying the time to impedance roll-off, extending the ablation duration, and finally leading to deeper ablation zones.

The effect of device IP spacing was also assessed with computational models. The model with shorter inter-pair spacing led to shorter ablation time (faster impedance roll-off) and smaller tissue surface ablation while causing similar ablation depth and zone of impact when compared to the model with longer inter-pair spacing (see Table 4). Tissue thermal conduction plays a significant role in the size of ablation depth when electrode pairs are closer to each other. This leads to sufficiently deep ablation zones despite a short ablation time and early impedance roll-off. Thus, IP spacing has an effect on lesion spread but not depth.

Table 4. Impact of device geometry on ablation results

Parameter	Ablation depth	Surface area (width and length)	Ablation time
Longer electrode	Larger	Larger	Longer
Longer inter-pair	Neutral	Larger	Longer

The combined effect of these parameters, EL and IP on lesion characteristics and treatment times were also evaluated. With the optimized configuration (long EL and long IP), the

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zone of impact is greater, ablation zones are deeper and larger as compared to the shallow ablation zones created using base configuration (short EP and short IP). However, as expected, the ablation times were also longer with the optimized configuration.

According to *ex vivo* simulation results (FIG. 17), delaying the impedance roll-off through duty cycle energy delivery resulted in similar ablation zone depth despite a prolonged ablation when compared to the ablation zones created by heating protocol with constant power delivery. This is likely due to significant contribution of the tissue thermal conductivity towards resistive heating when tissue is subjected to high temperature gradients during the RF ablation. Thus, an optimized delivery strategy could be pulsed energy delivery with a reasonable treatment time (less than 120 s for impedance roll-off). The *ex vivo* experimentation was carried out to validate the simulation models. The device end effector used for ex vivo testing was designed with optimized geometry parameters, i.e., long EL and long IP spacing. In our simulations, we adjusted applied power levels so that time to roll-off in experiments and simulations were matched (FIG. 16). When applying the same power level in simulations, models predicted considerably faster impedance roll-off and shorter ablation times, consequently yielding decreased ablation zone sizes. We note that we are using an RF computational modeling approach that has previously been applied in several modeling studies, yielding good agreement with experimental findings. One key difference is that we are modeling RF ablation with very thin electrodes, considerably smaller than electrodes used for liver or cardiac RF ablation (typically ~1-2 mm diameter), and thus associated with a faster rate of heating due to a very high electric current density in regions close to the electrode. One explanation is that tissue electrical conductivity implemented in our model may not precisely predict the changes in tissue properties with regards to sudden rises in temperature. Also, in the experiment, power is controlled based on an effective impedance of 4 electrode pairs within one petal of the NEUROMARK™ device, and thus the power logged captures the equivalent impedance across all 4 pairs. Within the idealized modeling environment, power was applied to approximate equivalent power delivered to each individual bipolar electrode pair, although this may not be the case in experiment. We used the same model for simulating RFA with a 16 G monopolar needle (OD ≈1.6 mm), and simulation results including power level, impedance roll-off time and ablation zones matched quite well with experiment (data not shown)

A comparison of simulated and experimentally measured transient impedance profiles

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during RFA in *ex vivo* liver tissue is illustrated in FIG. 16, confirming the consistency in tissue impedance trends between simulation results and experimental observations ($R = 0.92$). An applied power of 1.1 W in simulations was considered to model an experimental ablation of low-medium power since these yielded similar impedance roll-off times (~120 s). The discrepancy between power levels may be due to the manner in which the heat-induced changes in tissue biophysical properties are implemented in our model. In particular, heating rates near the electrode tip for this application generally ranged between 1.5– 4.5 °C/s; however, tissue electrical conductivity changes during heating have previously only been reported for heating rates between 0.02– 0.54 °C/s. Nevertheless, a good agreement between simulation and experimental results were observed, confirming constant power delivery with longer impedance roll-off time as the potential heating protocol for creating deeper ablation zones.

Our model was further developed to evaluate the effect of sub-mucosal blood flow on ablation results during *in vivo* RFA. Unlike prior studies that reported blood perfusion as a major obstacle in RF heating treatments, we observed that blood perfusion effect on ablation results could be negligible during RFA treatment of nasal mucosa (see FIG. 18). This may be attributed to the large heating rate (~10^8 [$W\ m^{-3}$]) within the target tissue that outweighs blood heat sink effect. A short distance (in the order of mm) between active and ground electrodes likely leads to producing a significantly high electric current during the ablation procedure, leading to a high heating rate and consequent microvascular stasis (i.e., $\omega_b = 0$) within the first few seconds of thermal ablation.

A limitation of the presented study is reporting thermal ablation results in *ex vivo* liver tissue only. It would also be beneficial to further assess the ablation results based on nasal cavity model in *in vivo* tissue but was not feasible in this study due to the lack of data on thermal dose and temperature-dependent dielectric properties for nasal tissue. However, the liver tissue is widely used for RF ablation modeling, and since the model itself was also validated with the *ex vivo* experiments, this model offers immense value in being able to predict the ablation zones to optimize the device features.

In summary, we carried out single and multifactor optimization of electrode configuration and energy delivery strategy of NEUROMARK™ System and determined the optimum parameters to maximize the ablation depth; specifically creating isothermic contours between 55-60°C – 85-90°C to ensure submucosal neurogenic pathways are ablated while minimizing

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unintended tissue damage by maintaining a clinically relevant treatment duration. We employed a multi-physics computational approach which was successfully validated and co-registered the outcomes with *ex vivo* testing. We also showed that the impact of blood perfusion on ablation results might be negligible depending on heating rate during RF ablation.

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Claims

What is claimed is:

1. A system for treating a condition, the system comprising:

a treatment device including an end effector comprising one or more electrodes; and

a controller operably associated with the treatment device and configured to:

determine a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues;

receive and process real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes; and

control supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

2. The system of claim 1, wherein the identifying data is associated with one or more properties of the one or more tissues, the one or more properties comprising at least one of a type, a depth, and a location of each of the one or more tissues.

3. The system of claim 2, wherein a subset of the one or more electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense at least bioelectric properties of the one or more tissues at the target site.

4. The system of claim 3, wherein the bioelectric properties comprise at least one of complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

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5. The system of claim 4, wherein the controller is configured to process the identifying data to determine the treatment pattern.

6. The system of claim 5, wherein the processing of identifying data, via the controller, comprises comparing the identifying data received from the device with electric signature data associated with a plurality of known tissue types.

7. The system of claim 6, wherein the electric signature data comprises at least bioelectric properties of known tissue types.

8. The system of claim 5, wherein the comparison comprises correlating the identifying data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

9. The system of claim 1, wherein the treatment pattern comprises at least one of a predetermined treatment time, a level of energy to be delivered from the electrodes, and a predetermined impedance threshold.

10. The system of claim 9, wherein the feedback data comprises at least impedance measurement data associated with the targeted tissue at the target site.

11. The system of claim 10, wherein the controller is configured to process the impedance measurement data to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue.

12. The system of claim 11, wherein the controller is configured to process the active impedance value using an algorithm to determine efficacy of ablation/modulation of the targeted tissue based on a comparison of the active impedance value with at least one of a predetermined minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value.

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13. The system of claim 12, wherein, if the active impedance value is less than the predetermined minimum impedance value, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes.

14. The system of claim 12, wherein, if the active impedance value is greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the controller calculates a slope change for the detection of a slope event.

15. The system of claim 14, wherein:

if a negative slope event is detected, the controller determines that ablation/modulation is successful and disables energy delivery from the one or more electrodes upon detecting a negative slope event; and

if a negative slope event is not detected, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes.

16. The system of claim 15, wherein, in the absence of detecting a slope event, the controller determines that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and disables energy delivery from the one or more electrodes.

17. The system of claim 1, wherein the controller is further configured to transmit a signal resulting in an output, via an interactive interface, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue.

18. The system of claim 17, wherein the alert includes a visual alert comprising at least one of a color and text displayed on a graphical user interface (GUI) and indicating whether the ablation/modulation is successful or unsuccessful.

19. The system of claim 1, wherein condition comprises a peripheral neurological condition.

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20. The system of claim 19, wherein the peripheral neurological condition is associated with a nasal condition or a non-nasal condition of the patient.

21. A method for treating a condition, the system comprising:

providing a treatment device comprising an end effector including one or more electrodes and a controller operably associated with the treatment device;

positioning the end effector at a target site associated with a patient;

determining, via the controller, a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues;

receiving, from the device, and processing, via the controller, real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes; and

controlling, via the controller, supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site.

22. The method of claim 21, wherein the identifying data is associated with one or more properties of the one or more tissues, the one or more properties comprising at least one of a type, a depth, and a location of each of the one or more tissues.

23. The method of claim 22, wherein a subset of the one or more electrodes is configured to deliver non-therapeutic stimulating energy at a frequency/waveform to respective positions at the target site to thereby sense at least bioelectric properties of the one or more tissues at the target site.

24. The method of claim 23, wherein the bioelectric properties comprise at least one of complex impedance, resistance, reactance, capacitance, inductance, permittivity, conductivity, dielectric

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

properties, muscle or nerve firing voltage, muscle or nerve firing current, depolarization, hyperpolarization, magnetic field, and induced electromotive force.

25. The method of claim 24, wherein the controller is configured to process the identifying data to determine the treatment pattern.

26. The method of claim 25, wherein the processing of identifying data, via the controller, comprises comparing the identifying data received from the device with electric signature data associated with a plurality of known tissue types.

27. The method of claim 26, wherein the electric signature data comprises at least bioelectric properties of known tissue types.

28. The method of claim 25, wherein the comparison comprises correlating the identifying data received from the device with electric signature data from a supervised and/or an unsupervised trained neural network.

29. The method of claim 31, wherein the treatment pattern comprises at least one of a predetermined treatment time, a level of energy to be delivered from the electrodes, and a predetermined impedance threshold.

30. The method of claim 29, wherein the feedback data comprises at least impedance measurement data associated with the targeted tissue at the target site.

31. The method of claim 30, wherein the controller is configured to process the impedance measurement data to calculate an active impedance value during delivery of energy from the one or more electrodes to the targeted tissue.

32. The method of claim 31, wherein the controller is configured to process the active impedance value using an algorithm to determine efficacy of ablation/modulation of the targeted tissue based on a comparison of the active impedance value with at least one of a predetermined

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

minimum impedance value, a predetermined low terminal impedance value, and a predetermined high terminal impedance value.

33. The method of claim 32, wherein, if the active impedance value is less than the predetermined minimum impedance value, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes.

34. The method of claim 32, wherein, if the active impedance value is greater than the predetermined minimum impedance value and greater than the predetermined low terminal impedance value, the controller calculates a slope change for the detection of a slope event.

35. The method of claim 34, wherein:

if a negative slope event is detected, the controller determines that ablation/modulation is successful and disables energy delivery from the one or more electrodes upon detecting a negative slope event; and

if a negative slope event is not detected, the controller determines that ablation/modulation is unsuccessful and disables energy delivery from the one or more electrodes.

36. The method of claim 35, wherein, in the absence of detecting a slope event, the controller determines that ablation/modulation is unsuccessful if the active impedance value is greater than the predetermined high terminal impedance value and disables energy delivery from the one or more electrodes.

37. The method of claim 21, wherein the controller is further configured to transmit a signal resulting in an output, via an interactive interface, of an alert to a user indicating a status of the efficacy of ablation/modulation of the targeted tissue.

38. The method of claim 37, wherein the alert includes a visual alert comprising at least one of a color and text displayed on a graphical user interface (GUI) and indicating whether the ablation/modulation is successful or unsuccessful.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

39. The method of claim 21, wherein condition comprises a peripheral neurological condition.

40. The method of claim 39, wherein the peripheral neurological condition is associated with a nasal condition or a non-nasal condition of the patient.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

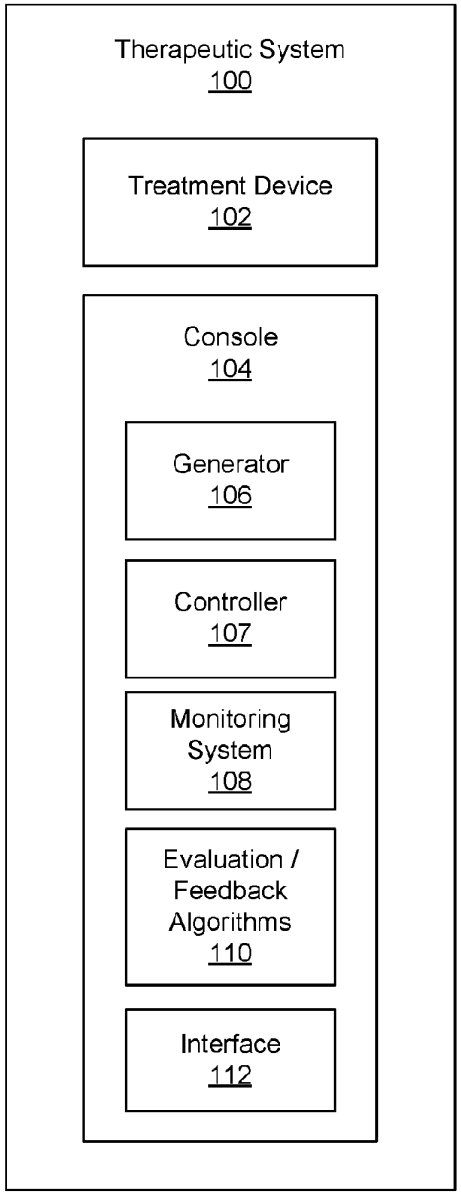

Therapeutic System
100
Treatment Device
102
Console
104
Generator
106
Controller
107
Monitoring System
108
Evaluation / Feedback Algorithms
110
Interface
112

