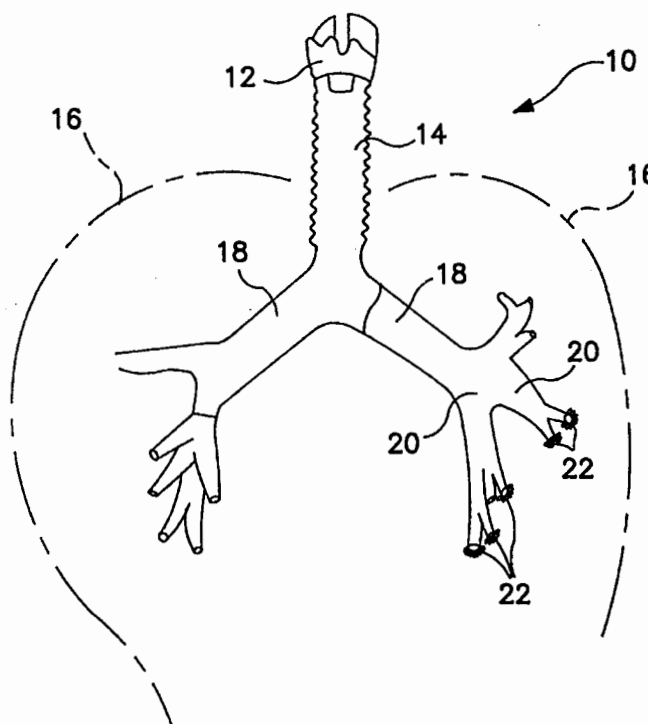


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(54) Title: NON-INVASIVE RADIOGRAPHIC METHOD FOR ANALYZATION OF A BODY ELEMENT**(57) Abstract**

This invention is a non-invasive process for analyzing the internal structure (10) of a patient. The process involves scanning a patient to acquire data representing a portion of the patient's internal structure. The scanned data is processed into three-dimensional volumetric and functional renderings. Baseline data representing three-dimensional volumetric data for either a normal internal structure or a previous scan of the patient's internal structure is also used in the process. The selected portions of the scanned and baseline data are preferably compared to determine whether an abnormality exists in the patient. Output data is sent to a display for displaying information related to the selected portions of the scanned and baseline data. An apparatus is also disclosed and includes a scanner for scanning a portion of a patient. A processor is utilized to receive and convert the converted data into three-dimensional volumetric data.



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NON-INVASIVE RADIOGRAPHIC METHOD FOR ANALYZATION OF A BODY ELEMENT

Cross-Reference to Related Application

5 The present application is a continuation-in-part of co-pending
Application Serial No. 08/805,787, entitled NON-INVASIVE RADIOGRAPHIC
METHOD FOR ANALYZATION OF A BODY ELEMENT, filed February 25,
1997.

Field of the Invention

10 The present invention is directed to a system for imaging internal
body structures and, more particularly, to a system for non-invasively analyzing and
diagnosing abnormalities in a body element.

Background of the Invention

15 Direct bronchoscopy of the tracheobronchial tree and endoscopy of
hollow visci, such as the gastrointestinal (GI) tract and pharynx, have been
performed for years. They are used to directly visualize masses, caliber changes,
surface or mucosal abnormalities, and traumatic injuries. However, direct
endoscopy requires the invasive introduction of a scope into the lumen of the
structure under consideration to visualize its inside surface. Apart from the surgical
requirements and complications involved in inserting the scope into the patient, the
20 actual physical advancement of a scope within the patient may be hampered by
obstructions which prevent or limit viewing of distal abnormalities. Furthermore,
the presence of a scope traversing the airways may in itself impose abnormalities
in airway structure or function by altering the diameter or by inducing mechanical
stimulation to airway components (i.e., mucous glands, smooth muscle, cilia).

25 Radiological and sonographic imaging has been used for decades to
non-invasively determine the internal status of the human body. Radiographic

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procedures, such as computed tomography (CT) and magnetic resonance imaging (MRI), operate on the basis of distinct physical principles by detecting and mapping differences in the composition of a target object.

5 Conventional radiographic procedures utilize a beam of x-rays to pass through a target object and expose an underlying photographic film. The film captures an image of the radiodensity pattern of the object. Areas of less radiodensity (e.g., air pockets) produce a greater blackening of the film. More radiodense objects (e.g., bones) produce a light image. Contrast agents are chosen so as to provide either less or more radiodensity than body tissues of interest.

10 Computed tomography is superior to conventional radiography in its ability to image a sequence of thin sections of an object at specific planes along the X, Y or Z axis of the target object and to do so with extremely high resolution.

Nuclear magnetic resonance imaging systems for body imaging operate on a different physical principle. Some atomic nuclei, such as, for
15 example, hydrogen nuclei, have both nuclear spin and nuclear magnetic moment. As such, these nuclei can be manipulated by applied magnetic fields. In the convention MRI system, a magnetic field is established across a body to align the spin axes of the nuclei of a particular chemical element, usually hydrogen, with the direction of the magnetic field. The aligned, spinning nuclei execute precessional
20 motions around the aligning direction of the magnetic field. For the aligned, spinning nuclei, the frequency at which they precess around the direction of the magnetic field is a function of the particular nucleus involved and the magnetic field strength. The selectivity of this precessional frequency with respect to the strength of the applied magnetic field is very sharp, and this precessional frequency is
25 considered a resonant frequency.

After alignment of the selected nuclei, a burst of radio frequency energy at the resonant frequency is radiated at the target body to produce deflection of the spin alignment of the selected nuclei. When the radio frequency energy is terminated, the deflected spin axes start to realign. The realignment of the spin
30 axis emits a characteristic radio frequency signal which can be detected by an external coil. The differences in the emitted radio frequency signal establish contrast between the different tissues.

Since tissue cells of body parts are primarily composed of water, radiography procedures typically do not sufficiently distinguish between contiguous
35 body parts. In the diagnosis of disorders of the digestive tract, for example,

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blockage or abnormalities in the conformation of loops of intestine lying one on the other are difficult to identify. Currently, assessment of pulmonary function requires the use of supplemental equipment or procedures (i.e., pneumotachography, spirometry, bronchoscope).

5 In order to assist in distinguishing between contiguous body parts, contrast agents have recently been utilized in imaging processes. The use of contrast agents in combination with radiological imaging make it possible to determine the location, size and conformation of organs or other structures of the body in the context of their surrounding tissues.

10 Contrast agents may be introduced into the body space in various ways depending on the imaging requirement. In the form of liquid suspensions or emulsions they may be placed into the area of interest by oral ingestion or injection into the bodily space (either directly or by channeling through selected vessels). A suitable contrast agent must be biocompatible, that is non-toxic, and chemically
15 stable, minimally absorbed or reactive with the tissue, and eliminated from the body within a short time.

 Fluorinated hydrocarbons (FCs) have been demonstrated to be useful in several clinical applications including vitreous fluid replacement, emulsions for blood substitutes, and have been used as contrast media in the lung and liver. FC
20 liquid can be used as an alternative respiratory media to support gas exchange. FC liquids are characterized by high respiratory gas solubility, are bioinert, nonbiotransformable, minimally absorbed, and have no deleterious histological, cellular, or biochemical effects. These properties combined with FC's radiopacity suggest that they may be ideal contrast agents for the mucosal surface of the
25 tracheobronchial tree.

 It is known to use fluorocarbons as a contrast enhancement medium, see for example, Wolfson, et al., Utility of a Fluorochemical Liquid for Pulmonary Diagnostic Imaging", Artificial Cells Blood Substitutes Immobilization Biotechnology, Volume 23, Number 4, pp. 1409-1420 (1994). Fluorocarbon (FC)
30 liquids are derived from common organic compounds by the replacement of all carbon-bound hydrogen atoms with fluorine atoms. These liquids are typically, clear, colorless, odorless, nonflammable and essentially insoluble in water. Perfluorinated compounds (e.g., perfluorocarbons or PFCs) are generally the preferred form of fluorinated hydrocarbons. FC liquids are denser than water and
35 soft tissue, and have low surface tension. fluorocarbon liquids have a high affinity

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for gases, dissolving more than 20 times as much O₂ and over three times as much CO₂ as water. FCs are also nontoxic and biocompatible.

5 The advent of helical computerized tomography (helical CT) has allowed for non-invasive volumetric data acquisition. This technique provides markedly improved multiplanar reconstruction as well as three dimensional rendering. However, current pulmonary imaging techniques, including helical CT, are limited by the presence of air on both sides of the walls of the progressively narrowing airway inhibiting visualization of small airways.

10 Recently developed post-processing software based on virtual reality techniques has permitted changing the viewer frame of reference and allowing direct visualization of the inside of hollow visci and tubes. This has been referred to as "endoscopic CT" or "virtual endoscopy." The technique has been applied to air distended bladders, colons, stomachs, tracheobronchial trees, as well as blood vessels. Major requirements of the technique are 1) a marked contrast difference
15 between the lumen and its wall; and 2) advanced novel software-design for edge detection and branch point detection of the structures. Air within the lumen of most structures supplies the contrast; or in the case of blood vessels, intravascular contrast agents provide the contrast between the lumen and the wall. In the case of magnetic resonance, fluid or moving protons provide the contrast with the wall.
20 See, for example, Rubin et al., "Perspective Volume Rendering of CT and MR Images: Applications for Endoscopic Imaging", Radiology, pages 321-330, May 1996, incorporated herein by reference in its entirety.