FIG. 1A

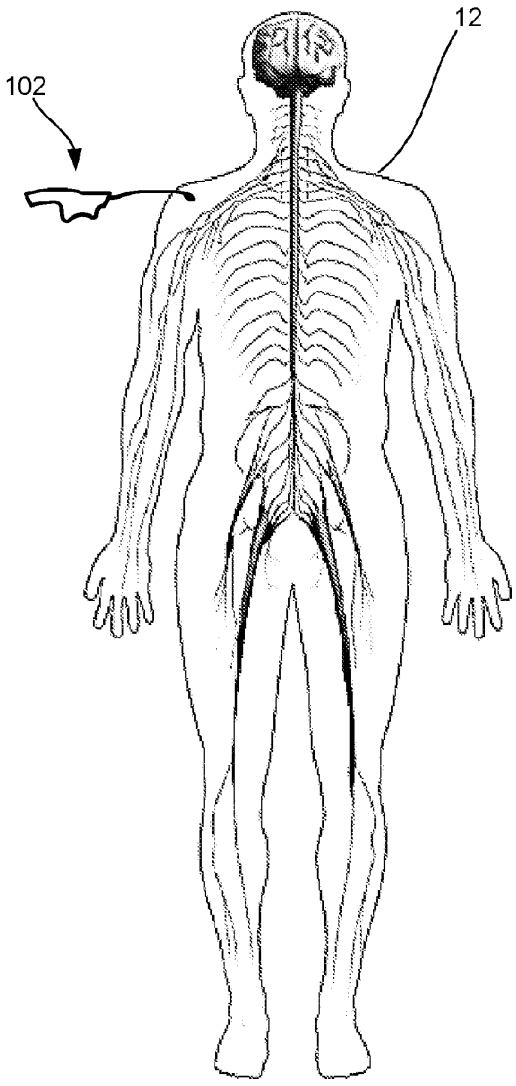

102
12

FIG. 1B

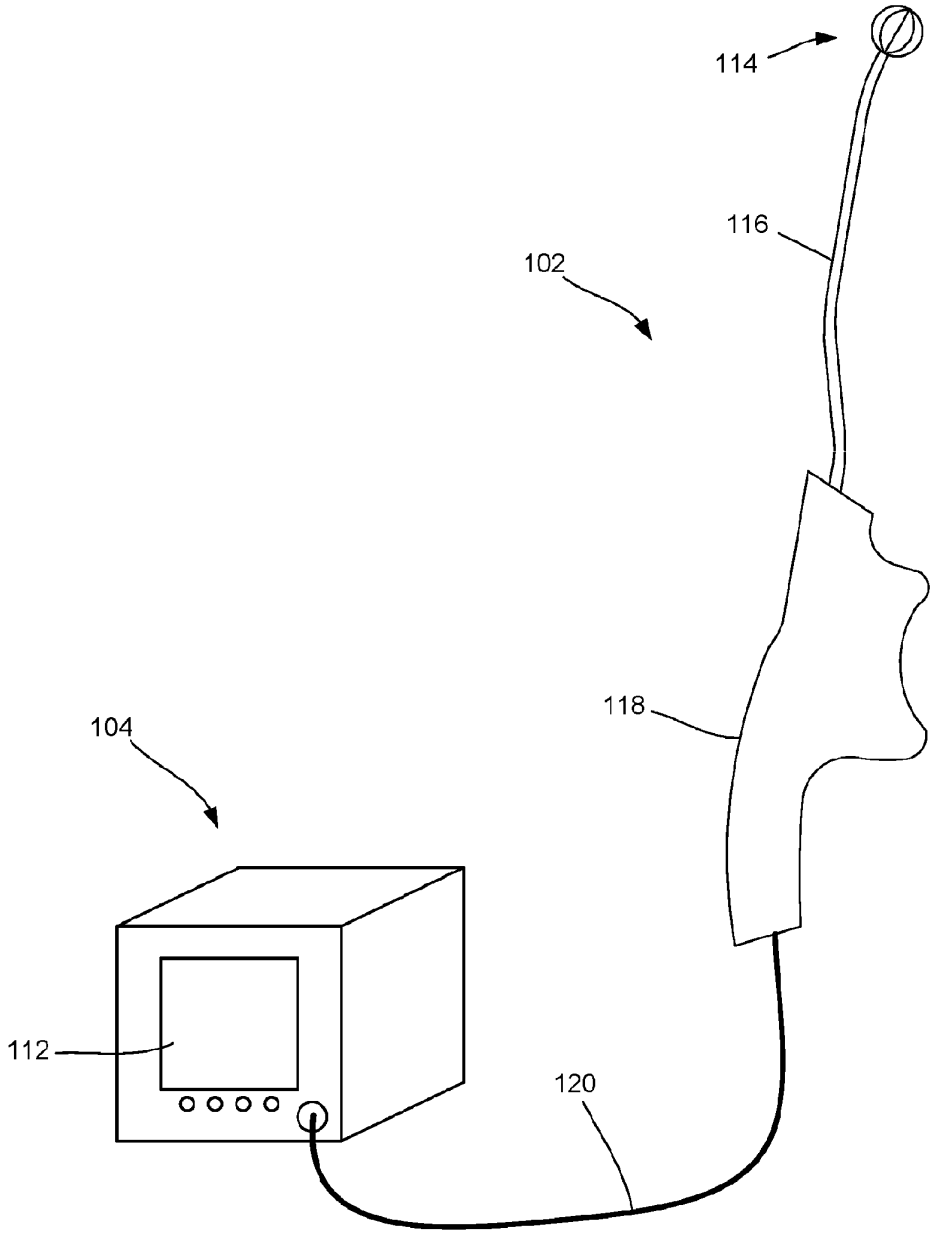


FIG. 2

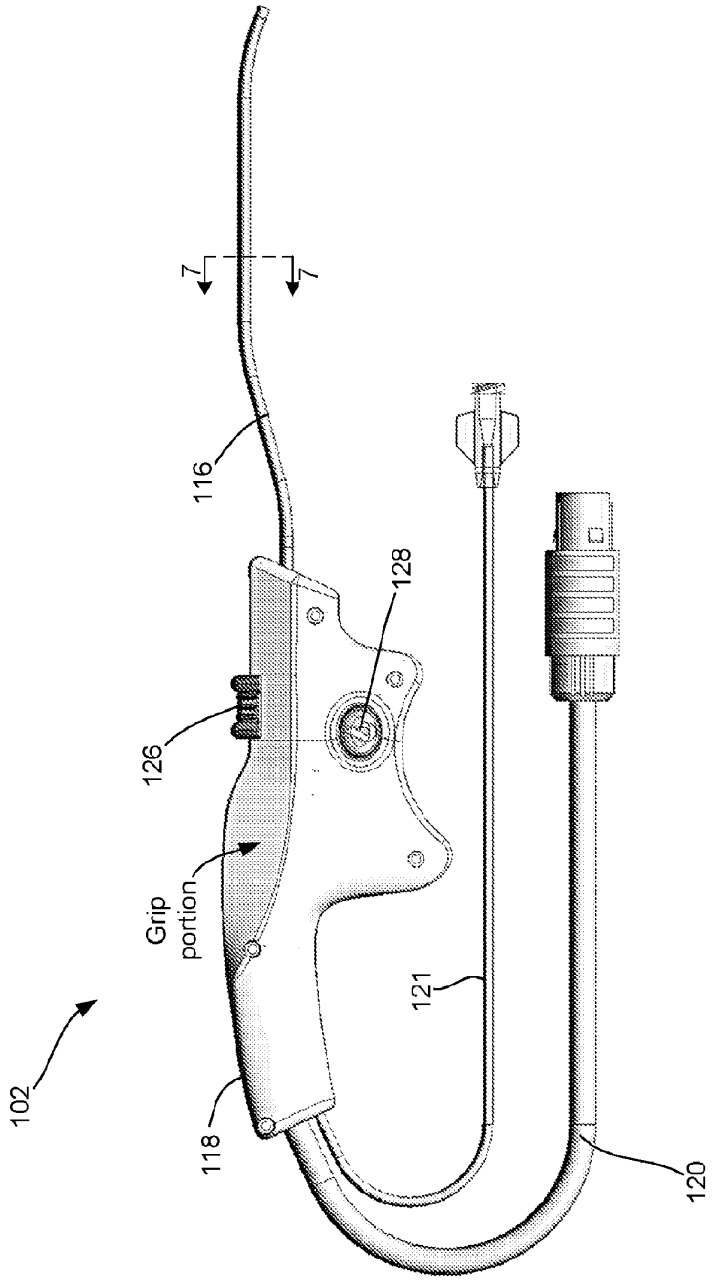


FIG. 3

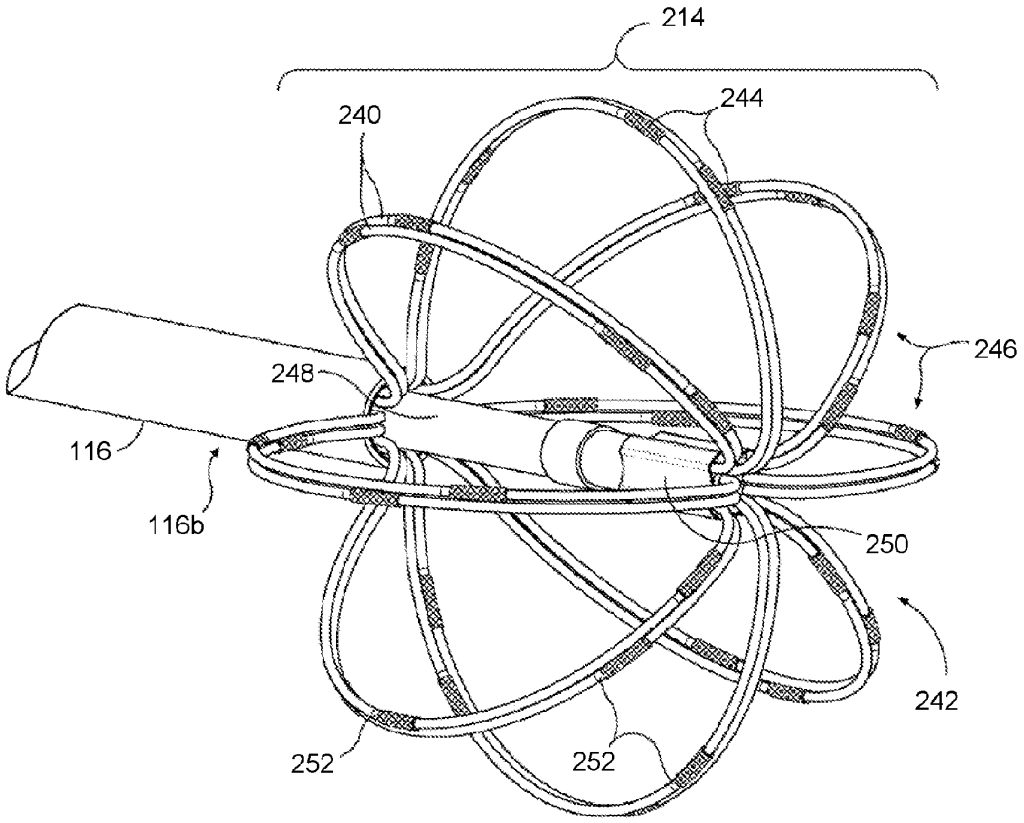


FIG. 4

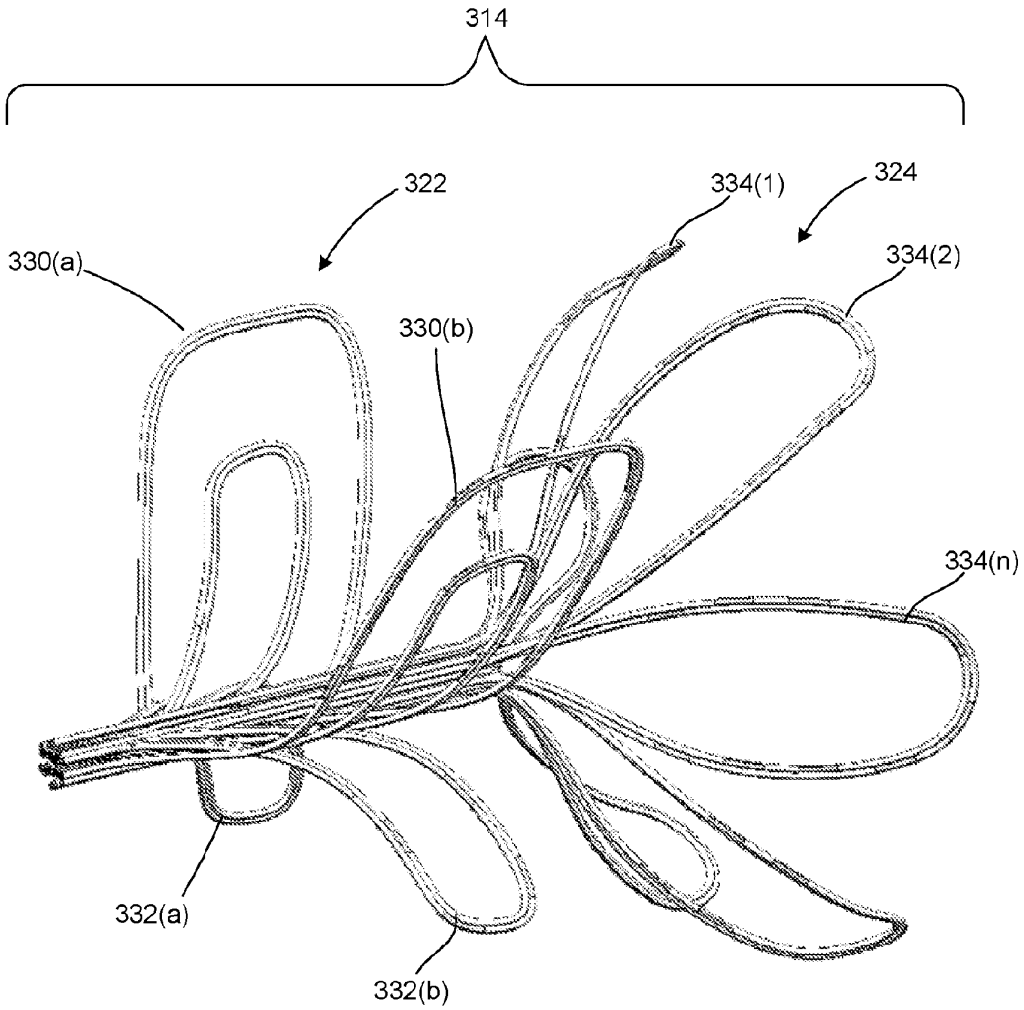


FIG. 5A

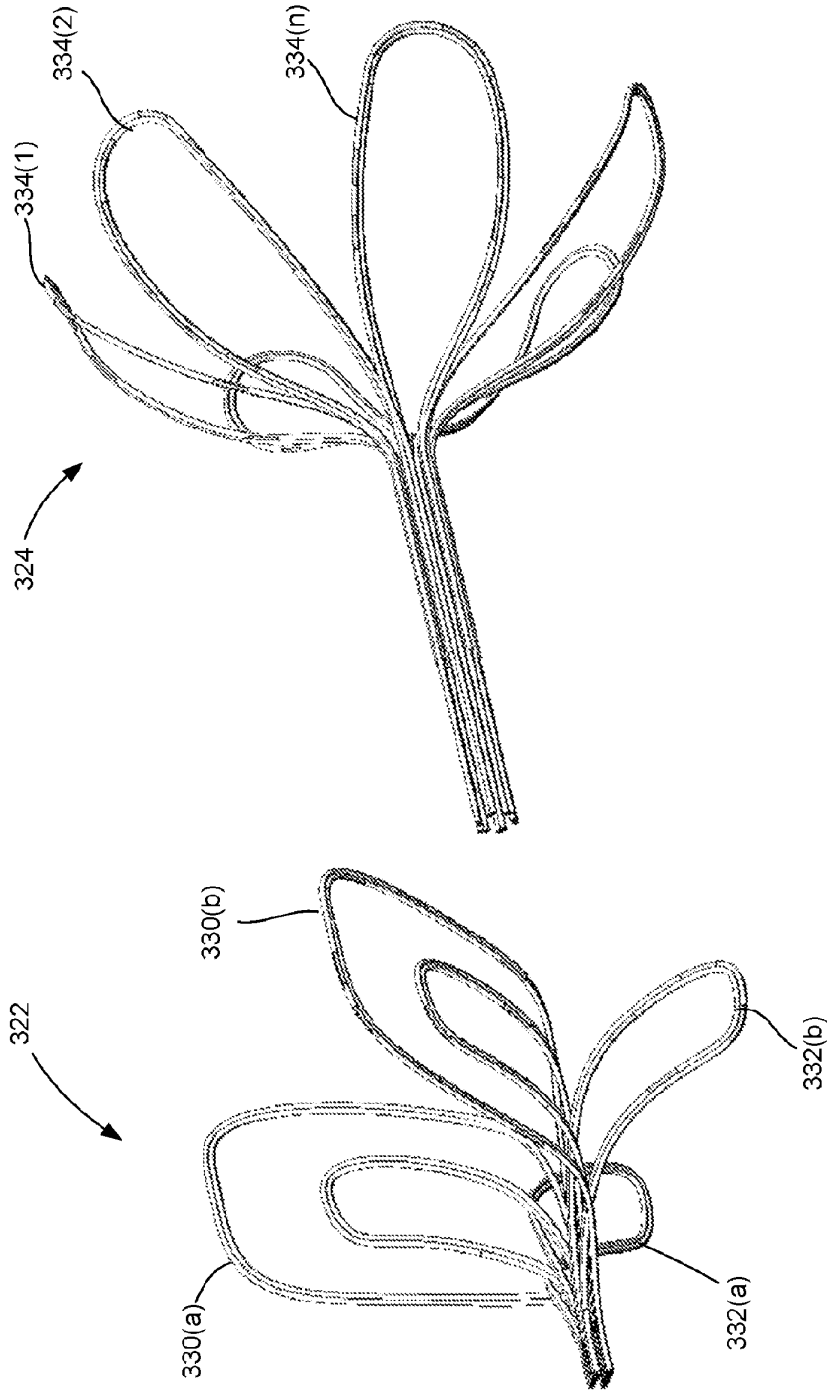


FIG. 5B

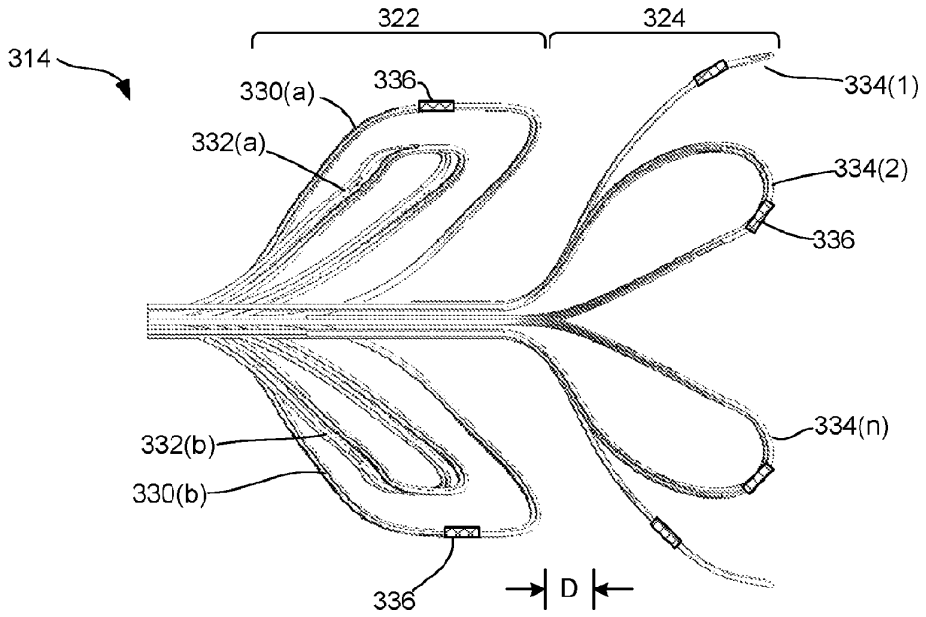

322
324
314
330(a)
336
334(1)
332(a)
334(2)
336
332(b)
334(n)
330(b)
336
D

FIG. 5C

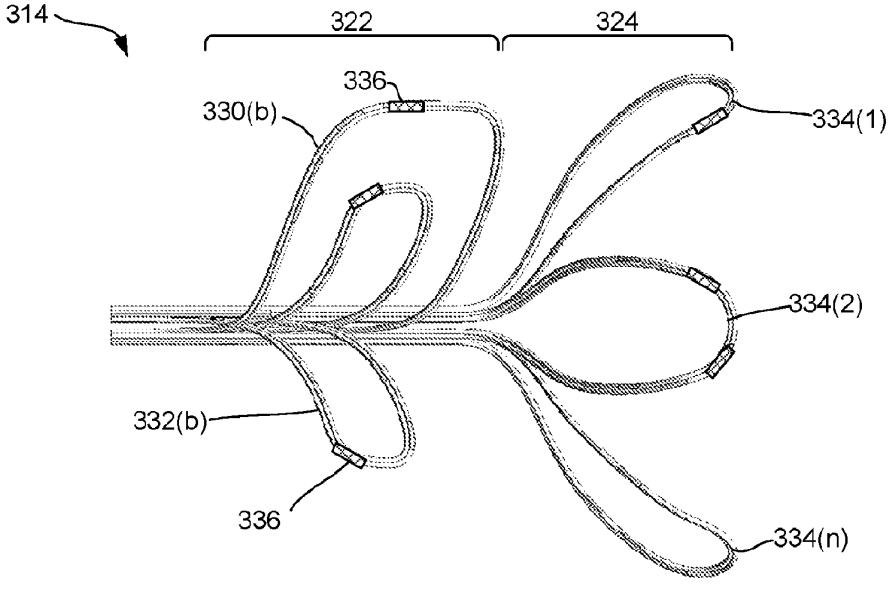

314
322
324
336
330(b)
334(1)
334(2)
332(b)
336
334(n)

FIG. 5D

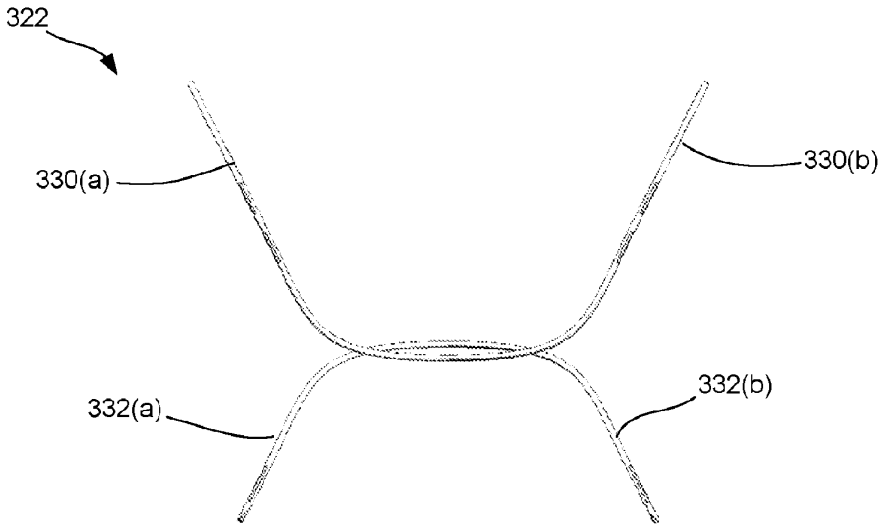


FIG. 5E

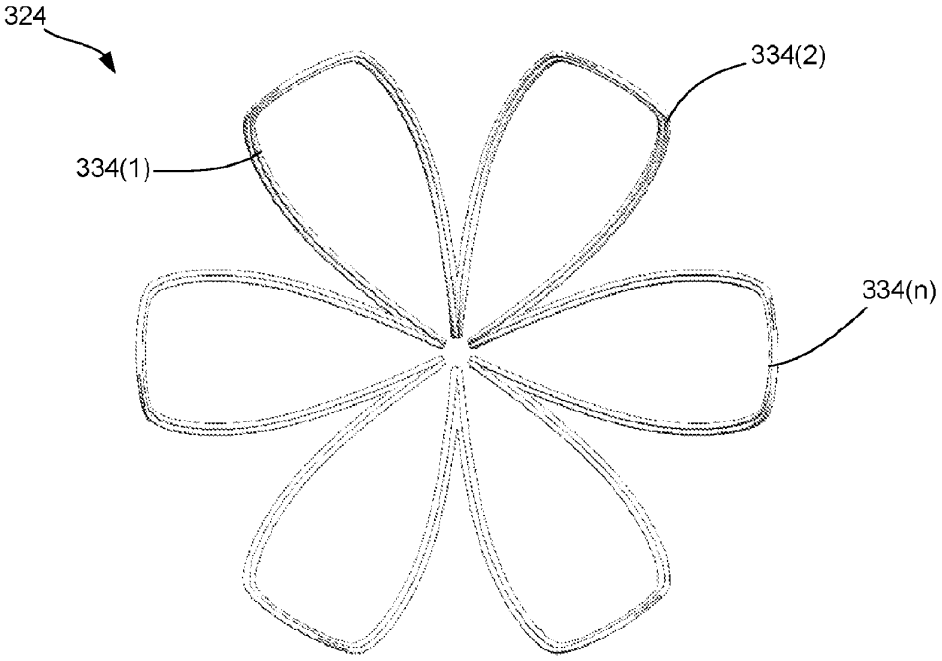


FIG. 5F

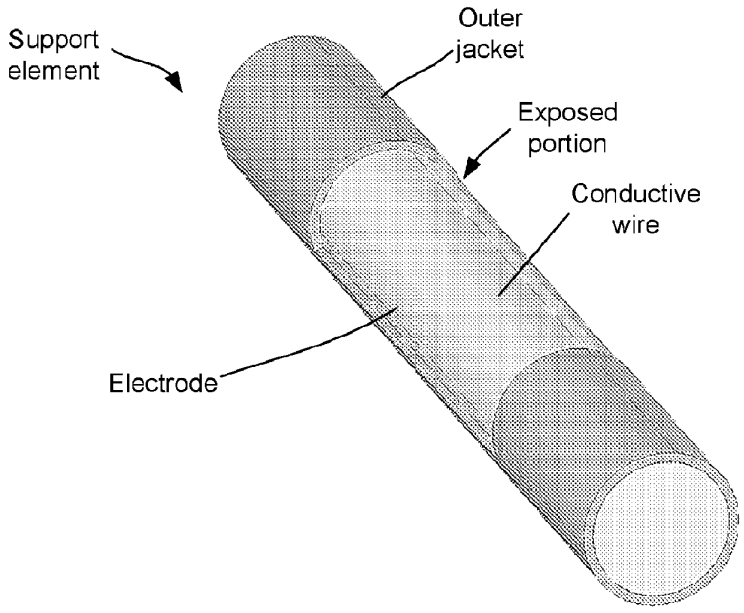

Support element
Outer jacket
Exposed portion
Conductive wire
Electrode

FIG. 6

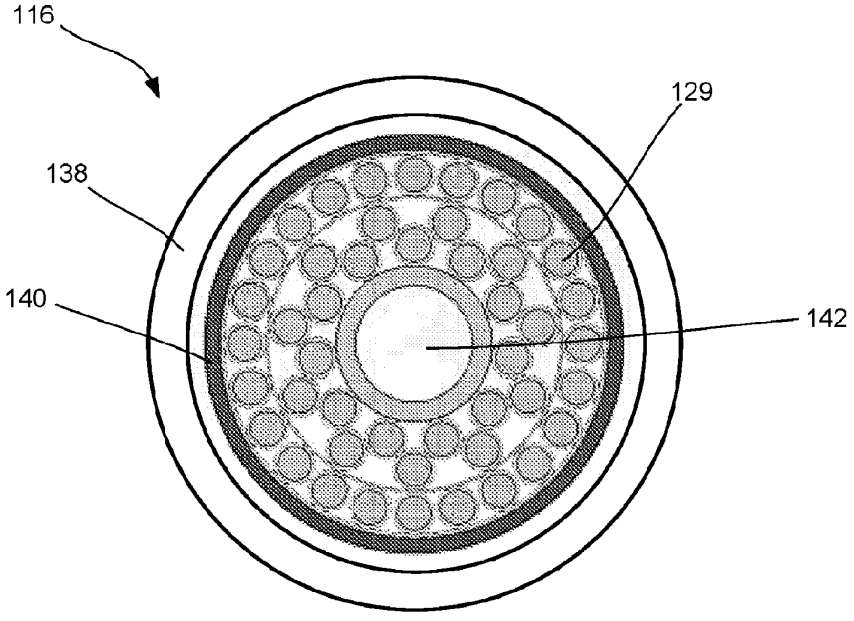

116
129
138
140
142

FIG. 7

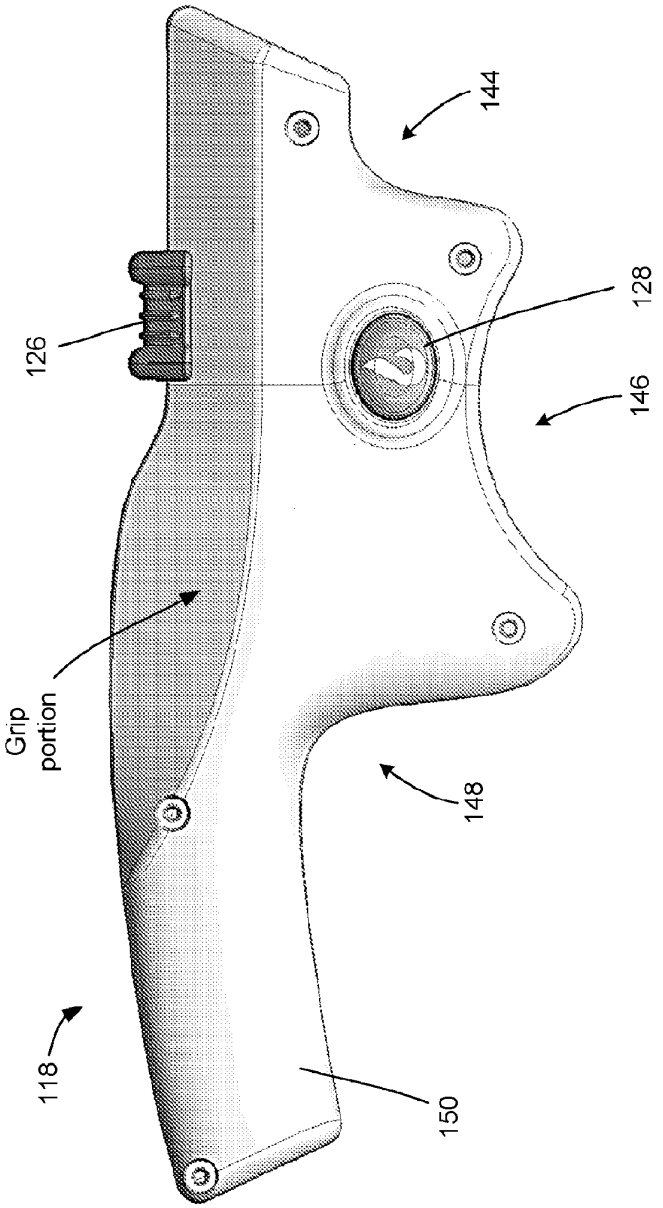


FIG. 8A

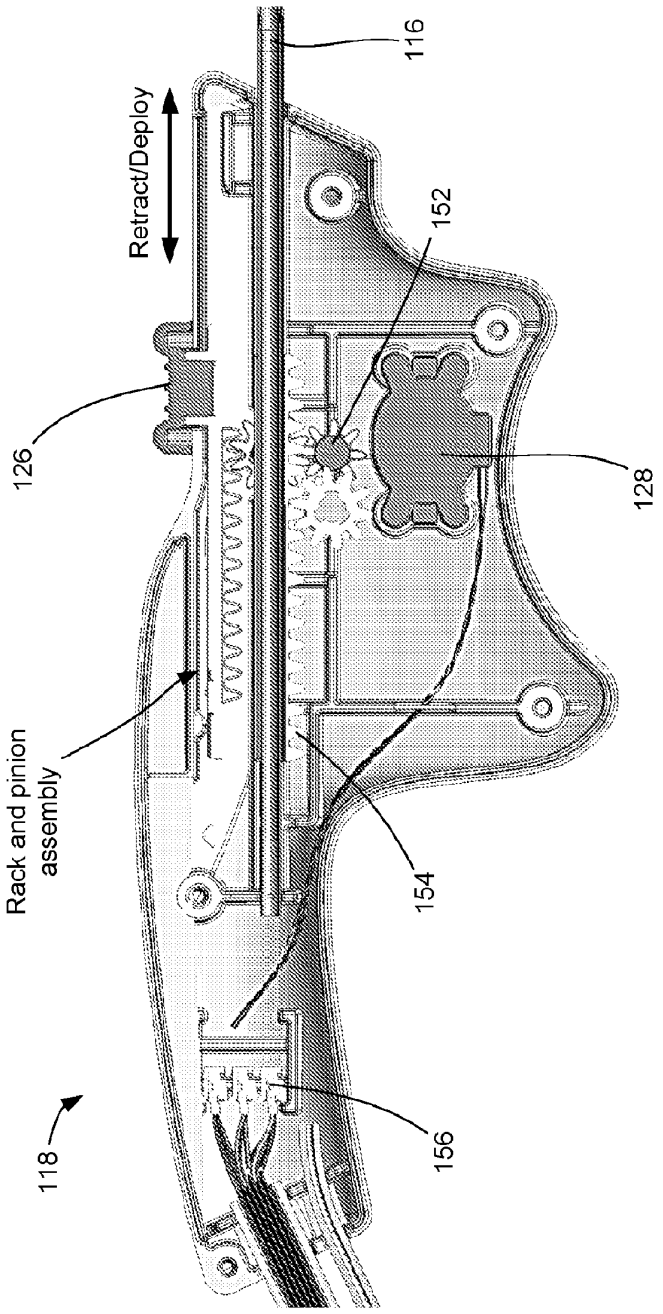

116
Retract/Deploy
152
126
128
Rack and pinion assembly
154
156
118

FIG. 8B

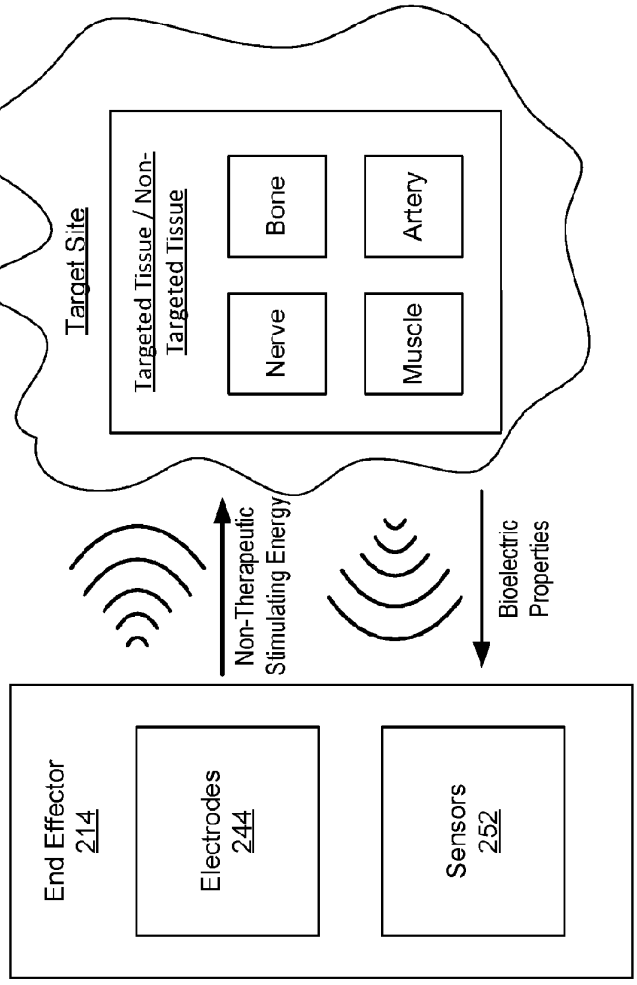

Target Site
Targeted Tissue / Non-Targeted Tissue
Nerve
Bone
Muscle
Artery
Non-Therapeutic Stimulating Energy
Bioelectric Properties
End Effector 214
Electrodes 244
Sensors 252

FIG. 9A

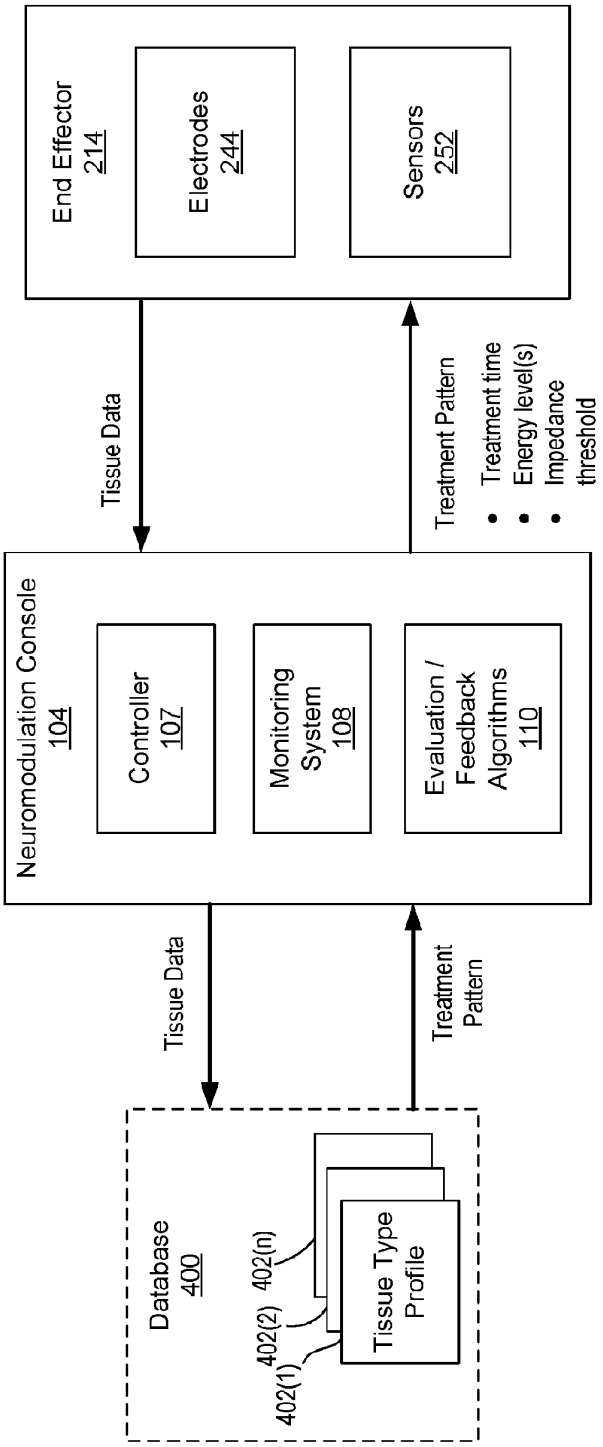

End Effector
214
Electrodes
244
Sensors
252
Tissue Data
Treatment Pattern
• Treatment time
• Energy level(s)
• Impedance threshold
Neuromodulation Console
104
Controller
107
Monitoring System
108
Evaluation / Feedback Algorithms
110
Tissue Data
Treatment Pattern
Database
400
402(n)
402(2)
402(1)
Tissue Type Profile