Volume rendering is an alternative to conventional surface display and projectional techniques and has significant advantages. Because volume
25 rendering uses information from all "voxels" within the volume, there is no information loss. As a result, it is not subject to the limitations caused by the information loss that is inherent in maximum intensity projection or to thresholding that occurs in surface displays. The basic drawback to volume rendering is that it is computationally more time consuming and expensive than other methods.

30 An additional advantage of volume rendering is that the images can be displayed as perspective views. That is, the images are rendered from a point source at a finite distance to approximate the human visual system. As a result, a close object appears larger than an object of identical size at a greater distance from the viewer. Surface displays of convention CT and MR data are rendered without
35 perspective. Hence, the distance between objects is not readily apparent. Although

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a lack of perspective is not critical when visualizing CT and MR data, three dimensional volumetric rendering allows striking visualization of nearly any surface or anatomic feature that has sufficient contrast (attenuation in CT or signal intensity difference in MR imaging) compared with neighboring structures.

5 At present, volumetric or three dimensional rendering of internal structures has been used to provide either a static or dynamic depiction of the scanned objects for viewing by medical personnel. The data accumulated has not, to date, been utilized in combination with a computer software and/or hardware system for analyzing and diagnosing abnormalities.

10 A need therefore exists for a system for scanning, analyzing and/or diagnosing abnormalities or deviations in a scanned body structure from a baseline set of data with subsequent displaying of the results.

Summary of the Invention

15 A non-invasive process is disclosed for analyzing an internal element in a body of a human or animal. The process involves scanning the body to acquire data representing a portion of the body's internal structure. The data is processed into three dimensional volumetric data representing the scanned internal body element. A portion of the volumetric data is selected from the processed scanned data. Baseline data representing three dimensional volumetric data for either a
20 normal internal body element or the patient's actual internal body element as determined from previous scanning processes is also used in the process. A portion of the baseline data is selected which corresponds to the selected portion of the scanned data. The selected portions of the scanned and baseline data are preferably compared to determine whether an abnormality exists in the patient. Output data
25 is sent to a display for displaying information related to the selected portions of the scanned and normative data.

 In one embodiment of the invention, the internal body element is a tracheobronchial tree within the human or animal body. The scanned bronchiole on a selected generation is compared against a baseline bronchiole on a
30 corresponding generation. Fluorochemicals can be administered to enhance the scanned data and, thereby, facilitate the visualization and selection of the portion of the scanned data by determining branching along the tracheobronchial tree.

 An apparatus according to the present invention is also disclosed. The apparatus includes a scanner for scanning a portion of a body. A processor is

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utilized to receive the scanned data. The processor converts the scanned data into three dimensional volumetric and functional data based on analytical models. The processor compares the converted data to baseline data. A monitor is utilized to display and compare data related to the scanned and baseline volumetric/functional data.

The present invention is useful for analyzing the pulmonary function of a patient, such as the patient's airway capacity or resistance, pulmonary volumes and capacities, and airway reactivity of pharmaceutical agents. The present invention is also useful for determining congenital anomalies, locating obstructions or masses, and/or reducing tissue damage during surgery. The present invention is also useful for determining changes in a patient's internal structure as caused by disease processes, therapeutic or diagnostic intervention.

The foregoing and other features and advantages of the present invention will become more apparent in light of the following detailed description of the preferred embodiments thereof, as illustrated in the accompanying figures.

Brief Description of the Drawings

For the purpose of illustrating the invention, the drawings show a form of the invention which is presently preferred. However, it should be understood that this invention is not limited to the precise arrangements and instrumentalities shown in the drawings.

Figure 1 is a diagrammatical representation of a portion of a normal respiratory system.

Figure 2 is a schematic representation of the Meyer model of the tracheobronchial tree.

Figure 3 represents the process flow of the present invention.

Figures 4a through 4c are graphical representation of a comparison between the frequency distribution in a baseline structure and a scanned structure.

Figure 5 illustrates a display of a lobar or segmental abnormality.

Figure 6 illustrates a display of a branch abnormality.

Detailed Description of the Preferred Embodiments

The present invention relates to a method for processing images into structural mathematical models from which structure, function, and reactivity of the bodily system can be determined. For the sake of simplicity, the method is

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discussed herein as it is contemplated for use in analyzing the structure, function and reactivity of a pulmonary system. The invention, however, is equally applicable to many other systems within the human body. Referring now to the drawings wherein like reference numerals indicate corresponding or similar elements throughout the several views, Figure 1 illustrates a diagrammatical representation of a portion of a normal respiratory system 10. The respiratory system 10 channels air from a larynx 12 through a trachea 14 into the lungs 16. The lungs 16 include right and left bronchus 18 and segmental bronchi or bronchioles 20. Air sacs or alveoli 22 are formed on the terminal ends of the bronchioles 20. Air exchange occurs between the alveoli 22 and blood capillaries (not shown) which surround the alveoli.

There are a number of theoretical and conceptual models which are useful for characterizing dichotomous, symmetrical, and asymmetrical nodes and branch points throughout the tracheobronchial tree. Some of the most well known are the Meyer, Horsfield, Strahler, and Weibel models. Figure 2 is a schematic representation of the "Meyer model" for characterizing the tracheobronchial tree. This model identifies the various branches of the bronchus 18 and bronchioles 20. The descending branches are identified as "generations" or "orders", the 1st order representing the right and left bronchus 18 and the subsequent orders representing the bronchioles 20. As shown in the figure, the numbering begins at the trachea, which is identified as generation 0. The numbering proceeds to the terminal airways, increasing by one at each dichotomy. This approach can be applied to both symmetric and asymmetric tree models. Other models, such as Horsfield or Strahler, have a different counting and numbering system for identifying branches and, therefore, in certain cases can end up with fewer orders. The generation system as described by the Meyer model is a useful method for locating a branch relative to the trachea (0) generation and, thus, is the most appropriate relationship for bronchoscopic or bronchographic investigations.

Referring to Figure 3, the process flow of the present invention is illustrated as it is contemplated for use as a non-invasive medical imaging and analyzing procedure. The procedure involves the steps of imaging or scanning the desired area of a patient, analyzing the scanned data to establish a baseline prior to an airway challenge or therapeutic intervention to determine if abnormalities or changes exist, and displaying any abnormalities or changes. The imaging step utilizes a standard imaging device, such as a computer tomography or nuclear

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resonance imaging machine. It is also contemplated that the present invention can be utilized with three dimensional data acquired by ultrasound. In one preferred embodiment, the imaging device is a Picker PQ 5000 helical CT device, manufactured by Picker International, Cleveland, Ohio.

5 Although the following procedure is not dependent upon the administration of a contrast agent, a contrast agent, such as a fluorochemical, is preferably administered into or near the area of interest prior to scanning the patient. For example, when imaging the internal bronchioles of the lung, it is preferable to fill at least a portion of the lung with a suitable contrast agent. The
10 contrast agent provides the high degree of differentiation between adjacent structures for subsequent three dimensional rendering. The preferred type of fluorochemical is a perfluorochemical (PFC). There are a large selection of PFCs' on the market and the one chosen for use in the present invention will depend upon the specific area of interest. For example, certain physicochemical characteristics
15 including, but not limited to, vapor pressure, viscosity, and spreading coefficients will influence the rate of evaporation and pattern dispersion of the FC. A fluid of high vapor pressure and low viscosity is useful when it is desirable to perform imaging throughout the entire lung over a short period of time. A FC viscosity above about 3 cS is generally considered to be a high viscosity. A FC viscosity at
20 or below 3 cS is generally considered to be a low viscosity. A fluid of lower vapor pressure and high viscosity may be preferred for local imaging over a longer time period. Those skilled in the art would readily appreciate the FC that is appropriate for the chosen site and the imaging desired.

 Another aspect of the FC is its radiopacity characteristic. A fluid
25 of marked radiopacity might be particularly useful to delineate larger regions but might in fact compromise detection of finer abnormalities. Thus, the physical characteristics of the FC will determine the preferred FC for the imaging desired. Table 1 provides a list of preferred FCs which are contemplated for use in the present invention. The table also provides the physical properties for each FC. In
30 general, all the listed FCs are inert, odorless and colorless. The FCs have low surface tension (between approximately 10 and 19 dynes/cm) and high solubility for oxygen (> 40 vol%). These FCs are insoluble in water, sparingly soluble in lipids (as noted by the logP values) and organic solvents, and completely soluble in other fluorinated compounds. Other fluorochemicals may provide the required contrast
35 and, therefore, can be substituted for the preferred FC's listed in the table.

TABLE 1
FC LIQUID COMPOUNDS AND PHYSICAL PROPERTIES

	Vapor Pressure	Viscosity	Density	Solubility
FC Compounds	(mmHg)	(cS)	g/ml	logP
PP-2	141	0.873	1.78	6.05
PP-5	13.5	2.61	1.95	7.97
PP-9	2.9	3.25	1.97	8.84
PP-11	< 1.0	14.0	2.00	7.81
RM-101	51	0.85	1.78	6.42
PFOB	10.5	1.0	1.89	7.87

wherein:

PP-2: perfluoromethylcyclohexane manufactured by BNFL Fluorochemicals Ltd.

PP-5: perfluorodecalin manufactured by BNFL Fluorochemicals Ltd.

PP-9: perfluoromethyldecalin manufactured by BNFL Fluorochemicals Ltd.

PP-11: perfluoroperhydrophenanthrene manufactured by BNFL Fluorochemicals Ltd.

RM-101: perfluoro-furan/pyran mixture manufactured by Mercantile Development, Inc.

PFOB: perfluorooctylbromide sold under the tradename LiquiVent[®] and manufactured by Alliance Pharmaceutical Corp.