FIG. 9B

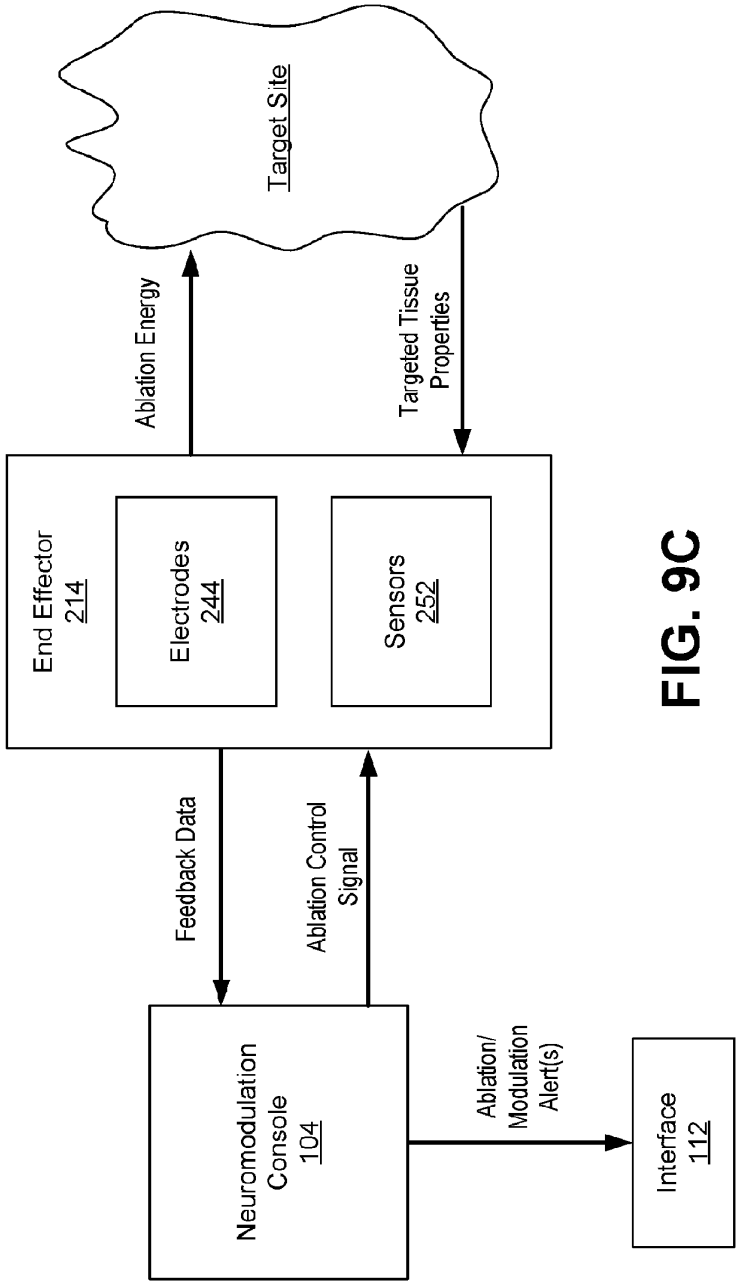

Target Site
Ablation Energy
Targeted Tissue Properties
End Effector 214
Electrodes 244
Sensors 252
Feedback Data
Ablation Control Signal
Neuromodulation Console 104
Ablation/ Modulation Alert(s)
Interface 112

FIG. 9C

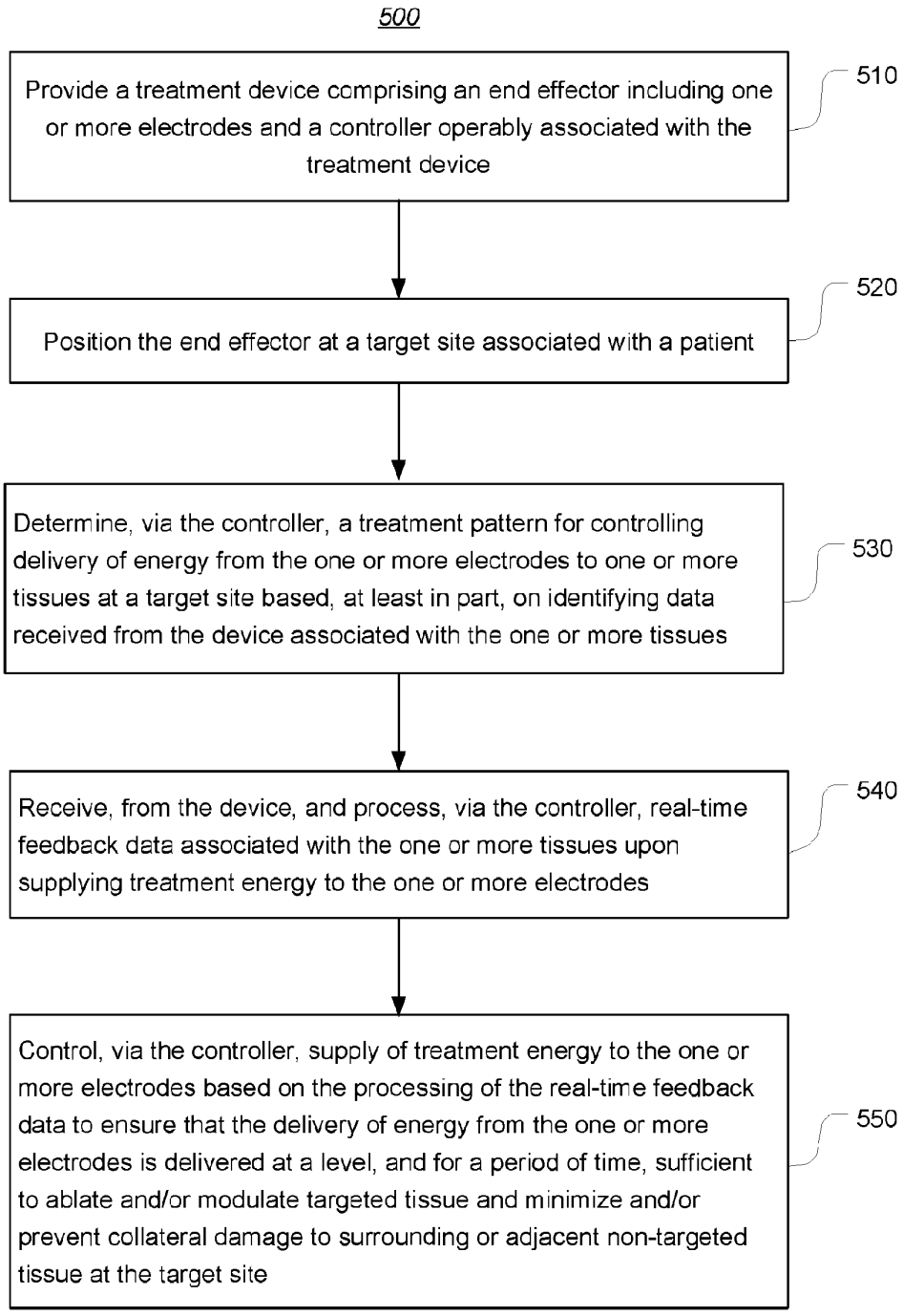

500
Provide a treatment device comprising an end effector including one or more electrodes and a controller operably associated with the treatment device
510
Position the end effector at a target site associated with a patient
520
Determine, via the controller, a treatment pattern for controlling delivery of energy from the one or more electrodes to one or more tissues at a target site based, at least in part, on identifying data received from the device associated with the one or more tissues
530
Receive, from the device, and process, via the controller, real-time feedback data associated with the one or more tissues upon supplying treatment energy to the one or more electrodes
540
Control, via the controller, supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site
550

FIG. 10

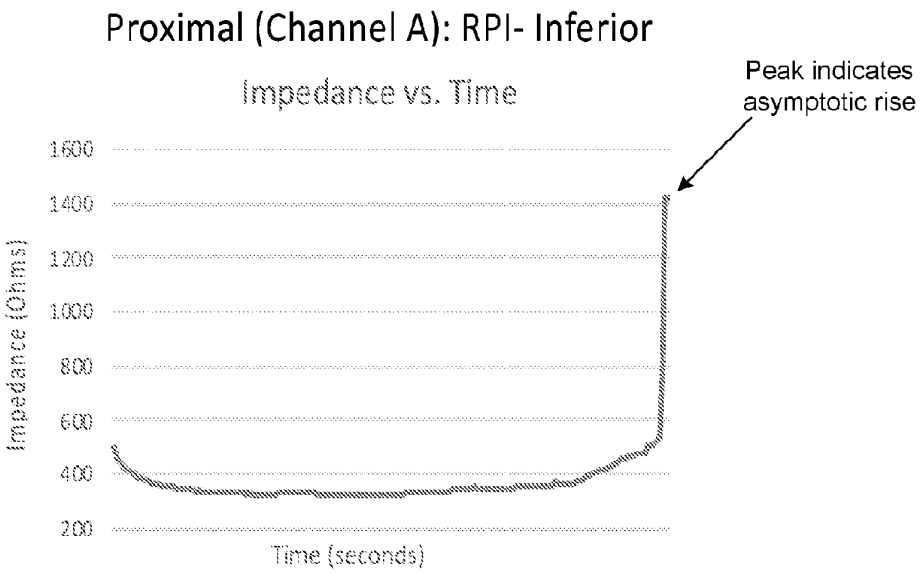


FIG. 11A

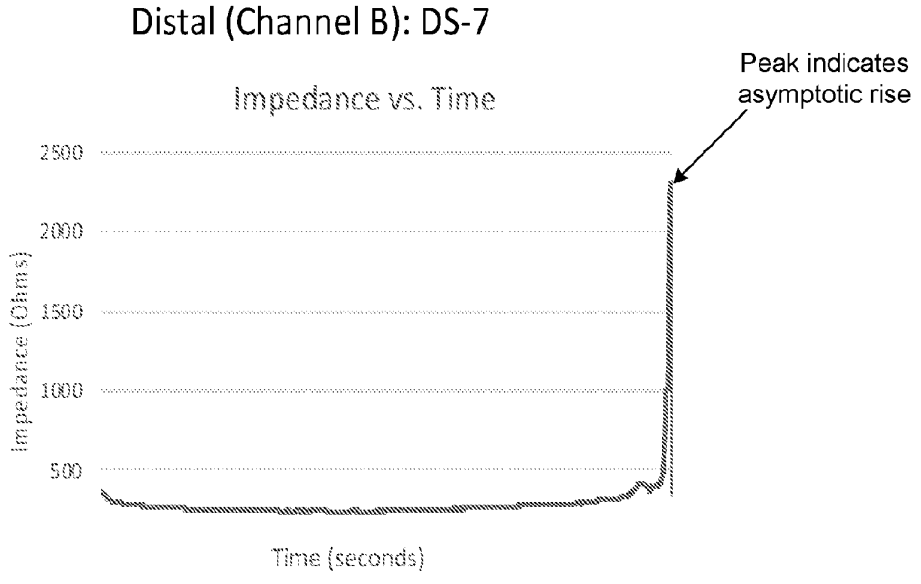


FIG. 11B

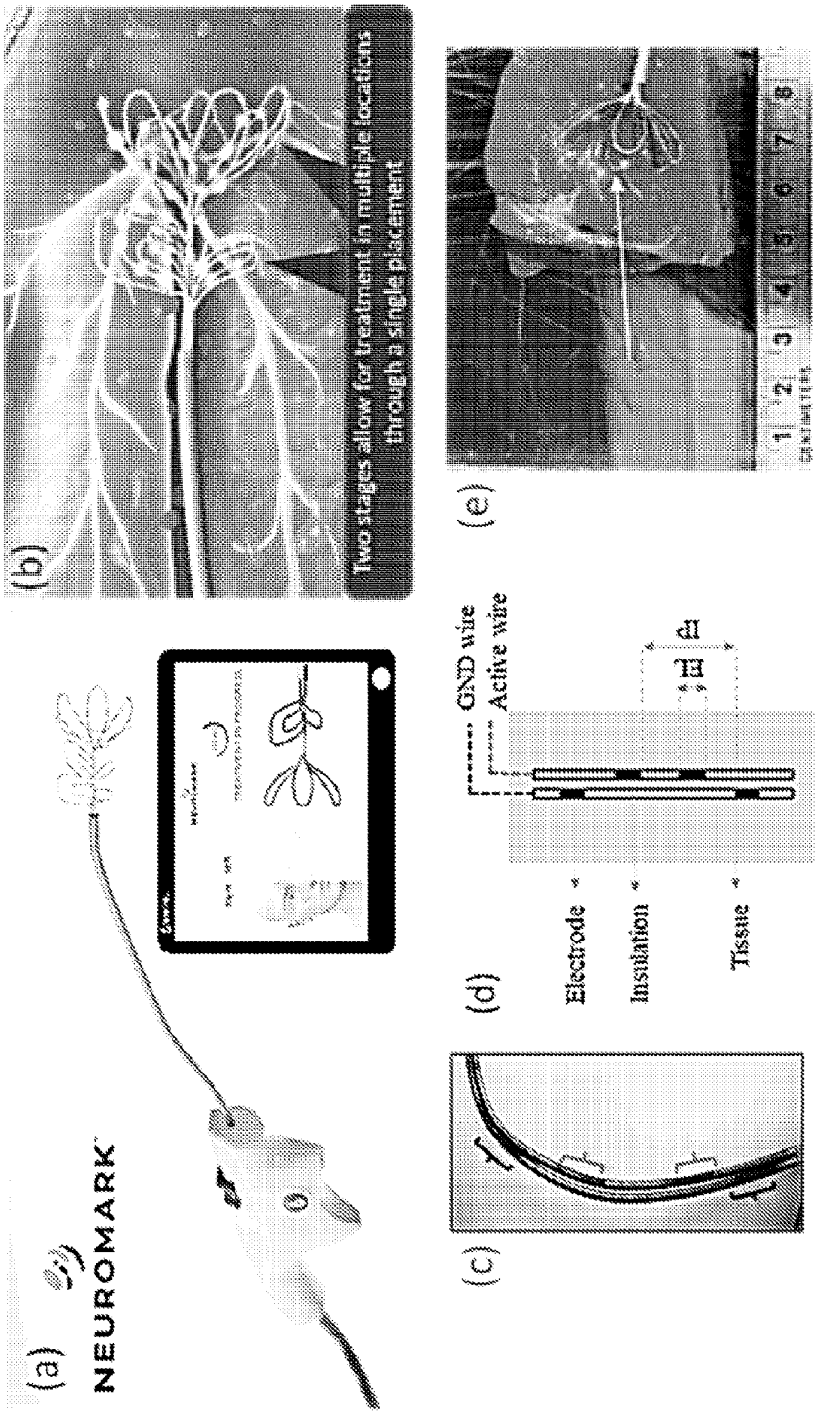

(a)
NEUROMARK
(b)
Two stages allow for treatment in multiple locations through a single placement
(c)
(d)
GND wire
Active wire
Electrode
Insulation
Tissue
d1
(e)

FIG. 12

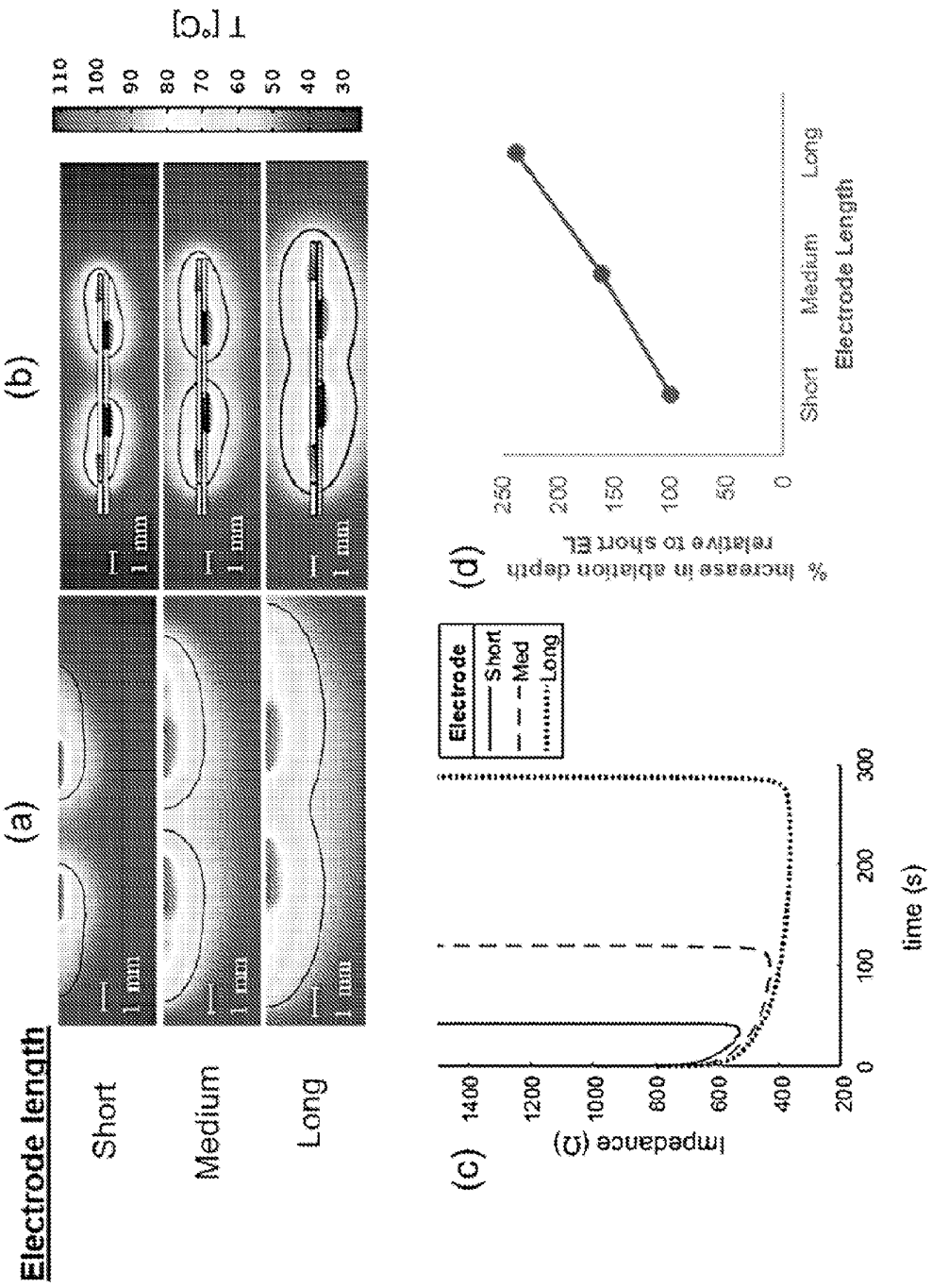

Electrode length
Short
Medium
Long
(a)
(b)
T [°C]
110
100
90
80
70
60
50
40
30
1 mm
(c)
Impedance (Ω)
1400
1200
1000
800
600
400
200
0
100
200
300
time (s)
Electrode
Short
Med
Long
(d)
% increase in ablation depth relative to short EL
250
200
150
100
50
0
Short
Medium
Long
Electrode Length

FIG. 13

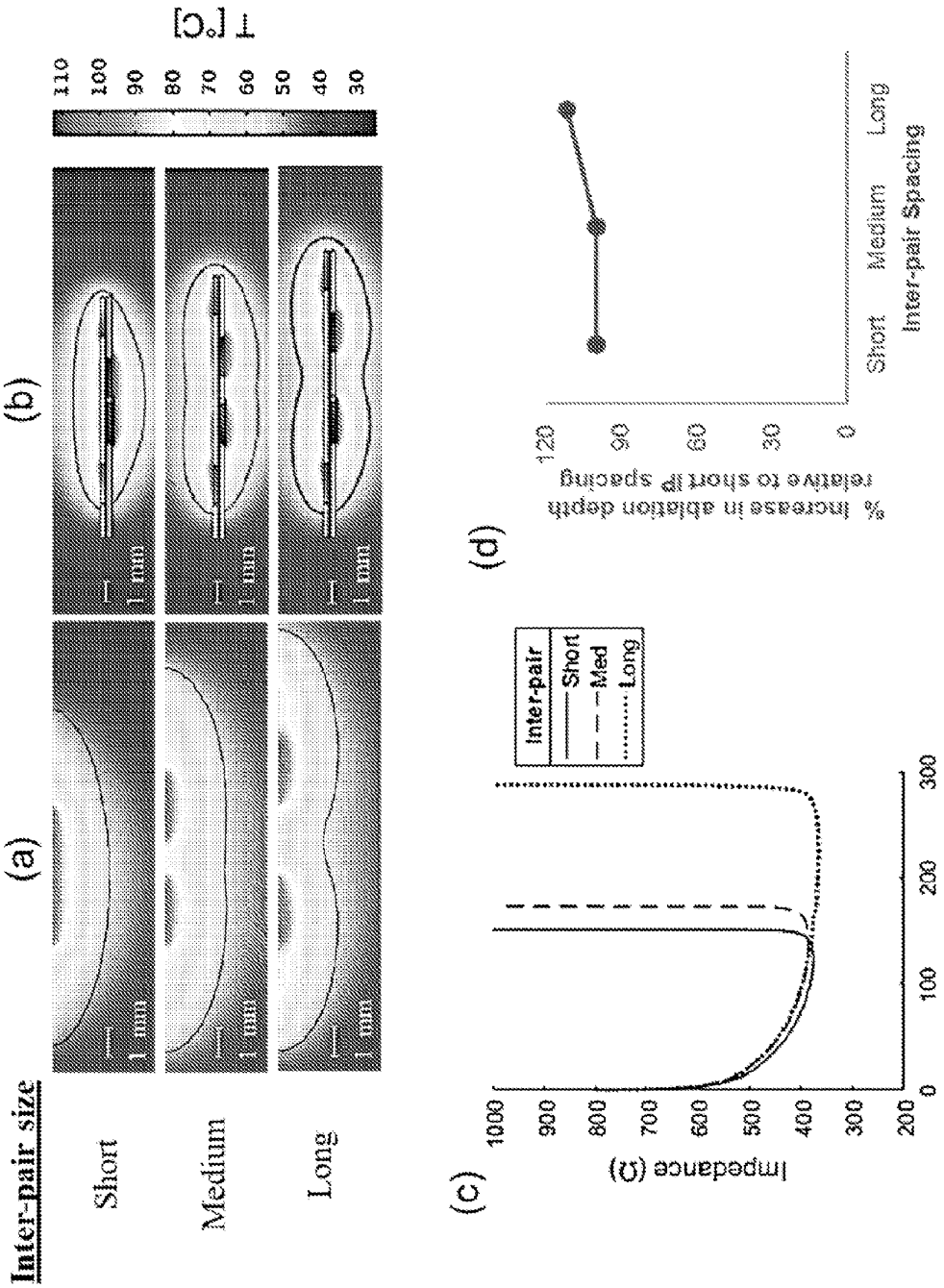

(a)
(b)
(c)
(d)
Inter-pair size
Short
Medium
Long
T [°C]
110
100
90
80
70
60
50
40
30
1 mm
Inter-pair
Short
Med
Long
Impedance (Ω)
time (s)
% increase in ablation depth relative to short IP spacing
Short
Medium
Long
Inter-pair Spacing

FIG. 14

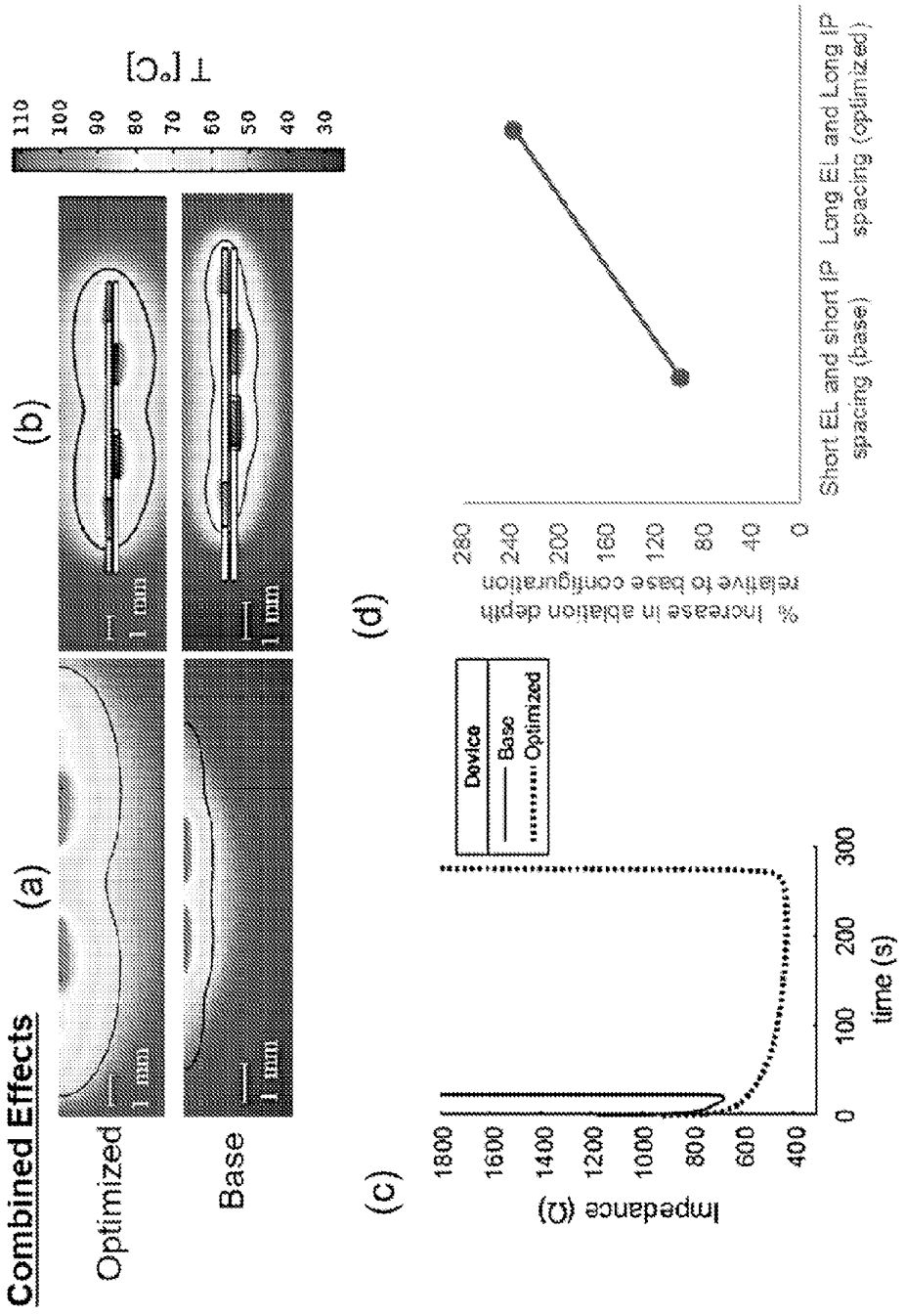

Combined Effects
(a)
(b)
(c)
(d)
Optimized
Base
T [°C]
110
100
90
80
70
60
50
40
30
Device
Base
Optimized
Impedance (Ω)
time (s)
% Increase in ablation depth relative to base configuration
Short EL and short IP spacing (base)
Long EL and Long IP spacing (optimized)

FIG. 15

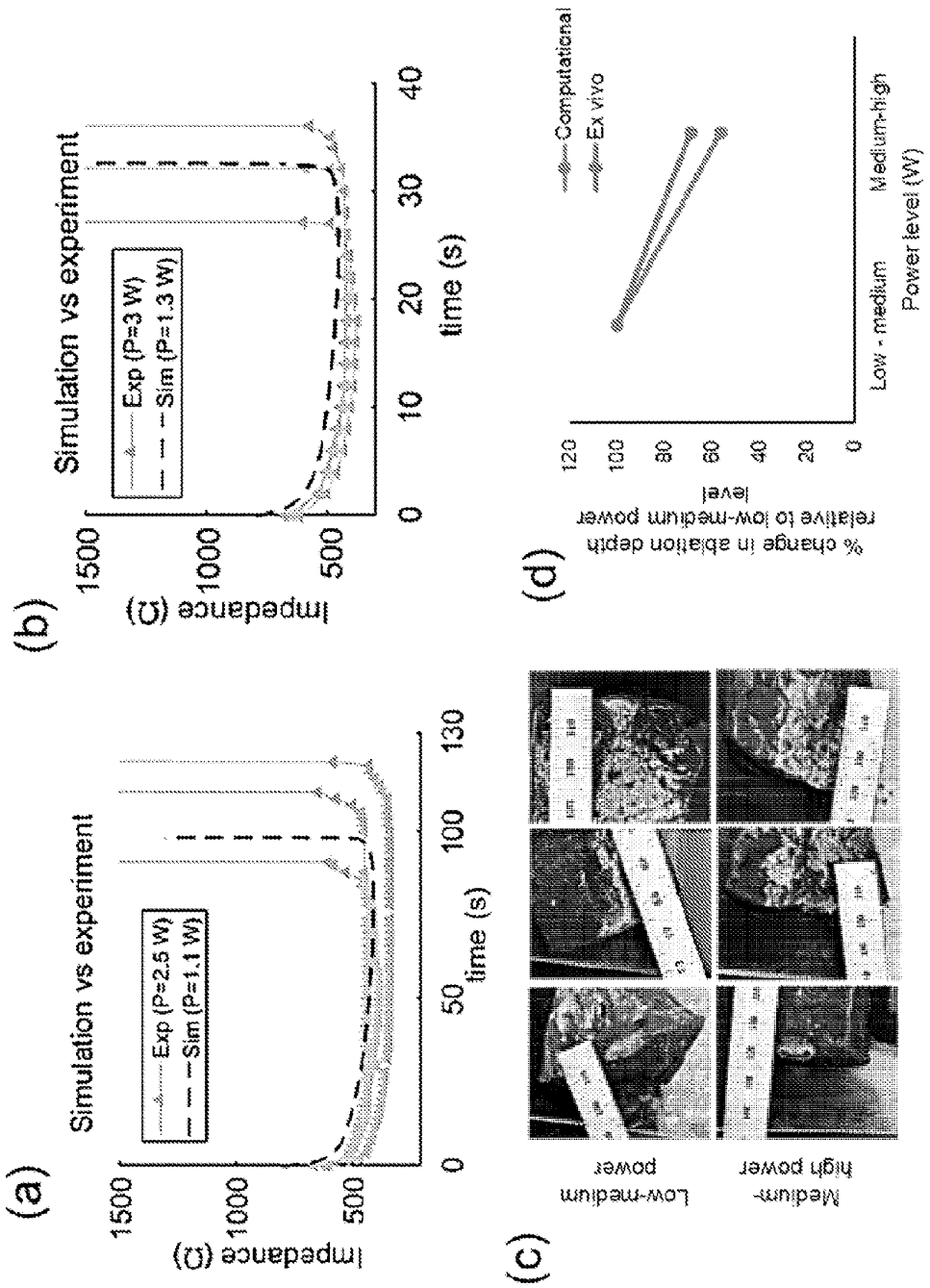

(a)
Simulation vs experiment
Exp (P=2.5 W)
Sim (P=1.1 W)
impedance (Ω)
1500
1000
500
0
50
100
130
time (s)
(b)
Simulation vs experiment
Exp (P=3 W)
Sim (P=1.3 W)
impedance (Ω)
1500
1000
500
0
10
20
30
40
time (s)
(c)
Low-medium power
Medium-high power
(d)
Computational
Ex vivo
% change in ablation depth relative to low-medium power level
120
100
80
60
40
20
0
Low - medium
Medium-high
Power level (W)

FIG. 16

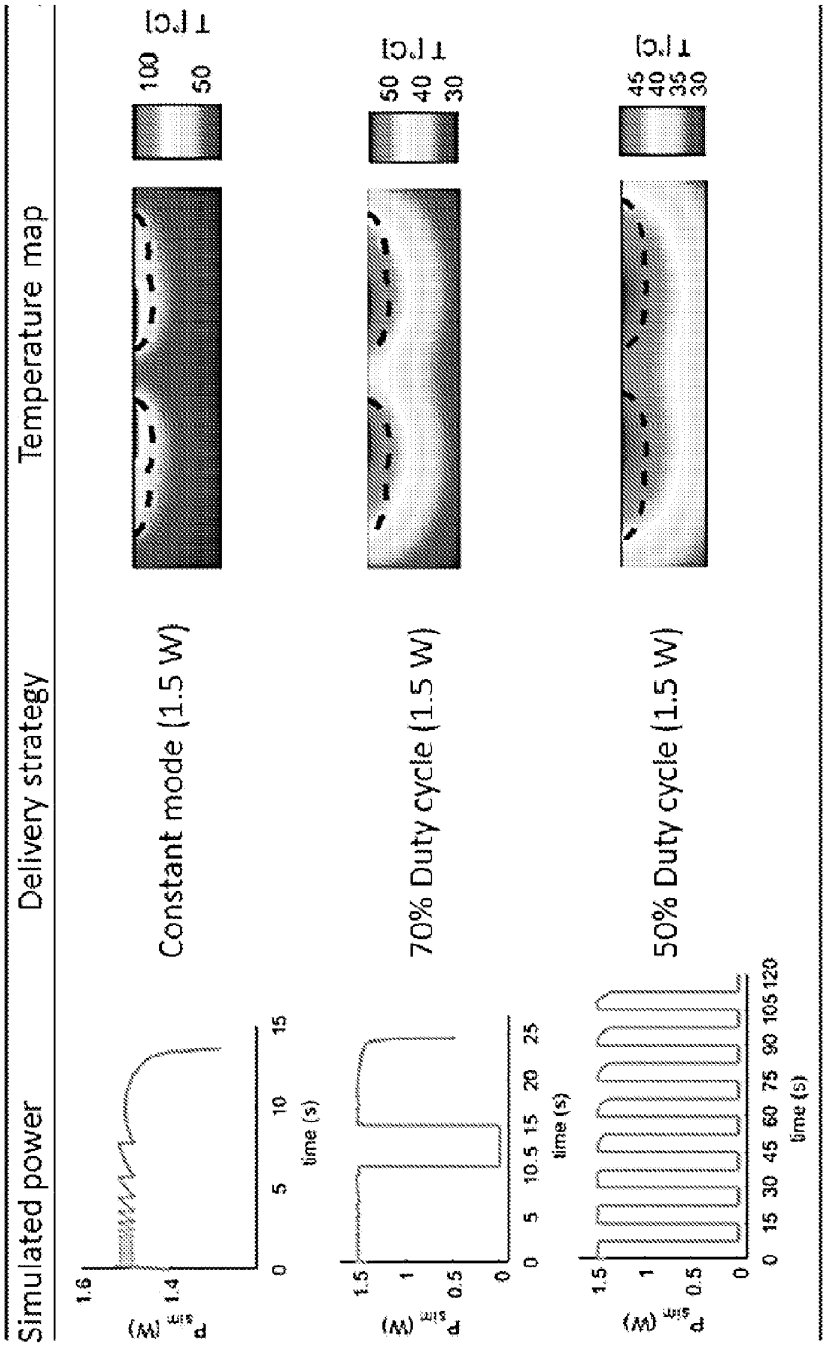

Simulated power
Delivery strategy
Temperature map
Constant mode (1.5 W)
70% Duty cycle (1.5 W)
50% Duty cycle (1.5 W)
T [°C]
100
50
50
40
30
45
40
35
30
P_{sim} (W)
1.6
1.4
1.5
1
0.5
0
time (s)
0 5 10 15
0 5 10.5 15 20 25
0 15 30 45 60 75 90 105 120