When viewing other organs in the body, it may be more preferable to provide a contrast agent external to the area of interest. Use of FCs as a contrast agent which enhances imaging is well known. See for example, U.S. Patent Nos. 4,993,415 and 5,350,359, which are both incorporated herein by reference in their entirety. The FC's can be provided to the patient in any suitable form, such as neat liquid, aerosol, vapor, or emulsion.

The preferred FC will have material properties which will allow for the FC to remain in or around the structure of interest or coat the walls until the scanning is complete. For example, when scanning the small bronchioles in the lungs, it is preferable to utilize a FC which will remain in the lung for a sufficient length of time to allow the FC to travel through the multiple branches of bronchioles. The Hounsfield unit (HU) number of a suitable breathable FC liquid is in the range of 800-2700. As discussed above, the preferred form of fluorocarbon is a perfluorocarbon.

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The amount of fluorocarbon necessary will vary depending on the portion of the body being imaged. For example, when imaging the lung, approximately 1 to 2 mils per kilo is needed if it is desired to coat only the alveoli. Approximately 20 mils per kilo is needed to coat everything, including the branches. It is desirable to provide a sufficient amount of fluorocarbon to leave the airways free. Also, the amount of contrast desired will effect the amount of fluorocarbon used.

The scanned or imaged data is transferred to a computer processor or other processing unit. A variety of processing units exist which would be capable of receiving and analyzing the scanned data. The processor may include one or more forms of memory (e.g., EPROM, ROM, RAM, etc.) for storing relevant data. The computations required to form volume rendered images necessitates a relatively high speed computer. Those skilled in the art are capable of selecting a suitable processor for receiving and analyzing the scanned data. The imaged data is preferably in the form of numerical data. Any conversions necessary to transform the scanned or imaged data to numerical data can be performed either prior to or after transmission to the processor.

The processor preferably utilizes the scanned data to develop a volumetric model of the scanned object. This is called volumetric rendering. Conventional software is available to perform volumetric rendering of a scanned image (see for example, U.S. Pats. Nos. 5,546,807, 5,315,512, and 5,594,842, which are incorporated herein by reference in their entirety). Picker International also distributes Voyager software which is capable of performing volumetric rendering. Therefore, no further discussion of the software is needed.

The processor also receives baseline data for comparing against the current scanned or imaged data. The present invention contemplates various types of baseline data which can be utilized. In one embodiment, the baseline data is data representing a previously scanned portion of the patient's body. For example, the patient's lung may have been scanned at an earlier point in time. When the previous scan was taken will depend on the intended analysis to be performed. For example, if it is desired to determine functional respiratory data, the first scan (previous scan) may be during inspiration and the subsequent scan may be during expiration. For this type of procedure, there may be only seconds or minutes between scans. Other types of analysis may require scans that are, for example, minutes, hours, weeks, months or years old. The previously scanned data is

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utilized in the present invention for comparison against the current scanned data. The processor determines whether a deviation exists between the prior scanned data and the current scanned data as described in more detail below. Hence, in this embodiment of the invention, the baseline data includes preexisting patient data.

5 In an alternate embodiment of the invention, the baseline data is scanned or stored data representing a "normal" structure. For example, data representing healthy or normally developing lungs is utilized for comparison against the patient's current scanned data. The data is preferably generated from scans of a large segment of patients having a normal internal structure of interest (e.g., a
10 normally developed lung structure). The data can be categorized based on various parameters, such as age, gender, etc. This data is referred to herein as "normative data".

 In this embodiment, the processor also preferably receives background information associated with the scanned data, for example, the age and
15 gender of patient and the location of the scanned area within patient. The processor preferably either receives this background information directly from the scanner (i.e., input into the scanner and transmitted along with the scanned image data) or the data can be entered directly into the processor (e.g., by medical personnel).

 Utilizing this background information, the processor (or the
20 operator) selects an appropriate set of data representing a "normal" or "average" object under consideration (e.g., bronchioles) for use as the baseline data for comparison against the patient's scanned image. As described above, the processor preferably has available to it data representing a plurality of normal body structures. This normative data is either stored internally in the processor, or is supplied
25 externally. The processor utilizes the background information to select the appropriate data for comparing with the actual scanned image.

 For example, if the patient is a 3 year old caucasian male, and the area of interest is the lungs, the processor will select predetermined data representing a "normal" or "average" lung in a 3 year old caucasian male. The
30 selected data is used as the baseline data for comparison against the imaged data for diagnostic analysis as described in more detail below. The criteria which is used to select the appropriate normative data can be, for example, age, gender, race, height, and/or weight, and is preferably based on a large segment of the "normal" population. Those skilled in the art would readily understand how to generate the
35 normative high resolution CT data for airway dimensions, geometry, and computer

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functional analysis (i.e., airway conductance) as a function of gender, race, age, lung pathophysiology, or differential diagnosis using airway challenge (e.g., cold air, pharmacologic). These criteria should not be considered all encompassing inasmuch as other criteria for separating the data can be substituted for any of the
5 above criteria and are well within the purview of the claims.

Alternately, the normative data can be separated by suitable background classifications or criteria and stored on individual data storage media, such as floppy disks. The appropriate storage media representing the appropriate "normal" object is selected by one of the medical personnel and input into the
10 processor. The normative data may be stored as raw numeric data similar to scanned data or, more preferably, may be stored as volume-rendered data (i.e., data converted into three-dimension volumes). Exemplary normative data for a tracheobronchial tree for use in the present invention include, but are not limited to, the number of bronchi in a generation, and the diameter, length, circumference,
15 cross-sectional area and volume of each bronchi in a given generation. This type of information can also be recorded from a prior scan of the patient according to the first embodiment of the invention described above.

The processor utilizes the two sets of data (scanned data and selected baseline data) to determine if and where abnormalities or deviations exist in the
20 current version of the patient's scanned data. As will be described in more detail below, the processor must first correlate or match the two sets of data in order to ultimately determine whether any differences exist. This can be achieved by initializing or identifying portions of each data set. For example, if the current scanned data and the baseline data represent the structure of a lung, it is desirable
25 to identify the data in both sets that corresponds to the trachea. The software identifies the branch point within the model. From that point, the processor (or more appropriately the software operating within the processor) can determine the structures that depend from the trachea and properly identify them according to the selected model.

30 An abnormality as determined by the processor is not necessarily indicative of a unhealthy condition. Instead, an abnormality is, in its broadest sense, a difference (deviation) between the scanned data and the normative data which requires closer inspection by a physician. What is considered to be an abnormality will vary depending on the organs that are being analyzed, the
35 procedures that are being performed, and/or the parameters that are being

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compared. A difference may exist between the current scanned data and the prior scanned data obtained in the same person, thus representing a return towards "normal", new abnormalities, or worsening of abnormalities identified on previous scans.

5 If the processor determines that an abnormality exists, it then displays the location of the abnormality and, preferably, the size of both the baseline object and the scanned object. The processor can also visually display the abnormal structure (e.g., cross-section) if desired. It is also possible to overlay the scanned image and the baseline image on the display. The differences can be
10 highlighted (such as by coloring or shading). Conventional software exists which permits such manipulation of computer data. The following examples further define and illustrate some of the capabilities of the present invention.

Obstruction or Mass (Radiologic Applications)

15 Small endobronchial masses which have resolvable thickness or distal obstructions can be identified using the present invention since the small bronchi are now navigable. The low surface tension of the FC liquid allows it to pass beyond any obstructions in the bronchi. The processor compares the cross-sectional properties of the scanned bronchus and bronchioles (by order) to the cross-section of the baseline bronchus and bronchioles. If the processor determines
20 that the cross-section of the scanned bronchi is sufficiently different than the baseline cross-section as indicated by the baseline data, the processor displays the location of the abnormality and its size. The processor could also display the size of a normal (baseline) bronchi. It is contemplated that a range of values around the baseline would be considered "normal" (i.e., not a significant deviation from the
25 baseline). A preferred range would be about ± 2 standard deviations from the mean. A reading outside of this range would represent an abnormality.

Congenital Anomalies

30 The caliber of the small bronchi could be determined which may be important in stricture or hypoplasia. Anomalous bronchial origins and congenital or acquired fistulas from the tracheobronchial tree to other organs or spaces could be evaluated. The processor can determine this from the acquired data. A branching pattern typically is characterized by progressively smaller diameter

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airways. If the dimensions become larger, this would indicate an abnormality, such as a bronchi-bronchi fistula, bronchiectasis, or entry into another organ.

Non-invasive Radiologic Determination of Pulmonary Function

5 The ability to visualize the small airways non-invasively permits non-pneumotach pulmonary function tests. The derivable information such as diameter, length, and volume of the airways from the imaging study can be broken down and analyzed. The use of ultrafast electron beam CT significantly decreases motion artifact, enabling a greater variety of pulmonary parameters to be determined at even high breathing frequencies.

10 a) Structural Analysis: Referring Figure 2 and Table 2, using the Meyer model for the tracheobronchial tree, a summarized structural profile table for each patient can be generated listing for each generation of bronchi, the number of that generation, mean diameter, mean length, cross-sectional area (CSA) and the volume.