FIG. 17

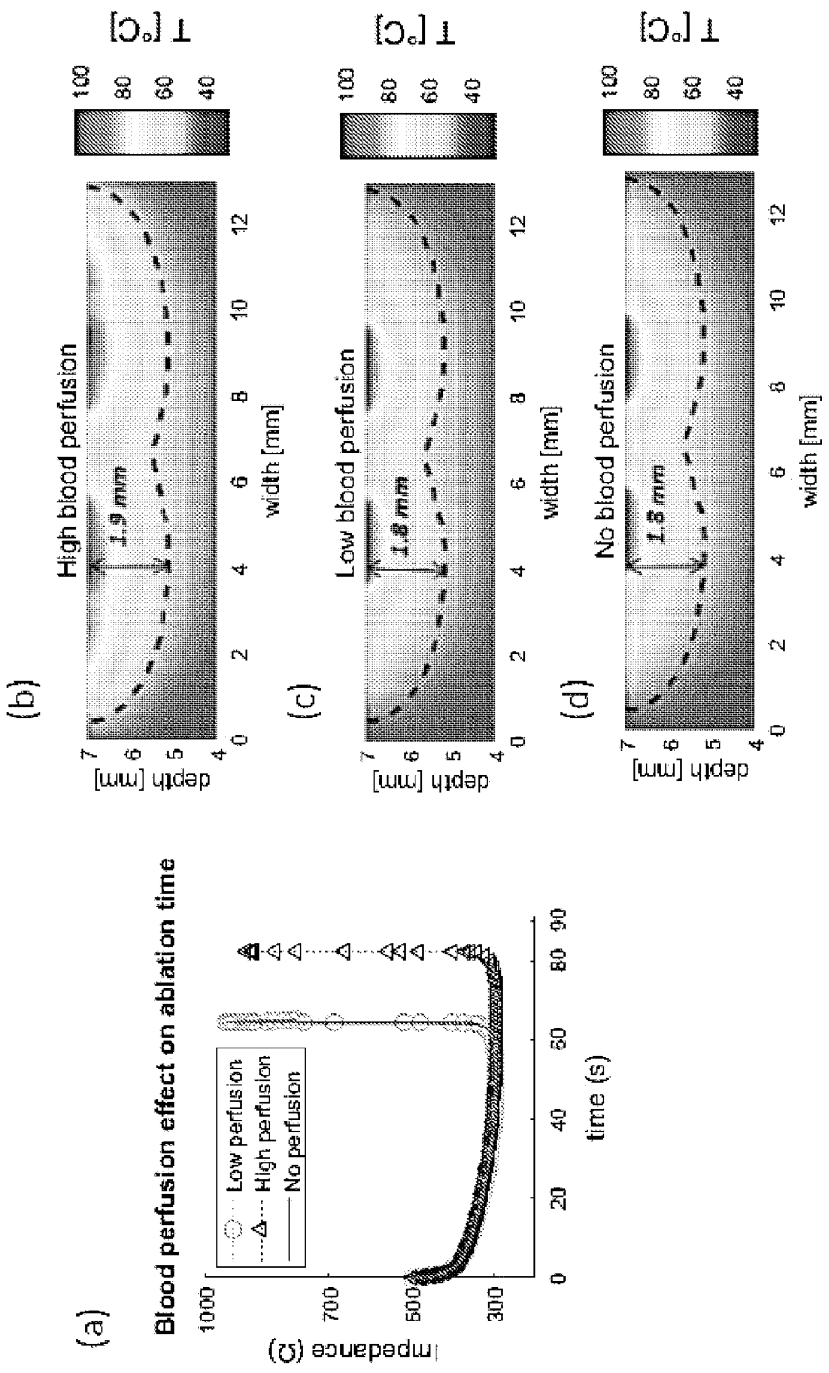

(a)
Blood perfusion effect on ablation time
Low perfusion
High perfusion
No perfusion
impedance (Ω)
time (s)
(b)
High blood perfusion
1.9 mm
depth [mm]
width [mm]
T [°C]
(c)
Low blood perfusion
1.8 mm
depth [mm]
width [mm]
T [°C]
(d)
No blood perfusion
1.8 mm
depth [mm]
width [mm]
T [°C]

FIG. 18

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000441

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/12 A61B18/14 A61B34/35 A61N1/00 G06N20/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61N G06N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17) cited in the application paragraphs [0002], [0006] paragraph [0031]; figure 3a paragraph [0053] - paragraph [0058] paragraph [0079] paragraph [0037] - paragraph [0038] paragraph [0072] paragraph [0065] ----- -/--	1-13, 17-20

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 November 2021	16/11/2021

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Ekstrand, Vilhelm

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000441

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 151 725 A1 (ETHICON ENDO SURGERY [US]) 7 November 2001 (2001-11-07) paragraph [0004] paragraph [0002] paragraph [0034] - paragraph [0037]; figures 1,10 paragraph [0066] - paragraph [0076]; figures 6-9 paragraph [0010]	1,9-20
X	US 2017/000541 A1 (YATES DAVID C [US] ET AL) 5 January 2017 (2017-01-05) paragraph [0283] - paragraph [0286]; figure 47 paragraph [0144]; figure 1 paragraph [0317] - paragraph [0318] paragraph [0240]; figure 30 paragraph [0342] paragraph [0287] - paragraph [0289]; figure 48 paragraph [0428] - paragraph [0429]; figure 89	1-13,15, 16,19,20
E	WO 2021/205231 A1 (NEURENT MEDICAL LTD [IE]) 14 October 2021 (2021-10-14) page 14, line 8 - page 15, line 30; figures 1,2 page 38, line 21 - page 45, line 5; figure 9a page 45, line 6; figure 9b page 51, line 17 - page 54, line 15; figure 9c page 55, line 4 - line 13	1-12,19, 20
A	US 2017/215952 A1 (NAIR ANUJA [US]) 3 August 2017 (2017-08-03) paragraph [0093]; figure 3	8

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000441

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 21-40
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 21-40

Claim 21 refer to a method of treatment and includes the step "supply of treatment energy to the one or more electrodes based on the processing of the real-time feedback data to ensure that the delivery of energy from the one or more electrodes is delivered at a level, and for a period of time, sufficient to ablate and/or modulate targeted tissue", which is performed on the human body (cl1: "positioning the end effector at a target site associated with a patient"). Thus, claims 21-40 refer to methods of treating the human body by surgery and therapy. According to Rule 39.1 (iv) PCT and to Art 43bis.1 PCT as well as Rule 67.1 PCT, neither a search nor an international preliminary examination is required to be carried out on these claims.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000441

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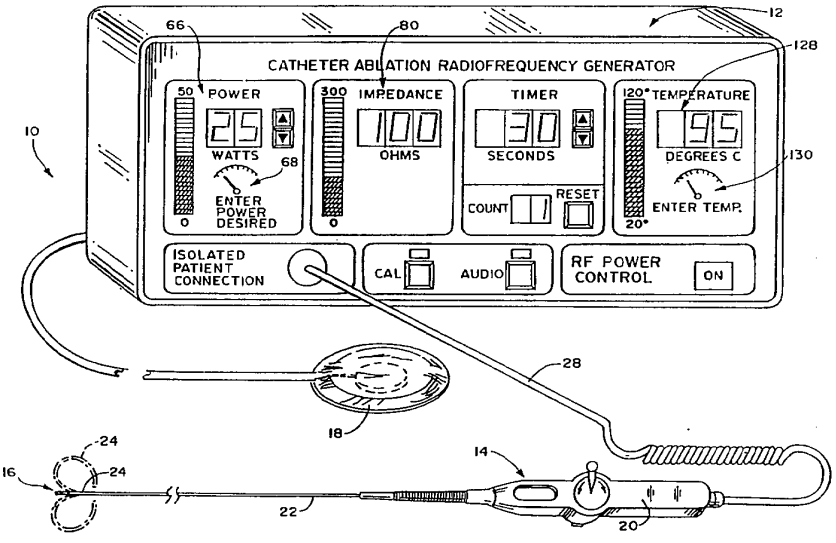
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(57) Abstract

A catheter (14) carries a functional component (16), like an ablating electrode, having a predetermined operating characteristic. The catheter (14) also electronically retains an identification code that uniquely identifies the predetermined characteristic. The catheter (14) is capable of transmitting the identification code to an external reader in response to a predetermined prompt. An associated apparatus, like an ablating energy source (12), reads the identification code and compares it to predetermined operating criteria. The apparatus (12) will not permit interaction with the functional catheter component (16) if the identification code indicates that the functional characteristics of the catheter (14) are not suited for the intended interaction. The catheter (14) can also store usage information to prevent reuse.

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SYSTEMS FOR IDENTIFYING CATHETERS AND MONITORING THEIR USE

Field of the Invention

The invention generally relates to catheters and associated power sources. In a more specific sense, the invention relates to ablation catheters and ablation methods that transmit energy to form lesions for therapeutic purposes.

Background of the Invention

Physicians make use of catheters today in medical procedures to gain access into interior regions of the body to ablate targeted tissue areas. It is important for the physician to control carefully and precisely the emission of energy within the body used to ablate the tissue.

The need for careful and precise control over the catheter is especially critical during procedures that ablate tissue within the heart. These procedures, called electrophysiological therapy, are becoming more widespread for treating cardiac rhythm disturbances.

During these procedures, a physician steers a catheter through a main vein or artery (which is typically the femoral vein or artery) into the interior region of the heart that is to be treated.

The physician then further manipulates a steering mechanism to place the electrode carried on the distal tip of the catheter into direct contact with the tissue that is to be ablated. The physician directs radio frequency energy from the electrode tip through tissue to an indifferent electrode to ablate the tissue and form a lesion.

Cardiac ablation especially requires the ability to precisely monitor and control the emission of energy from the ablation electrode.

Summary of the Invention

The invention provides systems and apparatus for identifying catheters and monitoring their use.

One aspect of the invention provides a catheter including a body carrying a functional component, like an ablating electrode, having a predetermined operating characteristic. The body also carries electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component. The electronic retaining means includes an output for transmitting the identification code to an external reader in response to a predetermined prompt.

Another aspect of the invention provides a catheter with a functional component, like an ablating electrode. In this aspect of the invention, the body also carries electronic means for retaining a code that represents the usage of the functional component. The electronic retaining means includes an output for generating the usage code in response to a predetermined prompt and an input for updating the usage code in response to use of the functional component.

Another aspect of the invention provides an apparatus for interacting with the functional component of the catheter. The apparatus includes a mechanism that prompts the electronic retaining means of the catheter to generate its identification code. The apparatus also stores predetermined criteria governing its interaction with the catheter. The apparatus compares the generated identification code to the predetermined interaction criteria. The apparatus generates a first control signal when the generated identification code meets the predetermined interaction criteria. The apparatus generates a second control signal, different than the first control signal, when the generated identification code does not meet the predetermined interaction criteria.

In one embodiment, the apparatus will not permit the intended interaction with the functional catheter component, if the identification code indicates that the catheter has been used too many times or if the functional characteristics of the catheter are not suited for the intended interaction.

In a preferred embodiment, the functional catheter component is an ablating electrode, and the apparatus is a source of ablating energy. In this embodiment, the apparatus sets the operating ablating power conditions depending upon the particular functional characteristics of the associated ablating electrode. In this way, the apparatus distinguishes among ablating electrodes of different functional characteristics and supplies ablating power accordingly.

The invention may be embodied in several forms without departing from its spirit or essential

characteristics. The scope of the invention is defined in the appended claims, rather than in the specific description preceding them. All embodiments that fall within the meaning and range of equivalency of the claims are therefore intended to be embraced by the claims.

Brief Description of the Drawings

Fig. 1 is a perspective view of a system for ablating tissue that embodies the features of the invention;

Fig. 2 is a schematic view of the generator and associated monitor and control circuits for the system;

Fig. 3 is a schematic view of the power monitor and control circuit for the system;

Fig. 4 is a schematic view of a catheter identification circuit that enables or prevents use of the catheter based upon functional and performance criteria; and

Fig. 5 is a schematic view of a catheter identification circuit that enables or prevents use of the catheter based upon prior use criteria.

Description of the Preferred Embodiments

Fig. 1 shows a system 10 for performing ablation on human tissue that embodies the features of the invention. The system 10 includes a radiofrequency generator 12 that delivers radiofrequency energy. The system 10 also includes a steerable catheter 14 carrying a radiofrequency emitting tip electrode 16.

In the illustrated embodiment, the system 10 operates in a monopolar mode. In this arrangement, the system 10 includes a skin patch electrode that serves as an indifferent second electrode 18. In use, the indifferent electrode 18

attaches to the patient's back or other exterior skin area.

Alternatively, the system 10 can be operated in a bipolar mode. In this mode, the catheter 14 carries both electrodes.

In the illustrated embodiment, the ablation electrode 16 and indifferent electrodes 18 are made of platinum.

The system 10 can be used in many different environments. This specification describes the system 10 when used to provide cardiac ablation therapy.

When used for this purpose, a physician steers the catheter 14 through a main vein or artery (typically the femoral vein or artery) into the interior region of the heart that is to be treated. The physician then further manipulates the catheter 14 to place the tip electrode 16 into contact with the tissue within the heart that is targeted for ablation. The user directs radio frequency energy from the generator 12 into the tip electrode 16 to form a lesion on the contacted tissue.

In the embodiment shown in Fig.1, the catheter 14 includes a handle 20, a guide tube 22, and a tip 24, which carries the tip electrode 16 (which also will be called the ablation electrode). The handle 20 encloses a steering mechanism 26 for the catheter tip 24. A cable 28 extending from the rear of the handle 20 has plugs (not shown). The plugs connect the catheter 14 to the generator 12 for conveying radiofrequency energy to the ablation electrode 16. The radiofrequency energy heats the tissue to form the lesion.

Left and right steering wires (not shown) extend through the guide tube 22 to interconnect the

steering mechanism 26 to the left and right sides of the tip 24. Rotating the steering mechanism 26 to the left pulls on the left steering wire, causing the tip 24 to bend to the left. Also, rotating the steering mechanism 26 to the right pulls on the right steering wire, causing the tip 24 to bend to the right. In this way, the physician steers the ablation electrode 16 into contact with the tissue to be ablated.

The generator 12 includes a radiofrequency power source 30 connected through a main isolation transformer 32 to first and second conducting lines 34 and 36.

In the illustrated environment, the power source 30 delivers up to 50 watts of power at a frequency of 500 kHz. The first conducting line 34 leads to the ablation electrode 16. The second conducting line 36 leads to the indifferent patch electrode 18.

As Figs. 2 and 3 show, the system 10 includes first monitoring means 38 for measuring the radiofrequency current and radiofrequency voltage delivered by the generator 12 to the patient. The first monitoring means 38 also derives control signals indicative of RMS (root mean squared) voltage (in volts), RMS current (in amps), and actual phase sensitive power (in watts) to support other control functions of the generator 12.

The first monitoring means 38 may be variously configured and constructed. In the illustrated embodiment, the first monitoring means 38 includes current monitoring means 40 for measuring the radiofrequency current passing from the first line 34 through the tissue to the second line 36 (i.e., from the ablation electrode 16 to the indif-

ferent patch electrode 18).

The first monitoring means 38 also includes voltage monitoring means 42. The voltage monitoring means 42 measures the radiofrequency voltage generated between the first and second conducting lines 34 and 36 (i.e., between the ablation electrode 16 and the indifferent patch electrode 18).

The first monitoring means 38 includes three control outputs 44, 46, and 48.

The first control output 44 carries a signal representative of RMS current conducted by the ablation electrode 16.

The second control output 46 carries a signal representative of the RMS voltage between the ablation electrode 16 and the indifferent patch electrode 18.

The third control output 48 carries a signal representative of actual phase sensitive power transmitted by the ablation electrode 16.

In the illustrated embodiment (as Figs. 2 and 3 show), the current monitoring means 40 includes an isolated current sensing transformer 50 connected in the second conducting line 36. In this arrangement, the current sensing transformer 50 directly measures the radiofrequency current passing through the ablation electrode 16 to the indifferent patch electrode 18.

The measured value is a radiofrequency signal varying at the selected rate, which in the illustrated embodiment is 500 kHz.

The current sensing transformer 50 is connected to the first control output 44, which derives RMS current. The first control output 44 includes an integrated circuit RMS converter 52 to do this

function. The RMS current converter first squares the radiofrequency current input signal from the current sensing transformer 50, and then averages the squared signal over a user prescribed period (which in the illustrated embodiment is about once every 0.01 second). The RMS current converter 52 then takes the square root of the average squared value. The resulting output represents RMS current.

The RMS current signal takes the form of a relatively slowly varying signal, compared with the rapidly varying radiofrequency current input signal.

As Figs. 2 and 3 show, the voltage monitoring means 42 includes an isolated voltage sensing transformer 54 that is connected between the first and second conducting lines. In this arrangement, the voltage sensing transformer 54 directly measures the radiofrequency voltage across the body tissue between the ablation electrode 16 and the indifferent patch electrode 18.

Like the value measured by the current sensing transformer 50, the measured voltage value is a radiofrequency signal varying at the selected 500 kHz rate.

The voltage sensing transformer 54 is connected to the second control output 46, which derives RMS voltage. The second control output 46 includes an integrated circuit RMS converter 56 to do this function. The RMS voltage converter 56 squares the radiofrequency voltage input signal and then averages it over the same user prescribed period used by the current converter 52. The RMS voltage converter 56 then takes the square root of the average squared voltage value.

The resulting RMS voltage signal (like the RMS current signal) takes the form of a relatively

slowly varying signal.

The voltage sensing transformer 54 is also connected to the third control output 48, which derives actual phase sensitive power. The third control output 48 includes an analog multiplier integrated circuit 58 to do this function. The multiplier circuit 58 receives as one input the radiofrequency input current signal directly from the current sensing transformer 50. The multiplier circuit 58 also receives as a second input the radiofrequency input voltage signal directly from the voltage sensing transformer 54.

The output of the multiplier circuit 58 is the product of these two inputs, which represents the actual radiofrequency power transmitted by the ablation electrode 16.

The power value is (like its component current and voltage inputs) a radiofrequency signal varying at a relatively high radiofrequency rate.

The third control output 48 also includes a low pass filter 60. In the illustrated embodiment, which operates with a radiofrequency rate of 500 kHz, the cut off frequency of the filter 60 selected is about 100 Hz. The rapidly varying measured input power value is low pass filtered by the filter 60 into a relatively slowly varying signal.

This signal represents the actual phase sensitive power signal of the radiofrequency energy that the ablation electrode 16 delivers to the targeted tissue.

The first, second, and third control outputs 44, 46, and 48 each includes appropriate inline scaling circuits 62. The scaling circuits 62 scale the RMS current signal, the RMS voltage signal, and

the actual phase sensitive power signal to a specified voltage range that can be usable by the remainder of generator 12 circuitry. In the illustrated embodiment, the scaled range is 0.0 to 5.0 volts.