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TABLE 2

Generation	# in Generation	Diameter (cm)	Length (cm)	Circumference	Cross Sectional Area	Volume
0	1	2.5	8	7.9	calculated	calculate
1	2	1.5	5	4.7	↓	↓
2	4	1.0	3	3.2	↓	↓
3	8	↓	↓	↓	↓	↓
4	16	↓	↓	↓	↓	↓
5	32	↓	↓	↓	↓	↓
6	64	↓	↓	↓	↓	↓
7	128	↓	↓	↓	↓	↓
8	256	↓	↓	↓	↓	↓
9	512	↓	↓	↓	↓	↓
10	1024	↓	↓	↓	↓	↓
11	2028	↓	↓	↓	↓	↓
12	4056	↓	↓	↓	↓	↓
13	8112	↓	↓	↓	↓	↓
14	16,224	↓	↓	↓	↓	↓
15	32,448	↓	↓	↓	↓	↓
16	64,896	↓	↓	↓	↓	↓
17	129,792	0.08	0.2	0.25	↓	↓

As discussed above, this scanned data is then compared to baseline data, which can be normative data based on age, sex/race, height and/or weight-matched controls, or the patient's prior scanned data. In addition to the summarized data for each generation (order), the scanned data would be displayed to demonstrate the frequency distribution of diameter, length, volume, and CSA relative to normative values. This comparative analysis permits quick and accurate determination of abnormalities. Figures 4a-4c are graphical illustrations of the frequency distribution of the number of airways (Y-axis) of a certain diameter (X-axis). As shown in Figure 4a, a frequency distribution of the cross-sectional diameter for the baseline 10th generation (order) bronchioles (solid line) is

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compared against the frequency distribution of the cross-sectional diameter for the current scanned data representing the 10th generation bronchioles for the patient (dashed line). From the visual display, the physician can readily determine whether or not any abnormalities exist in the scanned image of the patient. In the scanned data shown in Figure 4a, the physician can readily determine that the scanned data of the patient's 10th generation bronchiole shows abnormal development. Specifically, all the bronchioles on the 10th generation have a cross-sectional diameter that is smaller than the baseline 10th generation bronchioles. In order to further assist the physician, it may be preferable to display only the structures which are determined to be "abnormal".

Figure 4b is a graphical representation of the frequency distribution of the cross-sectional diameters for the baseline 10th generation (order) bronchioles (solid line) as compared against the frequency distribution of the cross-sectional diameters for the current scanned data representing the patient's 10th generation bronchioles (dashed line). In this figure, the processor displays (or determines) that most of the patient's 10th generation bronchioles have a normal cross-sectional diameter. However, a small population of bronchioles have cross-sectional diameters which are smaller than the baseline and may be localized to a single lung segment.

Figure 4c is a graphical representation of a frequency distribution of a patient's 10th generation bronchioles in which a diffuse abnormality is seen such that these airways are both larger and smaller than the baseline.

In addition, intrapulmonary variations can be assessed by the processor and the anatomical location (i.e., lobar, segmental etc.) of the abnormal bronchi can be determined. That is, lobes or segments, as well as bronchial generations within the lung, are compared against the baseline data and cross-correlated. The comparison would identify the location of any abnormality within the lung (e.g., generations five through ten are abnormal but only in the lower lobe). This could be graphically displayed to illustrate the branching tracheobronchial tree and identify the location and generation of the abnormal airways. Figure 5 illustrates one such display which is contemplated by the present invention.

Furthermore, diagnosis and therapy of the pulmonary function of a patient's lung may be determined by comparing ratios for various bronchi. The present invention utilizes the processor to determine ratios of diameter, length, volume, CSA for different generations. These ratios can be displayed to facilitate

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the rapid and accurate differential diagnoses. For example, it may be that in lymphocytic interstitial pneumonia (LIP) the ratio of the diameters of the 7th generation bronchioles to the 10th generation bronchioles is increased. This profile may occur only in the lower lobes. It is contemplated that the present invention would utilize the processor to compare the 7th and 10th generation bronchioles of the lower lobes. The ratio is displayed to allow the physician to diagnosis LIP earlier. A "normal" (or previous) ratio for the 7th and 10th bronchiole could also be displayed to facilitate comparison. This would also be important for demonstrating the anatomic patterns of disease (i.e., specific lobes, segments etc.). Alternately, an index of obstruction can be assigned to a scanned component (or portion thereof) and compared to a baseline index (which can be the patient's baseline or a normative baseline.)

b) Functional Analysis: Referring generally to Figure 2, the airways of the lung can be considered a large group of circuits in series and parallel. All of the same generation airways are in parallel and the airways from one generation to the next are in series. Utilizing the processor of the present invention, the overall and site specific pulmonary function can be calculated. That is, the processor can compare bronchi parameters for each generation against the baseline data. From this comparison, the processor can display the specific generation of bronchi where the abnormality exists. Figures 5 and 6 illustrate this aspect of the invention. Furthermore, if the processor determines that the diameter of the scanned bronchi is below a predetermined size (indicating substantially restricted flow), the display would also indicate the depending generations of bronchi as also being functionally abnormal.

Airway resistance: As part of the functional analysis of the lung, the following equation can be used to determine the resistance in the different airway generations, individually, combined, or in the overall lung model (figure 3).

$$R = 8L\mu / \pi r^4$$

Where: R = resistance;
L = length of airway;
r = radius of the airway; and
 μ = viscosity of air.

The viscosity (μ) of air is known. The length (L) and radius (r) of the airway can be determined from the scanned data. Accordingly, the resistance along each

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generation of airway can be derived. The processor can output the resistance for each airway or, alternately, can output airways which have a resistance below a normal resistance value as determined from the baseline data.

Airway Compliance (C_{AW}): Functional analysis of the lung also involves determining the airway compliance. The airway compliance of the scanned structures are calculated using the following formula.

$$C_{AW} = \Delta V / \Delta P$$

Where: ΔV = the calculated change in volume; and
 ΔP = the calculated change in pressure.

In order to calculate the change in pressure (ΔP), the imaging of the lung structure is performed twice under two different positive end distending pressure (PEEP) conditions. In the first condition, there is zero PEEP (i.e., no pressure applied to airways). In the second condition, the airways are subjected to a PEEP of 5 cm H_2O (i.e., induced positive pressure). Also, from the two sets of imaged lung structure the change in the airway volume (ΔV) can be calculated. The airway compliance C_{AW} can then be determined for any visible generation of airway.

It is also contemplated that a comparison of the calculated scanned airway impedance for the scanned data would be compared to the impedance for the baseline data. Airway impedance is a function of airway compliance and airway resistance.

Pulmonary Volumes and Capacities: As discussed above with respect to the airway compliance, volumes can be calculated from the scanned data. In order to determine the pulmonary capacity of the various airways, imaging is performed under different breathing conditions (i.e., static and dynamic). First, scanned or imaged data is acquired while the patient momentarily stops between inspiring and expiring. This provides an index of tidal volume within the airways. Next, scanned data is acquired while the patient maximally inspires and momentarily holds his/her breath. This provides data representing airway volume at total lung capacity (TLC). Lastly, scanned data is acquired while the patient maximally expires. This will provide data representing airway volume at residual volume (RV).

Lung volumes and capacities can then be derived by the processor from this scanned data, such as vital capacity (VC), inspiratory and expiratory reserve volumes (IRV and ERV, respectively), and functional residual capacity (FRC). Inspiratory and expiratory reserve volumes represent the volumes that one

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could inspire/expire above and below a normal tidal volume breath and, thereby, increase the depth of breathing. Functional residual capacity represents the volume of gas that is in the lung at the end of a normal breath. It is determined by a balance of recoil forces across the lung (chest wall pulling outward; lung pulling inward) and provides a "buffer" volume of gas in the lung which prevents large swings in arterial oxygen and carbon dioxide tension throughout a normal breath.

With the use of a very rapid CT electron beam scanner, a forced maximum expiratory maneuver, i.e., forced vital capacity (FVC) can be scanned and analyzed with respect to time to provide standardized indices of airway function, such as the forced expiratory volume per second (FEV_1) of maximum ventilation (V_{Emax}). From this data, the processor can analyze time dependent data relative to total effort (FEV_1/FVC) or resting conditions (FVC/VC) to provide indices of structural vs functional limitation of lung function.

Baseline datasets generated under any or all of the above conditions can be utilized to further characterize and identify regional differences in lung function in a similar manner as discussed above with respect to the Structural Analysis of the lung.

c) Airway Reactivity Analysis: It is also contemplated that the present invention can be used to determine airway reactivity to pharmacologic agents (e.g., vasodilator, bronchodilator, methacholine, etc.), physical agents (e.g., cold air, exercise, gases (O_2 , CO_2 , He, N_2O , NO_2 , etc.)), or various respiratory maneuvers (e.g., PIP, PEEP, inspiration, expiration, etc.). For example, after providing the FC contrast agent to the area of interest, the area is scanned before and after delivery of a pharmacologic agent. The scanned data would be compared to baseline values representing, for example, standardized dose-response and regional airway site-specific nomograms.

In the past, only the overall pulmonary response could be evaluated. However, by using the technique of the present invention, each generation of airway could be evaluated to determine if the challenge affected all the airways or only specific generations of airways. Airway challenge refers to a stimulus which might induce bronchoconstriction, such as inspiration of cold air, inhalation or intravenous administration of an airway smooth muscle agonist. Similarly, the present invention provides an important method for pharmacologic testing of drugs to determine which generations of airways are affected by which drugs. This would allow site specific pharmacologic intervention to ultimately be determined for

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improving therapeutic management. The FC could also be combined with pharmacologic agents and act as a carrier for delivery of the drug.

Improved Virtual Endoscopic Technique Anywhere in the Body

5 The present invention is not limited to performing analysis and diagnosis of the lung structure but, instead, is applicable to any element or component within the body. For example, the present invention can be used to provide virtual endoscopy and diagnosis for the following body elements: nasopharynx, nasal sinuses, peritoneum (i.e., virtual laparoscopy), GI tract, urinary tract, synovial spaces (i.e., virtual arthroscopy), pleural space, and auditory canal
10 among others. Additionally, this technique is applicable to intravasculture. When using this technique on the intravasculture, it is contemplated that FC liquid would be used as a blood substitute to assist in imaging. In the In each case, baseline data (either based on prior scanned images from the patient or normative data) would be acquired for subsequent comparison with the current scanned data. A skilled
15 artisan would readily appreciate the diverse capabilities of the present invention in light of the above discussion.

Imaging the Tracheobronchial Tree and Small Airways Externally

Using a more viscous FC or by delivering the FC so that it remains inside and fills the bronchial tree without entering the very tiny respiratory
20 bronchiolus and alveoli, the tracheobronchial tree could be viewed from the perspective of its outer walls. In this embodiment, the contrast would be between the air filled lung and the very dense FC filled airways. Comparison against baseline data would provide insight into the existence of any abnormalities in or on the walls.

Radiologic Assisted Surgery

25 It is also contemplated that the present invention can be utilized to assist during a surgical procedure. FC enhanced virtual endoscopy can be applied as an arthroscopy assistive modality in various procedures in which enhanced edge-detection would be advantageous and further minimize the need for invasive
30 procedures or production of iatrogenic trauma. In this embodiment tissue lined lumen may be protected from surgically related tissue trauma during diagnostic or therapeutic procedures, such as laparoscopy or "virtual laparoscopy". Scanned and

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processed data would provide the surgeon with actual dimensional data before or during surgery to facilitate an approximate surgical approach, choice of instruments, prosthetic devices, etc. One important advantage to using this information during surgery is the potential ability to minimize trauma and risk of infection by reducing tissue handling.

The present invention is extremely beneficial in the pediatric population where the size of the pediatric bronchial tree prevents navigation with a conventional bronchoscope. Similarly, the present invention permits analysis of small airways which heretofore have not been viewable through non-invasive procedures. For example, with the use of the present invention, it is possible to assess diseases down to approximately the 12th through 17th generation bronchi (about 1 mm diameter in the adult). This is a much smaller size than is reachable by a bronchoscope.

As discussed above, with the use of fluorochemical contrast agents, the present invention provides a non-invasive means for identifying and analyzing branching along the tracheobronchial tree to a degree previously unobtainable through conventional techniques.

The present invention also provides a novel non-invasive method for relating structure (e.g., normative data or prior patient scanned data, obstruction or mass identification, congenital abnormalities) to function (e.g., pulmonary function analysis section).

One key benefit of the present invention is the ability to provide medical personnel with real-time, on-line analysis. When used with a high speed processor, the monitoring of the changes in the structure of the patient can be performed nearly instantaneously. When using the patient's previously scanned data, it is possible to monitor changes in a body element due to therapy. For example, the change in the size of a previously scanned mass may provide an indication as to whether a change in therapy is warranted.

While the above discussion has described the use of a display for providing a comparison of the actual scanned data against the baseline data, or for identifying an abnormality, it is also contemplated that the desired information can be "displayed" in printed format.

Experimental Testing

Experimental tests were conducted utilizing several aspects of the present invention. An eight week old 1400 gram New Zealand white rabbit was locally anesthetized. A tracheotomy was performed with a Hi-Lo Jet endotracheal tube (Mallincrodt, Glen Falls, NY) inserted proximal to the carina. After systemic anesthesia, the rabbit was connected to a ventilator circuit and placed on a CT table in the supine position. The rabbit was gas ventilated at the same frequency (30 bpm), tidal volume (9-5 ml/kg), temperature (37°C) and inspiratory time (0.3 sec) for the duration of the protocol with continuous cardiovascular monitoring for data comparison. The rabbit received an initial dose (17cc/kg) of perfluorooctylbromide (PFOB)(LiquiVent®, Alliance Pharmaceutical Corp.) administered via the endotracheal tube which equated to the measured gas functional residual capacity (FRC) as was determined by closed circuit helium dilution (PANDA, Medical Associated Services, Hatfield, PA).

Imaging was performed on a Picker PQ 5000 helical CT scanner before and after the administration of the PFOB during ventilated respiration. Images were obtained using a targeted 10 cm FOV, 3 mm slice thickness with a pitch of 1.25, images reconstructed every 3 mm, smooth spatial reconstruction algorithm, and a mA/kVp of 200/120. Each revolution of the helical tube required 1 second. An additional set of images was obtained with the rabbit held at peak inspiratory pressure (PIP) with the same parameters except the images were reconstructed every 1 mm. The images were then transmitted to an independent work station (Voxel Q). Using software supplied by Picker International, three dimensional rendering of the images was performed with identical windowing. Using the three dimensional rendering, the operator was able to navigate through the lumen of the reconstructed tracheobronchial tree. The software permitted viewing the inside wall of the tracheobronchial tree at any angle, navigating from distal to proximal, or entering distal to an obstruction. The entire process required only ten minutes of post-processing time. The maximum tracheal diameter of the rabbit was approximately 5.2 mm.

The PFOB distributed evenly within the lungs with pooling in the bronchi occurring only immediately after the PFOB was administered. Initially, a small amount of pooled PFOB was seen in the proximal right and left mainstem bronchi on the reconstructed bronchoscopic CT. The PFOB rapidly distributed out

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of the larger airways into the very small airways and alveoli due to the application of PEEP (positive end expiratory pressure).

5 An endoscopic CT without PFOB was compared against the endoscopic CT with PFOB. Without PFOB, the endoscopic CT only allowed visualization of the trachea, carina, and the mainstem bronchi with very poor visualization of the third order branches. By comparison the endoscopic CT with PFOB allowed improved visualization of the tracheobronchial tree down to fourth order branches with visualization of the orifices of fifth order branches in some locations.

10 The above results were obtained without suspension of ventilated respiration. Respiratory motion results in the loss of resolution and contrast between the air in the smaller airways and the PFOB and prevents navigation into these small bronchi. Endoscopic CT was performed with PFOB and peak inspiratory breathhold to examine the effects of respiratory motion. The endoscopic
15 CT which was performed with PIP and reconstructed every 1 mm, allowed navigation into fifth order bronchi which were approximately 0.8 mm in diameter.

The rabbit tolerated the PFOB well, maintaining physiologic gas exchange and cardiopulmonary profile throughout the procedure.

20 The Hounsfield unit (HU) number of PFOB liquid is in the range of 2700-2800. The Hounsfield unit number of PFOB in the rabbit lung is 1400-1700. PFOB inspired in the trachea creates a marked contrast difference between the air in the bronchi and the contrast in the lung. Since the bronchial wall can be assumed to have similar CT density to soft tissue and have a Hounsfield unit number of approximately 40-60, the contrast difference achieved with FC is much
25 greater than can be achieved with endogenous tissue densities in the lung. The above described testing demonstrated that contrast improvement with PFOB allows markedly better visualization of significantly smaller bronchi with the bronchoscopic CT technique than the identical bronchoscopic CT technique without PFOB.

30 Since the airways of adult humans are much larger than those of the 1400 gram rabbit, the results of the testing in this small animal model indicate that the present invention would permit evaluation of small bronchi and be useful in the assessment of small airway disease down to approximately 12th order bronchi (about 1 mm diameter in an adult human). In addition, the testing demonstrates that the present invention might allow for the evaluation of changes in the caliber
35 of small airways under different conditions such as inspiration, expiration, PIP,

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PEEP (positive end expiratory pressure), bronchodilators or even slight negative pressure.

5 With respect to the pediatric population, the diameter of a steerable pediatric bronchoscope is about 3mm. The size of the tracheobronchial tree in premature infants is similar to the 1400 gram rabbit. As such, it is not easy to visualize the tracheobronchial tree in an infant utilizing conventional bronchoscopy. However, as demonstrated by the above tests, the present invention would be useful for non-invasively evaluating the bronchial tree in the pediatric population.

10 The present invention has been described thus far as it is intended to be used for imaging and analyzing a body element on a macroscopic level. However, it is contemplated that the present invention is also applicable for imaging and analyzing a body element on a cellular or molecular level. The capabilities of the invention are primarily dependent on the imaging resolution. Current and developing technology is such that the visualization of the dynamics at the level of
15 the cell membrane are readily foreseeable, even down to the molecular level. The present invention as described above would be readily applicable to such images. Hence, on both a cellular and molecular level, a comparison can be made between a body element of a patient and their own test profiles to evaluate a change from a prior state. Alternatively, cellular and molecular imaging of a body element can
20 be compared to normative values based on selected criteria, such as age and gender, to evaluate the patient relative to a population standard.

The present invention can be applied to a cellular membrane to calculate transmembrane flux of substrates by visualization of substrate concentration on the two sides of the membrane. Also, imaging and analysis
25 according to the present invention permit direct observation of drug uptake with the resulting measurement of diffusion and partition coefficients. This permits an assessment to be made of bioavailability. The drug can be marked with a biologically active or inert material, such as FC.

30 Using the present invention, physiologic responses on the cellular level can be determined for any agent, such as coil contraction, secretion, endocytosis, exocytosis etc. Also, direct observation can be performed of functional cell actions at the tissue level (*i.e.*, Osteoclast/osteoblast interaction on bone and changes/deviations from normal.

35 High resolution imaging permits the use of the present invention to analyze and evaluate branching structure in blood vessels, nerves, capillaries,

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lymphatics. As microscopic imaging techniques improve cellular and subcellular structures may be analyzed to evaluate microtubular structure, actin filaments, membrane structure, and extracellular "potential" space.