The first monitoring means 38 also includes an analog to digital converter 64. The converter 64 digitizes a selected one or more of the analog RMS current output signal, RMS voltage output signal, and the actual phase sensitive power signal.

The digital output(s) of the converter 64 can be used to display measurement results. In the illustrated embodiment, the system 10 includes a first digital display 66 on the generator 12 to show the user the actual phase sensitive power signal.

The digital output(s) of the converter 64 also can be used to control operation of the generator 12. In the illustrated embodiment, the system 10 uses the digitized outputs in a feedback loop that maintains radiofrequency output voltage within a desired range or at a constant value to control radiofrequency power at the ablation electrode 16. By controlling the power delivered by the generator 12, the physician can reproducibly form lesions of the desired depth during an ablation procedure.

In this arrangement, the system 10 includes an input 68 for the user to enter an operating value desired for the actual phase sensitive power for the generator 12. The system 10 includes power control means 70 that includes comparator 71 to compare desired power with actual phase sensitive power. The output of the comparator varies the output voltage of radiofrequency power source 30 to maintain minimum error between the measured actual power and

the set point power.

In the illustrated embodiment, the power control means 70 also monitors phase differences between radiofrequency voltage and current. The power control means 70 does this function by computing apparent power and by comparing the computed apparent power to the actual phase sensitive power. If the radiofrequency voltage and current signals are exactly in phase, the apparent power and actual phase sensitive power will be the same. However, if there is a phase difference, actual phase sensitive power will differ from the apparent power by a factor that represents the cosine of the phase angle.

In the illustrated embodiment, the power control means 70 includes a multiplier circuit 72 that obtains the product of the RMS current and RMS voltage. The resulting output of the multiplier circuit 72 forms the apparent (i.e., not phase sensitive) power of the system 10. The power control means 70 includes a comparator 74 to compare the derived apparent power with the actual phase sensitive power. The magnitude of the output of the comparator 74 quantifies the amount of the phase shift.

If the output of the phase shift comparator 74 exceeds a preselected amount, the power control means 70 generates a warning signal to show that a phase shift between the radiofrequency voltage and current has occurred. The system 10 may include a flashing light and audible alarm (not shown) to warn the user.

The power control means 70 operates to maintain a constant set power when the output of the phase shift comparator 74 remains within an allowable range above the threshold amount. The power

control means 70 operates to reduce the output voltage of the source 30 when the output of the phase shift comparator 74 increases beyond this range. If the output of the phase shift comparator 74 shows a phase shift beyond a maximum threshold value, the power control means 70 generates a signal to shut off all power to the ablation electrode 16.

According to the invention, the system 10 also includes means 76 for identifying and monitoring the physical and/or functional characteristics of the catheter 14 that is connected to the radiofrequency generator 12.

The resulting control functions of the catheter identification means 76 can vary.

In one preferred arrangement (shown in Fig. 4), the identification means 76 assures that the catheter 14 and its intended use meet predetermined functional and therapeutic criteria.

In this embodiment, the identification means 76 senses the actual functional characteristics of the catheter 14 connected to the generator 12. The identification means compares these actual characteristics to the characteristics required for the intended use, based upon predetermined criteria. Based upon this comparison, the identification means 76 generates a variety of output control signals.

The control signals either actively control or passively monitor the operational characteristics of catheter 14 used in association with the power generator 12. The system 10 thereby guards against the use of a catheter 14 that does not meet the performance characteristics required.

More particularly, when the sensed physical and/or functional characteristics of the catheter 14 meet the predetermined use criteria, the output

control signal generated by the identification means 76 actively permits the intended use of the catheter 14. Alternatively, the output control signal generates a passive, user discernible "Use Permitted" message under this condition. Still alternatively, the output control signal can simultaneously permit use while generating a confirming, user discernible message.

Likewise, when the sensed physical and/or functional characteristics of the catheter 14 do not meet the predetermined use criteria, the output control signal generated by the identification means 76 actively intervenes to prevent the intended use of the catheter 14. Alternatively, the output control signal generates a passive, user discernible "Use Not Permitted" alarm under this condition. Still alternatively, the output control signal can simultaneously prevent use while generating a confirming, user discernible alarm.

In another preferred arrangement (shown in Fig. 5), the identification means 76 generates signals that track the use of the catheter 12. This aspect of the invention guards against the reuse or overuse of a given catheter 14.

The particular details of these arrangements will now be discussed.

Controlling/Monitoring the Catheter-Generator Interface

In Fig. 4, the identification means 76 senses the actual physical and/or functional characteristics of the attached catheter 14 and compares these to predetermined criteria.

As shown in Fig. 4, the identification means 76 includes means 88 carried within the

catheter handle 20 for automatically generating a uniquely coded identification signal 90 when the catheter 14 is attached to the system 10. The signal 90 is coded to uniquely identify the particular performance and/or physical characteristics of the catheter 14 and attached electrode 16.

The selected catheter characteristics identified by the code can vary. They may include electrode surface area, electrode configuration, electrode orientation, and electrode field dispersion properties. They also indicate the presence of a temperature sensor or thermistor and its associated resistance calibration value. They may simply identify catheter product numbers or other commercial designations.

The catheter identification means 88 carried within the handle can vary.

In one embodiment, the catheter identification means 88 can comprise a resistor having a prescribed ohm value, which varies according to the physical and/or performance characteristics of the catheter 14. The sensed ohm value then becomes the identification code for the catheter.

In an alternative and preferred embodiment, instead of the resistor, the catheter identification means 88 can comprise a solid state micro-chip, ROM, EEROM, EPROM, or non-volatile RAM carried within the handle 20. The micro-chip can be pre-programmed with a digital value representing the catheter identification code and other information. In this way, the catheter itself can be programmed to store information about its operational and functional characteristics.

The identification means 76 includes a register means 92 that latches the sensed catheter

identification code when the catheter 14 is attached to the generator 12.

The identification means 76 also includes a catheter criteria look-up table 86 in system ROM. The table 86 specifies the catheter types that are approved for use in association with the system 10, as well as those catheter types that are not approved for use. The selection criteria takes into account the performance and/or physical characteristics necessary for safe and efficacious therapeutic use, based upon empirical testing, governmental regulatory approval, and similar relevant considerations.

The approved catheter types in the look-up table 86 are coded to correspond with the identification codes the catheter 14 carries.

Preferably, the codes in the look up table 86 further classify the physical and/or performance characteristics of different catheters 14 at different set power conditions, as determined by empirical testing.

In this arrangement, the table 86 permits the identification means 76 to distinguish between acceptable and unacceptable catheter types on an interactive basis, taking into account the particular power condition set for the generator 12.

When the identification means 76 takes into account the selected power output of the generator 12, one catheter code may be acceptable for use at low selected power outputs, whereas the same catheter code may not be acceptable at selected higher power outputs.

The identification means 76 also includes a comparator 96. The comparator 96 looks to the input 68 to determine the set power condition and

compares the sensed catheter type (latched in the register means 92) with the catheter types listed in the catheter criteria table 86.

When the sensed physical and/or functional characteristics of the catheter 14 and the predetermined criteria at the set power condition match, the comparator 96 generates a first control signal 78. When the sensed physical and/or functional characteristics of the catheter 14 and the predetermined criteria at the set power condition do not match, the comparator 96 generates a second control signal 80.

The first control signal 78 enables the physician to operate the system 10 with the catheter 14 selected and at the set power condition. In addition, the first control signal 78 preferably generates a confirming, user discernible "Use Permitted" message 79.

The second control signal 80 disables or at least discourages operation of the system 10 at the set power condition. The particular operative effect of second control signal 80 can vary.

In a preferred embodiment, the second control signal 80 activates an interlock 82 that disables the power generator 12. The interlock 82 prevents operation of the system 10, thereby preventing the intended use of the catheter 14.

Alternatively, the second control signal 80 generates a user discernible "Use Not Permitted" alarm message 84 under this condition. Most preferably, the second control signal 80 simultaneously activates the interlock 82 while generating a confirming, user discernible alarm 84.

The identification means 76 also preferably serves as an information source for the physician.

In this mode, the identification means 76 includes a look-up table 87 that correlates the catheter identification codes with a user readable message that contains useful physical and performance information about the selected catheter 14. The message can list the manufacturer of the catheter, the surface area and other relevant characteristics of the ablating electrode, including the presence or absence of temperature sensing elements. The message can also list the set power conditions approved or recommended for the catheter.

In this embodiment, the identification means 76 includes a second comparator 97. The comparator reads the code latched in the register means 92 looks to the table 87 to obtain the corresponding message. The comparator 97 outputs the message to a display device 99 for the physician to read.

Monitoring Catheter Use

As Fig. 5 shows, the identification means 76 can also serve to monitor the use of the catheter 14.

In this preferred embodiment, the identification means 76 includes a use register 98 carried within the catheter handle 20. The use register 98 latches a digital value representing the number of times the catheter 14 has been used.

Preferably, the use register 98 comprises a solid state micro-chip having non-volatile RAM carried within the catheter handle 20.

The use register 98 is initially programmed by the manufacturer with a digital value of zero. The use register 98 includes an output 100 for generating this digital value. The use register 98 also includes an input 102 for incrementing the

digital value after each use.

The identification means 76 includes means 104 for incrementing by one the digital value carried by the use register 98 after each permitted use of the catheter 14.

The identification means 76 also includes means 106 for determining the digital value resident within the use register 98 before allowing use of the catheter 14 with the generator 12.

In this arrangement, the identification means 76 includes a comparator 108 that compares the resident digital value with a set value in a use criteria table 110, which represents the maximum number of uses allowed.

If the resident value is less than the set value, the comparator generates a signal 114 that permits continued use of the catheter 14 with the power generator 12.

If the resident value equals or exceeds the set value, the comparator 108 generates a signal 116 to activate the previously described power interlock 82. The interlock 82 prevents use of the catheter 14 with the generator 12.

Alternatively, the comparator 108 simply activates a display 112 to warn the physician, counseling against reuse of the chosen catheter 14. Of course, the identification means can both activate the interlock 82 and the display 112.

Various features of the invention are set forth in the following claims.

Claims

We Claim:

1. A catheter including a body carrying a functional component having a predetermined operating characteristic, the body also carrying electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component, the electronic retaining means including output means for transmitting the identification code to an external reader in response to a predetermined prompt.

2. A catheter according to claim 1 wherein the functional component includes an energy emitting electrode.

3. A catheter according to claim 1 wherein the body comprises a handle having an interior area, and wherein the electronic retaining means is carried within the interior area of the handle.

4. A catheter according to claim 3 wherein the functional component includes a guide body that carries an energy emitting electrode.

5. A catheter according to claim 1 wherein the electronic retaining means comprises a component having a predetermined resistance value that comprises the identification code.

6. A catheter according to claim 1 wherein the electronic retaining means includes a microchip holding the identification code as a digital value.

7. A catheter according to claim 1 wherein the electronic retaining means comprises non-volatile RAM.

8. A catheter according to claim 6 wherein the electronic retaining means comprises ROM.

9. A catheter according to claim 6 wherein the electronic retaining means comprises EPROM.

10. A system comprising

a catheter carrying a functional component having a predetermined operating characteristic, the catheter also carrying means for electronically retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component, the electronic retaining means including output means for generating the identification code in response to a predetermined prompt, and

apparatus means for interacting with the functional component of the catheter including

means for coupling the catheter to the device for interaction,

means operative, when coupled to the catheter, for prompting the electronic retaining means to generate the identification code,

means for registering the generated identification code,

means for storing predetermined criteria governing the interaction between the catheter and the apparatus means, and

means connected to the register means and the storage means for comparing the generated identification code to the predetermined interaction criteria and for generating a first control signal when the generated identification code meets the predetermined interaction criteria and for generating a second control signal, different than

the first control signal, when the generated identification code does not meet the predetermined interaction criteria.

11. A system according to claim 10 wherein the apparatus means includes control means for operating in a first interaction mode with the attached catheter in response to the first control signal and for operating in a second interaction mode with the attached catheter, different than the first interaction mode, in response to the second control signal.

12. A system according to claim 10 wherein the apparatus means includes interlock means for permitting interaction with the attached catheter in response to the first control signal and for preventing interaction with the attached catheter in response to the second control signal.

13. A system according to claim 10 wherein the apparatus means includes means for generating a first user discernible signal in response to the first control signal and for generating a second user discernible signal, different than the first user discernible signal, in response to the second control signal.

14. A catheter including a body carrying a functional component having a predetermined operating characteristic, the body also carrying electronic means for retaining a code that represents the usage of the functional component, the electronic retaining means including output means for generating the usage code response to a predetermined prompt and input means for updating the usage code in response to use of the functional component.

15. A catheter according to claim 14 wherein the functional component includes an energy emitting electrode.

16. A catheter according to claim 14 wherein the body comprises a handle having an interior area, and wherein the electronic retaining means is carried within the interior area of the handle.

17. A catheter according to claim 16 wherein the functional component includes a guide body that carries an energy emitting electrode.

18. A system comprising

a catheter carrying a functional component having a predetermined operating characteristic, the catheter also carrying means for electronically retaining a code representing the number of times the functional component has been used, the electronic retaining means including output means for generating the usage code in response to a predetermined prompt and input means for updating the usage code, and

apparatus means for interacting with the functional component of the catheter including

means for coupling the catheter to the device for interaction,

means operative, when coupled to the catheter, for prompting the electronic retaining means to generate the usage code,

means for registering the generated usage code,

means for storing a predetermined value representing the maximum number of times the functional component can be used, and

means connected to the register means

and the storage means for comparing the generated usage code to the predetermined usage value and for generating a first control signal when the generated usage code is less than the predetermined usage value and for generating a second control signal, different than the first control signal, when the generated usage code is equal to or exceeds the predetermined usage value.

19. A system according to claim 18 wherein the apparatus means includes control means for permitting operation in interaction with the attached catheter in response to the first control signal and for preventing the operation in interaction mode with the attached catheter in response to the second control signal.

20. A system according to claim 18 wherein the apparatus means includes means for generating a first user discernible signal in response to the first control signal and for generating a second user discernible signal, different than the first user discernible signal, in response to the second control signal.

21. A system according to claim 18 wherein the apparatus means include means for generating a signal to the input means of the electronic retaining means for updating the usage code after operation in interaction with the attached catheter.

22. A system comprising

a first catheter carrying a functional component having a first predetermined operating characteristic, the first catheter also carrying means for electronically retaining a first identification code that uniquely identifies the first predetermined operating characteristic of the

functional component, the storage means including output means for generating the first identification code in response to a predetermined prompt,

a second catheter carrying a functional component having a second predetermined operating characteristic different than the first predetermined operating characteristic, the second catheter also carrying means for electronically retaining a second identification code, different than the first identification code, that uniquely identifies the second predetermined operating characteristic of the functional component, the storage means including output means for generating the second identification code in response to a predetermined prompt, and

apparatus means for interacting with the functional component of either the first catheter or the second catheter including

means for coupling either the first or second catheter for interaction,

means for providing the predetermined prompt to generate the first or second identification code from the electronic retaining means of the attached catheter,

means for generating a first control signal when the first identification code is received and for generating a second control signal, different than the first control signal, when the second identification signal is received.

23. A tissue ablation catheter including a body carrying an ablating electrode having a predetermined operating characteristic, the body also carrying electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the

ablating electrode, the electronic retaining means including output means for transmitting the identification code to an external reader in response to a predetermined prompt.

24. A tissue ablation catheter including a body carrying an ablating electrode having a predetermined operating characteristic, the body also carrying electronic means for retaining a code that identifies the number of times the ablating electrode has been used, the electronic retaining means including output means for transmitting the usage code to an external reader in response to a predetermined prompt and input means for updating the usage code in response to use.

25. Apparatus for supplying energy to a tissue ablation electrode comprising

generating means for producing ablating energy for the electrode in a first power mode and in a second power mode different than the first power mode,

means for connecting an electrode to the generating means,

means for registering a first control condition when an ablating electrode having a first characteristic is connected to the generating means and for registering a second control condition when an ablating electrode having a second characteristic, different than the first characteristic, is connected to the generator means, and

control means responsive to the register means for operating the generating means in the first power mode when the first control condition is registered and for operating the generating means in the second power mode when the second control condition is registered.