5 Contrast agents bound to antibodies for certain structures could create boundaries (similar to cell membranes) which would allow evaluation of extracellular space. In this regard, indium or gadolinium could be targeted to the epithelium/endothelium tissue of various organs which would enable the epithelium/endothelium tissue to then be imaged. Epithelium or endothelium could be visualized in ureter, bile duct, pancreatic duct, lymphatic ducts, epidural space,
10 meninges, inner ear/semi-circular canals, or other epithelium or endothelium containing structures.

It is also contemplated that ultra miniaturization will permit tiny robot probes or sensors to be placed within the body at desired locations. These devices, operating in conjunction with an ultrasonic or magnetic resonance imaging
15 system, would send back structural information from within the body that is analyzed using the above-disclosed techniques.

Cellular and molecular imaging also permits evaluation of important pulmonary structures and functions. For example, such imaging would permit direct observation of ciliary function and clearance, single isolated airway smooth
20 muscle cell assessment of airway contractility secondary to agonist stimulation, and assessment of other airway cell functions including secretory cells to assess mechanisms of mucous secretion and surfactant production.

While the present invention has generally referred to radiographic scanning as the preferred form of scanning, other non-invasive methods for
25 producing scanned images of a body element, such as sonographic imaging, are also contemplated for use in the present invention.

Although the invention has been described and illustrated with respect to the exemplary embodiments thereof, it should be understood by those skilled in the art that the foregoing and various other changes, omissions and
30 additions may be made therein and thereto, without parting from the spirit and scope of the present invention.

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CLAIMS

1. A non-invasive process for analysis of an internal element in a body of a human or animal comprising the steps of:

receiving scanned data reflective of a portion of a human or animal body in a processor;

processing the scanned data in the processor into three dimensional volume and functional data based on mathematical models representative of an internal body element;

selecting a portion of the processed scanned data;

providing baseline data representing three dimensional volume and functional data reflective of a version of the internal body element;

selecting a portion of the baseline data corresponding to the selected portion of the scanned data; and

displaying data which is a function of the selected portions of the scanned and baseline data.

2. A non-invasive process according to claim 1 wherein the baseline data is normative data for a normal version of the internal body element.

3. A non-invasive process according to claim 1 wherein the baseline data is acquired from a previous scan of the patient.

4. A non-invasive process according to claim 1 further comprising the steps of:

providing a fluorochemical in the vicinity of the internal body element to be scanned to enhance the scanned image data; and

scanning the human's or animal's body.

5. A non-invasive process according to claim 4 wherein the fluorochemical is placed in the body element being scanned.

6. A non-invasive process according to claim 4 wherein the fluorochemical is placed around the body element being scanned.

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7. A non-invasive process according to claim 4 wherein the fluorochemical has a high viscosity, the process further comprising the step of comparing a wall structure of the selected portion of the scanned data to a wall structure of the selected portion of the baseline data.

8. A non-invasive process according to claim 1 the process further comprising the steps of:

comparing the selected portions of the scanned data and the baseline data; and

determining if an abnormality exists in the selected portion of the scanned data based on the comparison;

wherein the step of displaying involves displaying only the selected portions of the scanned and baseline data when an abnormality exists in the selected portion of the scanned data.

9. A non-invasive process according to claim 8 wherein the selected portion of the scanned data includes a bronchiole generation in a lung and wherein the step of comparing includes comparing frequency and impedance distributions for the selected portions of the scanned and baseline data.

10. A non-invasive process according to claim 1 wherein the internal body element is a lung, the process further comprising the steps of:

selecting a portion of the processed image data representing a desired segment of the lung;

selecting a portion of the baseline data;

the selected portions representing the same segment of the lung; and

comparing the selected portions of the data.

11. A non-invasive process according to claim 10 wherein the selected portions represent a bronchiole generation.

12. A non-invasive process according to claim 10 wherein the selected portions represent a bronchiole.

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13. A non-invasive process according to claim 8 wherein the selected portion of the scanned data includes a bronchiole in a human's lung, wherein the step of comparing includes comparing scanned data for successive bronchiole generations, and wherein an abnormality is determined when the cross-sectional diameters of the bronchiole on successive generations become smaller.

14. A non-invasive process according to claim 8 wherein the selected portion of the scanned data includes a bronchiole in a human's lung, wherein the step of comparing includes comparing scanned data for successive bronchiole generations, and wherein the step of determining includes forming a ratio of selected parameters of the bronchiole and comparing the ratio to a ratio of selected parameters of the baseline data.

15. A non-invasive process according to claim 1 wherein the scanned data includes scanned data representing the lung in at least two states.

16. A non-invasive process according to claim 15 wherein the at least two states of the lung represent different pressure conditions.

17. A non-invasive process according to claim 15 wherein the at least two states of the lung represent a point between normal inspiring and expiring, a point after maximal inspiring, and a point after maximal expiring.

18. A non-invasive process according to claim 1 the process further comprising the steps of:

comparing parameters of the selected portions of the scanned data and the baseline data; and

determining if the differences between the parameters of the selected portions of the scanned data and baseline data is greater than about ± 2 standard deviations from the baseline which may be indicative of an abnormality;

wherein the data that is displayed is the selected portions of the scanned and baseline data where an abnormality may exist.

19. A non-invasive process according to claim 2 wherein the step of providing baseline data includes choosing normative data based on at least one

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parameter associated with the human selected from a group consisting of age, gender, race, height and weight.

20. A non-invasive process according to claim 1 wherein the scanned data includes scanned data representing a lung, the process further comprising the step of determining a total lung capacity, a tidal volume, and a residual volume of the lung for the selected scanned data and baseline data, and wherein the data that is displayed is the total lung capacity, tidal volume, and residual volume for the selected scanned data and baseline data.

21. A non-invasive process according to claim 1 wherein the scanned data includes scanned data representing a lung, the process further comprising the step of determining the airway compliance of the lung for the selected scanned data and baseline data, and wherein the data that is displayed is the airway compliance for the selected scanned data and baseline data.

22. A non-invasive process according to claim 1 wherein the scanned data includes scanned data representing a lung, the process further comprising the step of determining the airway resistance of the lung for the selected scanned data and baseline data.

23. A non-invasive process according to claim 22 wherein the step of displaying the scanned and baseline data includes displaying only the scanned and baseline data when the airway resistance is below the airway resistance of the baseline data.

24. A non-invasive process according to claim 1 wherein the selected portion of the scanned data includes the internal body element before and after delivery of a pharmaceutical agent, the process further comprising the step of comparing the scanned data to baseline data representing standardized dose responses for the pharmaceutical agent that was delivered.

25. A non-invasive process according to claim 9 wherein the step of comparing includes comparing at least one bronchiole parameter for each generation against a bronchiole parameter for the corresponding generation of the

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baseline data to determine if an abnormality exists; and wherein the step of displaying includes displaying data representing specific generations where an abnormality exists based on the comparison.

26. A non-invasive process according to claim 9 wherein the scanned data represents a tracheobronchial tree in a patient's lung, the process further comprising the step of determining a bronchiole diameter for each bronchiole, wherein step of comparing includes comparing the bronchiole diameter for each bronchiole against baseline data for a corresponding bronchiole; and wherein the step of displaying includes displaying data for each scanned bronchiole with a diameter less than the baseline data diameter.

27. A non-invasive process according to claim 10 further comprising the step of summarizing the data for the bronchiole generation, wherein the step of comparing includes comparing the summarized data for the bronchiole generation with corresponding baseline summarized data, and wherein the data that is displayed is the summarized bronchiole generation and baseline data.

28. A non-invasive process according to claim 1 wherein the internal body element is a tracheobronchial tree in a lung and wherein the step of selecting a portion of the processed scanned data includes determining a branch in the tracheobronchial tree which is indicative of a generation.

29. A non-invasive process according to claim 1 wherein the scanned data is computer tomography generated image data.

30. A non-invasive process for analysis of an internal body element of a human or animal body comprising the steps of:

scanning a portion of the body with a scanner to produce imaged data representative of an internal body element;

transmitting the imaged data to a processor;

processing the imaged data into three dimensional data representing the internal body element;

providing baseline three dimensional data related to the internal body element;

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comparing the processed imaged data to the baseline data; and
displaying data reflective of the comparison.

31. A non-invasive process according to claim 30 wherein the body element is a tracheobronchial tree in a lung, wherein the step of comparing includes comparing data for bronchiole on successive generations, and wherein the step of determining includes determining whether cross-sectional diameters of the bronchiole on successive generations become smaller.

32. A non-invasive process according to claim 30 wherein the imaged data is processed into three dimensional volume and functional data, and wherein baseline data is three dimensional volume and functional data.

33. A non-invasive process according to claim 30 wherein the baseline data is from a prior scan of the internal body element of the patient.

34. A non-invasive process according to claim 30 wherein the baseline data is for a normal version of the internal body element.

35. A non-invasive process for analysis of an internal body element of a human or animal comprising the steps of:

receiving scanned data of a portion of a human or animal body which includes an internal body element;

converting the scanned data into three dimensional data representative of the internal body element;

retrieving stored baseline data representing three dimensional data related to the internal body element;

comparing the data representing the scanned internal body element to the baseline data; and

displaying the results of the comparison.

36. A non-invasive process according to claim 35 wherein the scanned data is processed into three dimensional volume and functional data, and wherein baseline data is three dimensional volume and functional data.

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37. A non-invasive process according to claim 35 wherein the baseline data is from a prior scan of the internal body element of the patient.

38. A non-invasive process according to claim 35 wherein the baseline data is for a normal version of the internal body element.