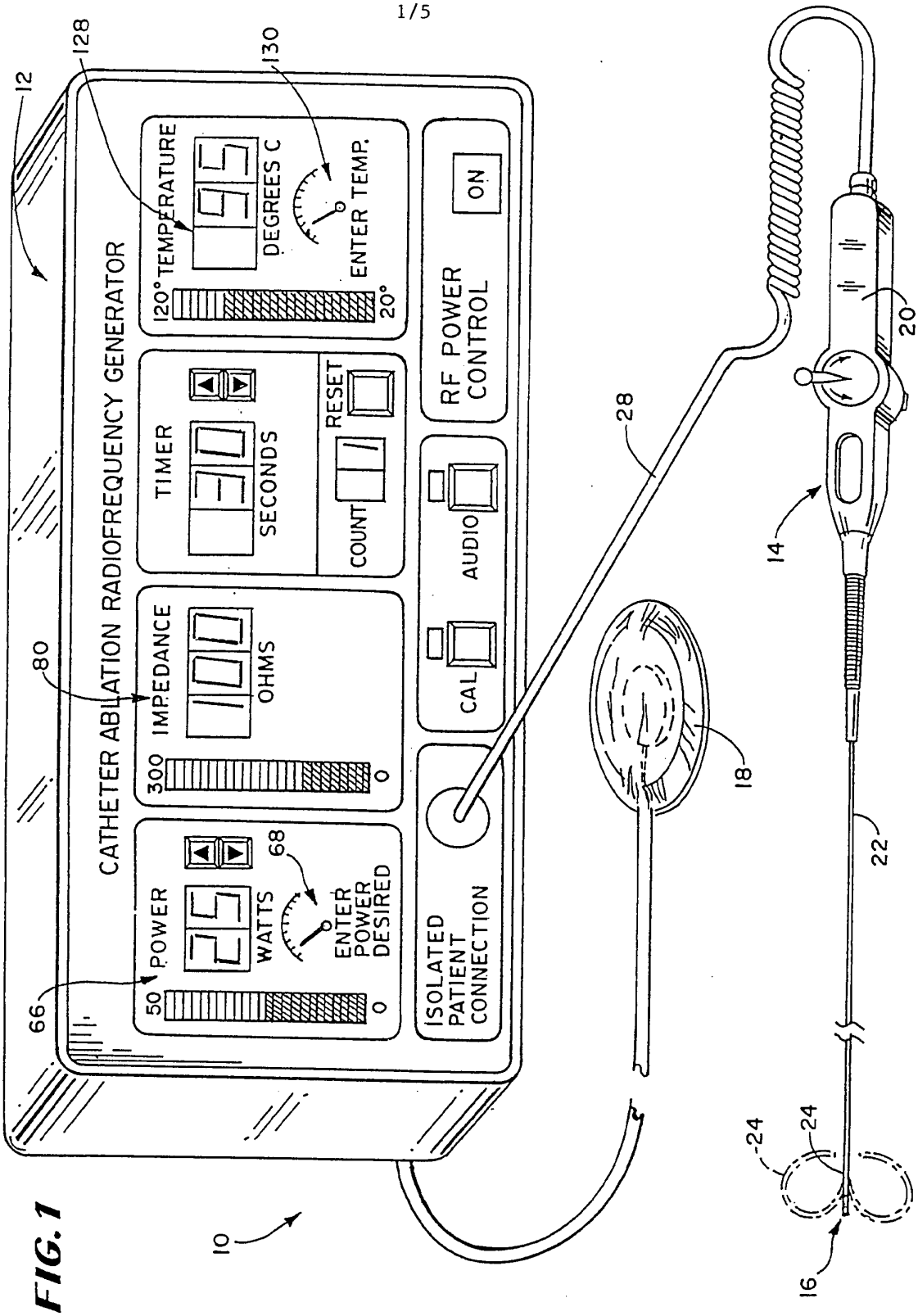


FIG. 1

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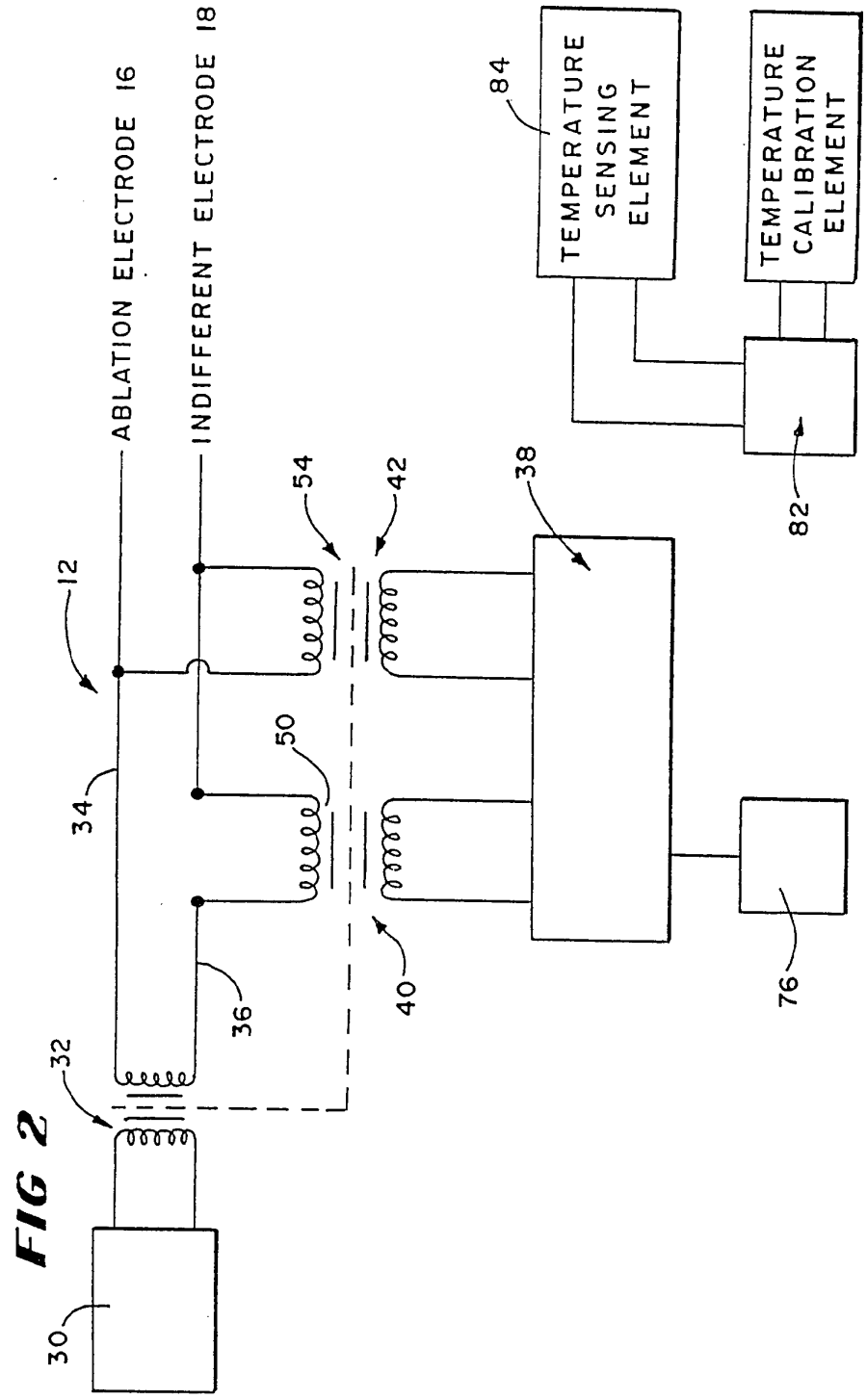


FIG 2

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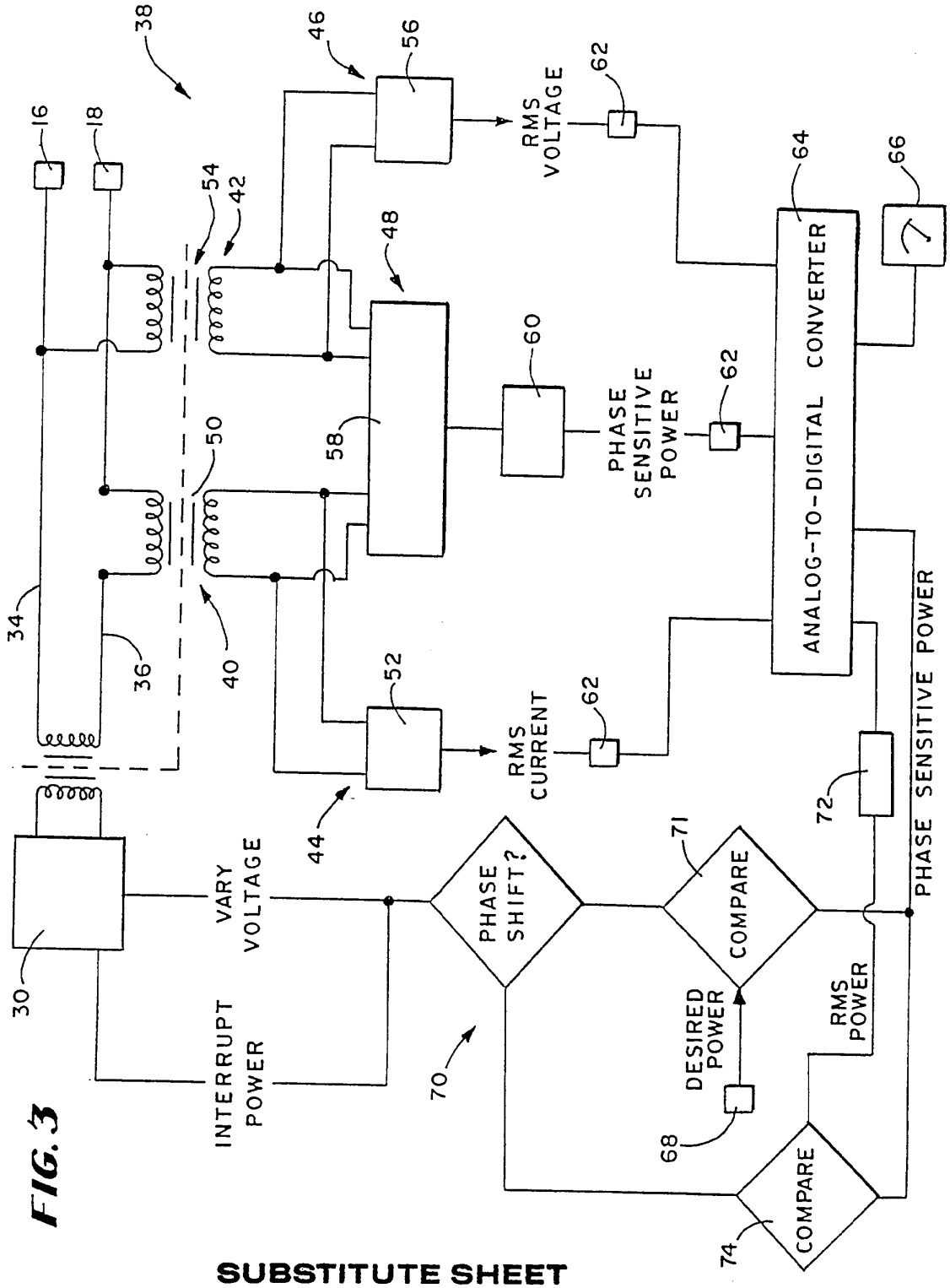
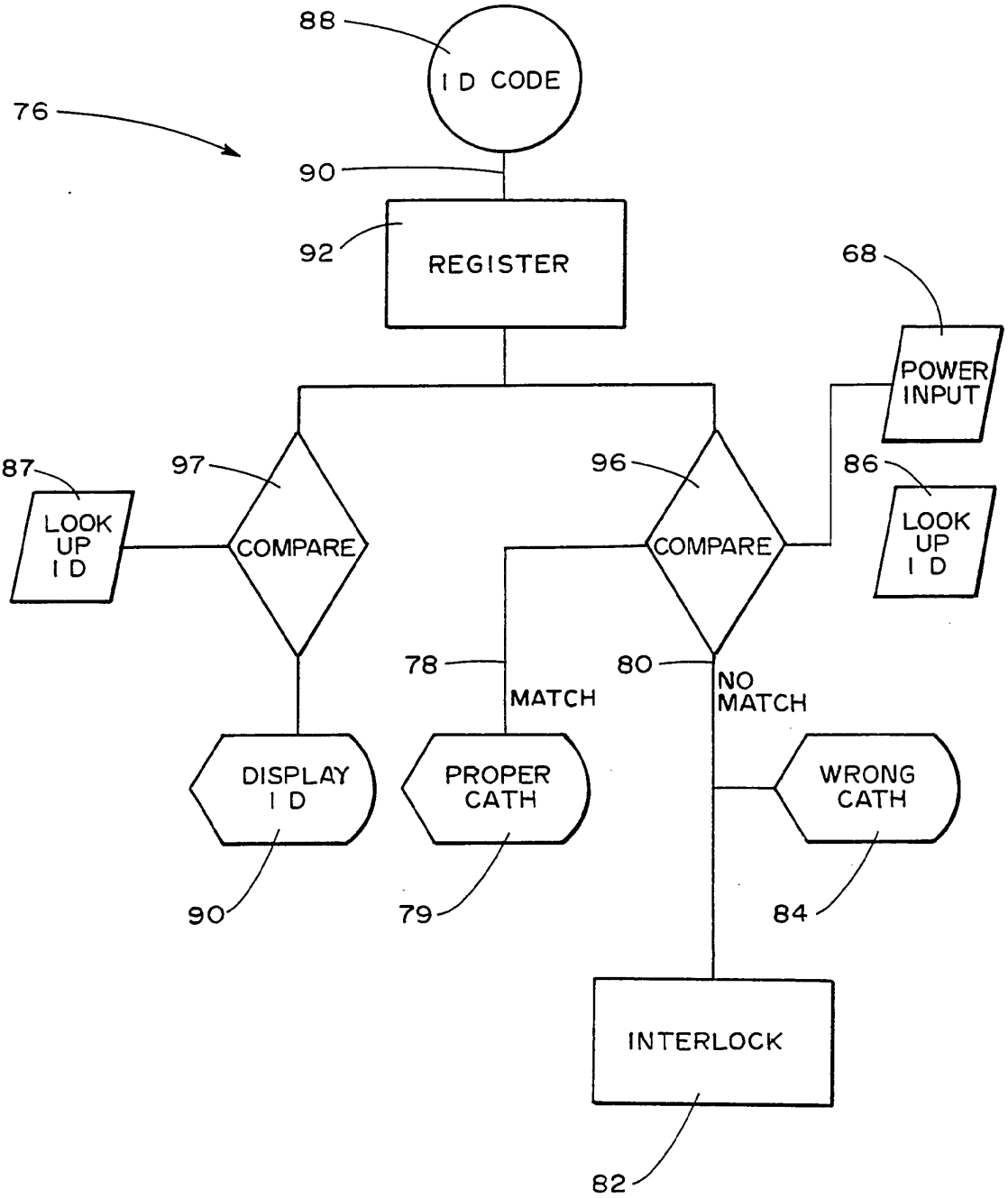


FIG. 3

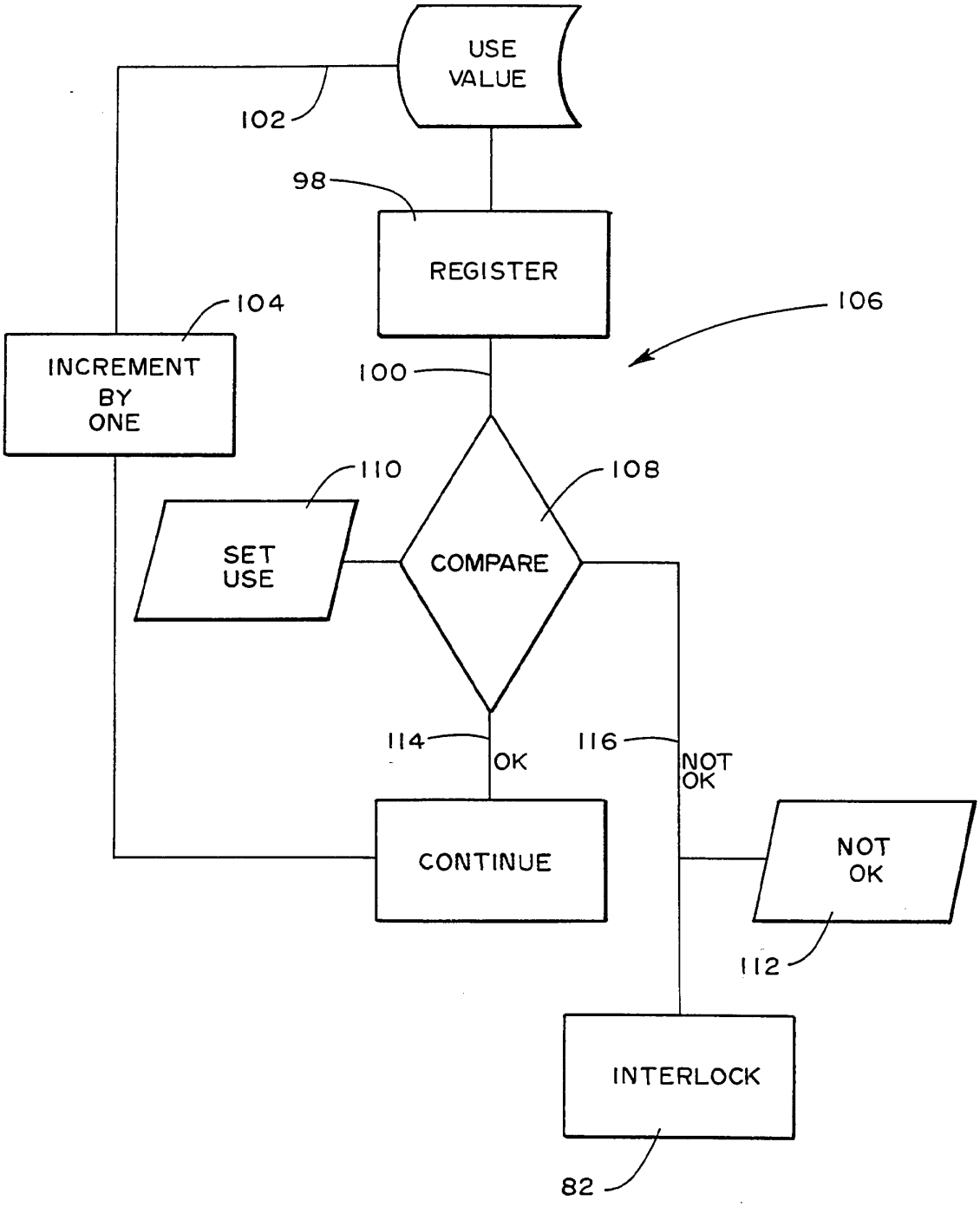
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FIG. 4



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FIG. 5



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/10902

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61B 17/36
US CL :606/32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/1, 10-12, 32-35, 41-42, 45-50; 604/20, 21

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US, A, 4,580,557 (Hertzmann) 8 April 1986, Figure 3, column 6	1, 10, 14, 22, 23, 25 --- 2-5, 11-13, 15-17
Y	US, A, 3,929,137 (Gonser) 30 December, 1975, whole document	2-5, 11-13, 15-17
Y	US, A, 4,936,842 (D'Amelio et. al.) 26 June 1990, see Abstract, whole document	2-5, 11-13, 15-17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 15 December 1993	Date of mailing of the international search report 17 FEB 1994
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE	Authorized officer MICHAEL PEFFLEY Telephone No. (703) 308-4305

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