39. An apparatus for non-invasive analysis of internal body elements of a human or animal comprising:

a scanner for scanning a portion of a human's or animal's body, the scanner providing data signals representing an internal body element within the scanned portion of the body;

a processor for receiving the data signals, the processor adapted to create three dimensional data from the data signals, the three dimensional data representing the scanned internal body element, the processor also adapted to receive three dimensional baseline data representing the internal body element, the processor adapted to compare the data representing the scanned internal body element to the baseline data to determine differences between the two, and the processor adapted to output signals reflective of the scanned internal body element data and the baseline internal body element data; and

a display for receiving and displaying the output signals.

40. An apparatus according to claim 39 wherein the internal body element is a tracheobronchial tree in a lung, and wherein the processor is adapted to select a portion of data by locating a branch in the tracheobronchial tree.

41. An apparatus according to claim 39 wherein the baseline data is three dimensional volume and functional data, and wherein the scanned data is three dimensional volume and functional data.

42. An apparatus according to claim 39 wherein the baseline data is normative data representing a normal version of the body element.

43. An apparatus according to claim 39 wherein the baseline data is from a prior scan of the patient's internal body element.

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44. An apparatus according to claim 39 further comprising a storage media for storing the baseline data.

45. A non-invasive process according to claim 6 wherein the fluorochemical is perfluorooctylbromide.

46. A non-invasive process according to claim 1 wherein the baseline data represents an imaged portion of the internal body element before delivery of a pharmaceutical agent and the scanned data represents the internal body element after delivery of the pharmaceutical agent.

47. A non-invasive process according to claim 8 wherein the selected portion of the scanned data includes a bronchiole generation in a lung and wherein the step of comparing includes comparing frequency and resistance distributions for the selected portions of the scanned and baseline data.

48. A non-invasive process according to claim 1 wherein the step of comparing includes comparing frequency and impedance related data distributions for the selected portions of the scanned and baseline data.

49. A non-invasive process according to claim 36 wherein the step of comparing includes comparing frequency and impedance related data distributions for the scanned and baseline data.

50. A non-invasive process according to claim 1 wherein the scanned data is radiographic data.

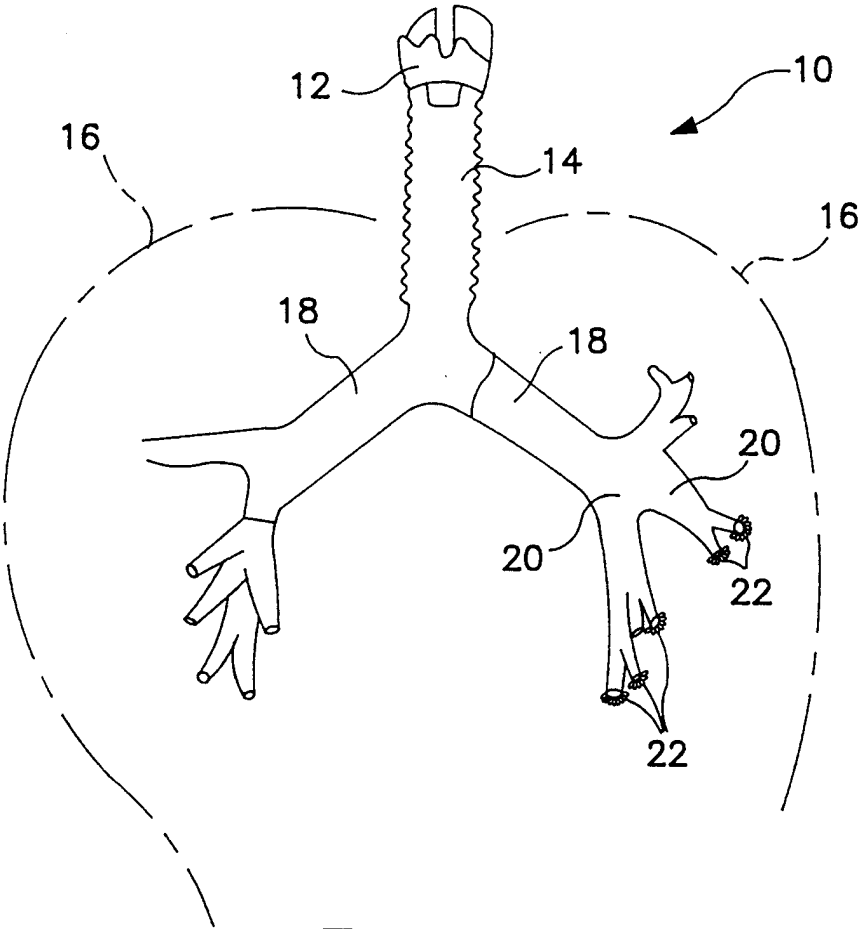


FIG. I

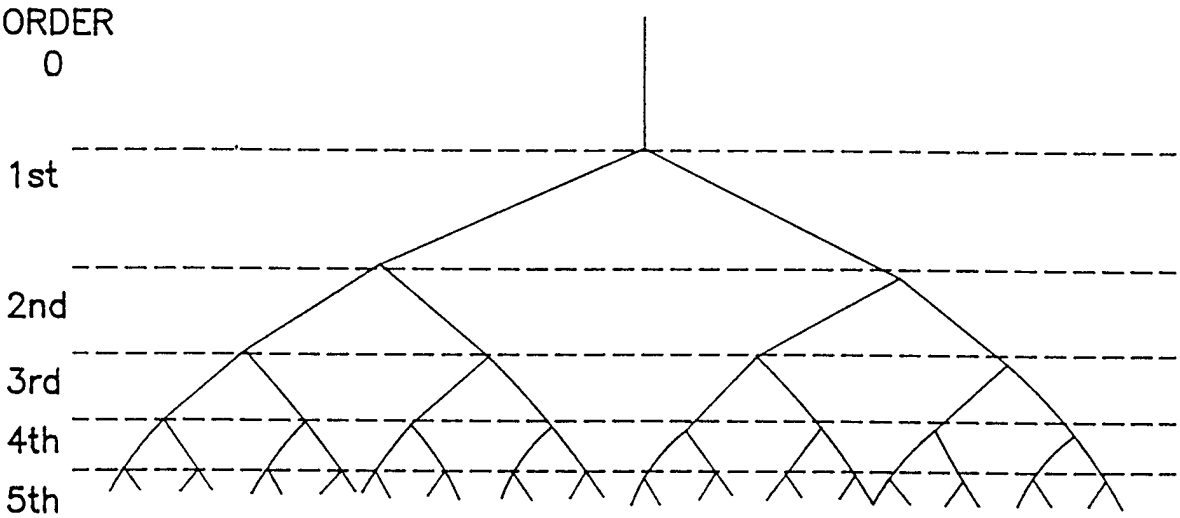


FIG. 2

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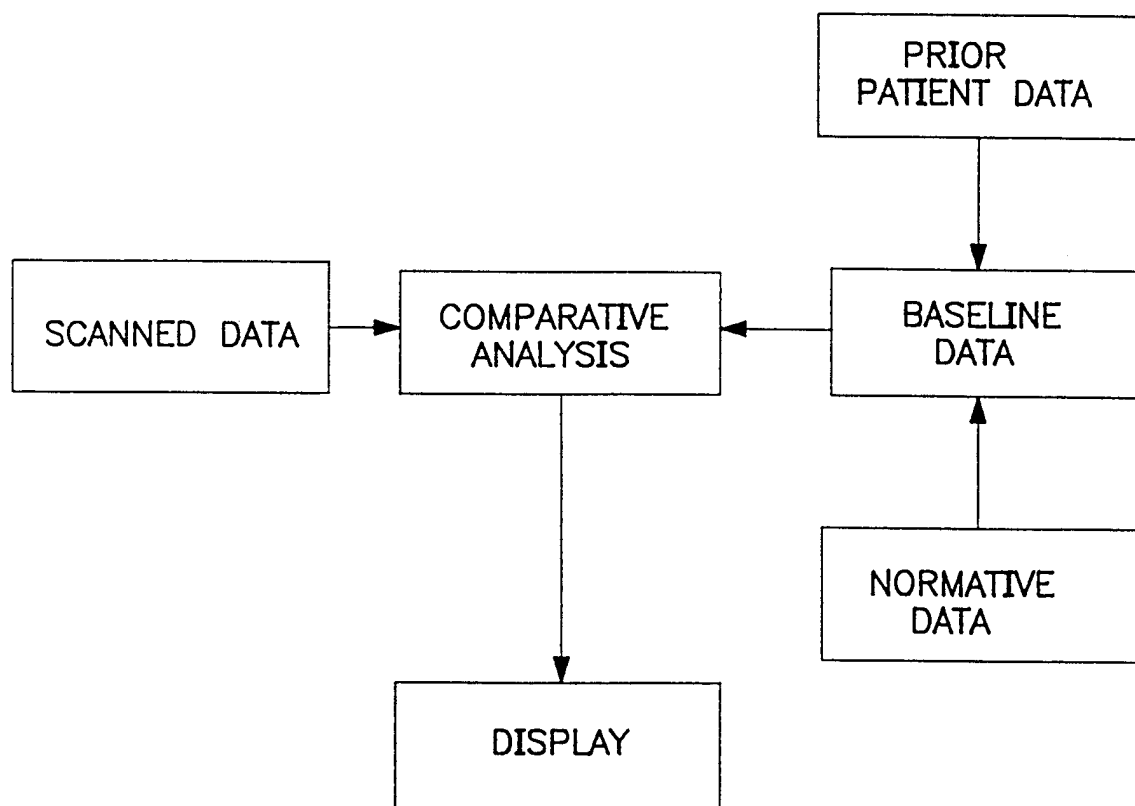


FIG. 3

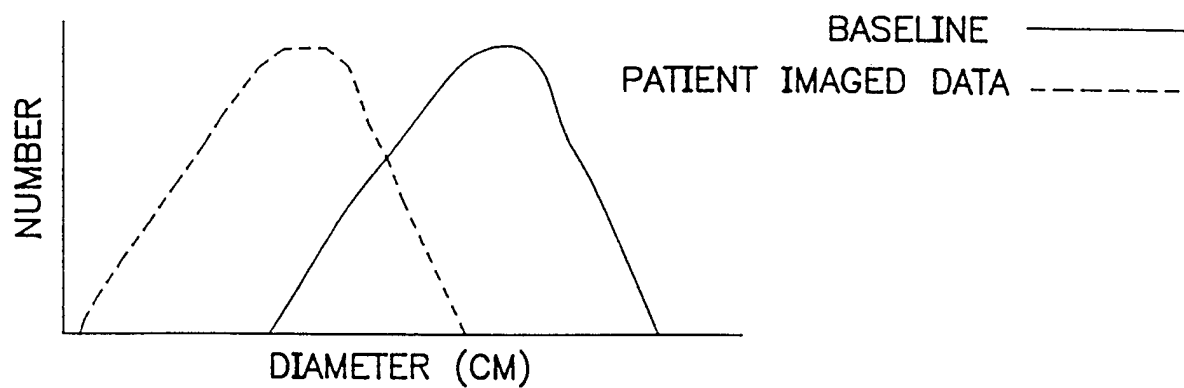


FIG. 4A

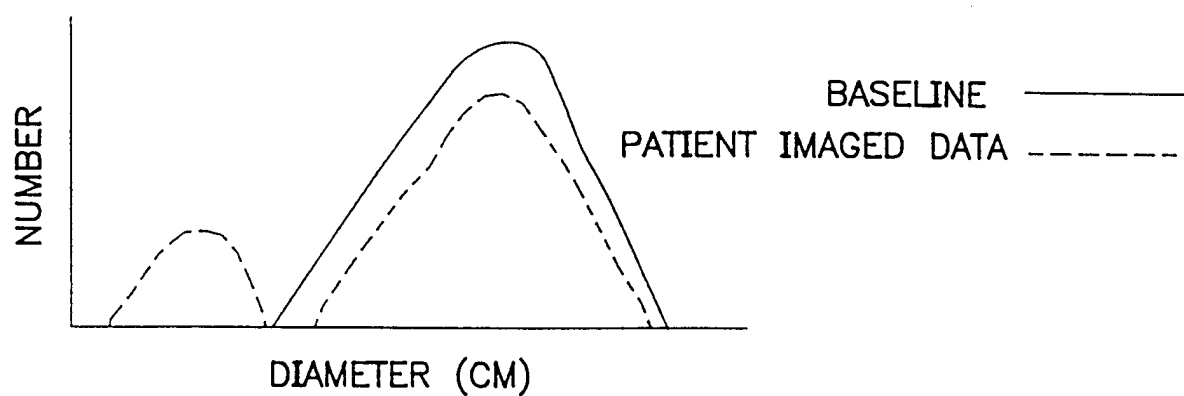


FIG. 4B

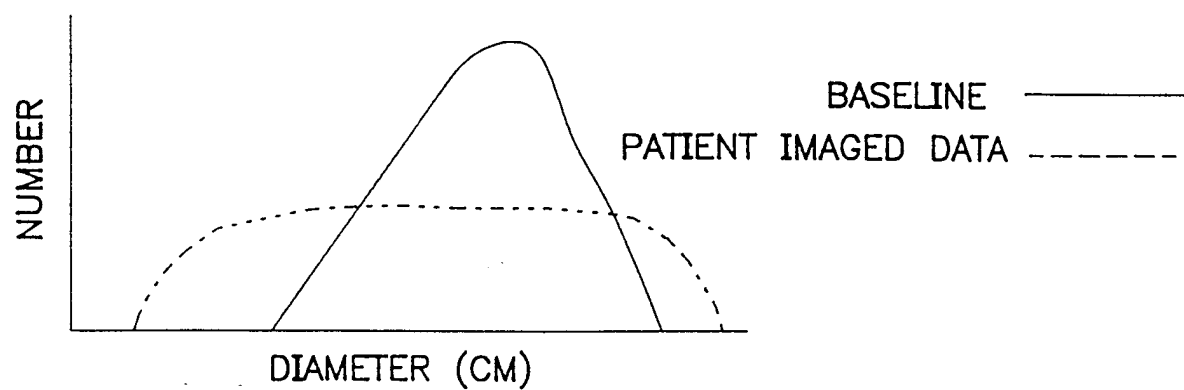


FIG. 4C

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----- LOBAR OR SEGMENTAL DISTRIBUTION

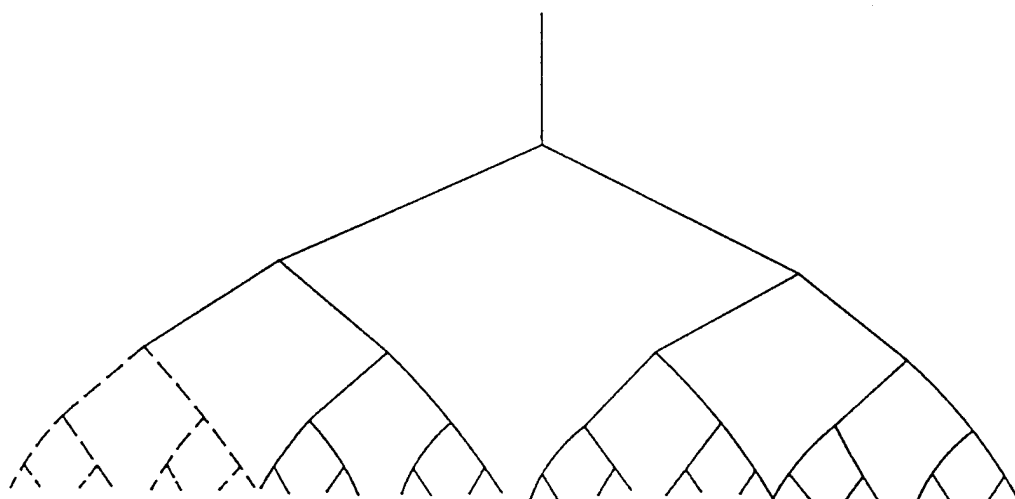


FIG. 5

----- SPECIFIC BRANCH ORDER ABNORMALITY

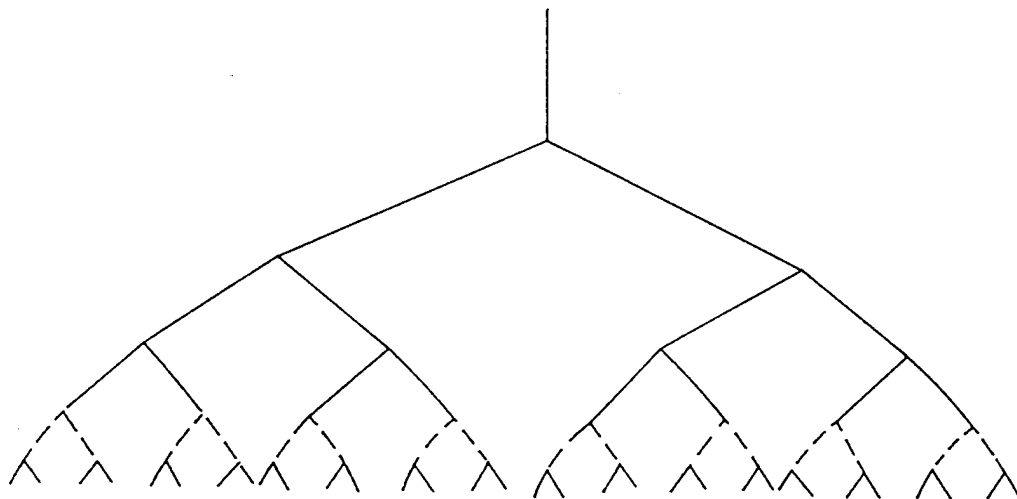


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/03464

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/00

US CL :600/407

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. : 128/913, 916, 920, 922, 923; 382/128, 131, 132, 305; 600/407, 410, 425, 529, 538

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 5,398,684 A (HARDY) 21 March 1995, Abstract, col, 6 line 25 to col. 7 line 30, col. 7 line 59 to col. 8 line 68, col. 9 lines 4-13, col. 11 lines 32-45, col. 15 line 28 to col. 16 line 26, and claims 53-58 and 70.	1-3, 8, 29, 30-39, 41-44, 50 ----- 1-6, 40, 45, 47
X --- Y	VINING et al. Virtual Bronchoscopy Relationships of Virtual Reality Endobronchial Simulations to Actual Bronchoscopic Findings. CHEST/109/2:. February 1996. pages 549-553.	1, 8-15, 27-29 ----- 1-6, 40, 45, 47

☒ 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
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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

10 APRIL 1998

Date of mailing of the international search report

28 APR 1998

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/03464

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	STERN et al. High-Resolution Computed Tomographic Bronchiolography Using Perfluorooctylbromide (PFOB): An Experimental Model. Journal of Thoracic Imaging. 1993. Vol 8. No. 4. pages 300-303.	1-6, 24, 25, 45
Y	US 5,590,651 A (SHAFFER et al.) 07 January 1997, Abstract, Figs. 13 and 18, and col. 18 lines 13-29.	1-6, 24, 25
A, P	US 5,638,458 A (GIGER et al.) 10 June 1997, Abstract, and claims 1-48.	1-50