

First Subject Evaluated with Simulated BION™ Treatment in Posterior Genioglossus to Prevent Obstructive Sleep Apnea

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Abstract—We are using percutaneous electrical stimulation to simulate BION™ activation of posterior genioglossus during sleep to prevent occurrences of obstructive sleep apnea (OSA). Patients with OSA due to tongue prolapse are recruited in this ongoing clinical study for an overnight session in a sleep laboratory. Bipolar hooked wires are inserted percutaneously into the tongue muscle, from under the chin at midline, and used for neuromuscular stimulation. Data are collected with polysomnography and analyzed to compare the efficacy of proposed treatment to conventional CPAP or the untreated state. Encouraging preliminary results from the first study participant are described.

Keywords—BIONs, obstructive sleep apnea, genioglossus, percutaneous, asynchronous, repetitive, intermittent, neuromuscular stimulation.

I. INTRODUCTION

Obstructive Sleep Apnea (OSA) is a common breathing disorder caused by repetitive upper airway obstruction that stops breathing during sleep [1]. The primary mechanism causing the obstruction is the pronounced decrease in muscle tone during sleep [2], permitting the tongue to prolapse, closing the airway during the negative pressure of inspiration. As the airway obstructs, the sleeping patient typically produces a prolonged inspiratory effort, attempting to open the airway. Usually this is not successful and the negative pressure causes the flaccid tongue to seal the airway tighter. Eventually, the patient is awakened by the resulting hypoxia and hypercapnea, muscle tone returns to the tongue and breathing becomes unobstructed. After a few breaths, the patient falls back to sleep, muscles relax, and the obstruction occurs again. The repeated pattern results in loss of sleep and risks hypoxic damage to the heart and brain. Estimated 20 million Americans (50 millions world wide) are afflicted with obstructive sleep apnea [3]. Preventing obstructive sleep apnea will reduce the patient's susceptibility to cardiovascular and cerebrovascular diseases and will improve their quality of life.

We proposed using a single intralingual BION™ microstimulator to prevent airway obstruction in patients with OSA [4,5]. Each BION is a single channel, wireless microelectronic stimulator (2mm diameter x 16mm long) that can be injected into a muscle such as the tongue, as illustrated in Fig. 1. Each BION receives power and digital command data from a nearby RF transmission coil to

produce stimulation pulses with controlled current (0-30mA) and duration (4-512 μ s) [6]. In theory, the BION could be used to stimulate the tongue muscle to move it out of the airway of the sleeping patient and help prevent OSA. Preclinical studies in pigs for 2-4 weeks have shown that BIONs implanted into the tongue are well tolerated and become anchored in a stable position by a thin, biocompatible capsule of connective tissue [4,5].

To assess the feasibility of the proposed BION treatment, we used percutaneous electrical stimulation to simulate BION activation of the genioglossus [5]. We used fine wire electrodes in place of the BION as a study model to gather specific information to support a proposed clinical trial of BION treatment for OSA. The primary objectives of this study are to evaluate: 1. Insertion approach and target search technique; 2. Optimal stimulation site for selective tongue protrusion; and 3. Stimulation parameters that prevent prolapse without disturbing sleep. We here describe the preliminary results from the first study participant in our ongoing clinical study.

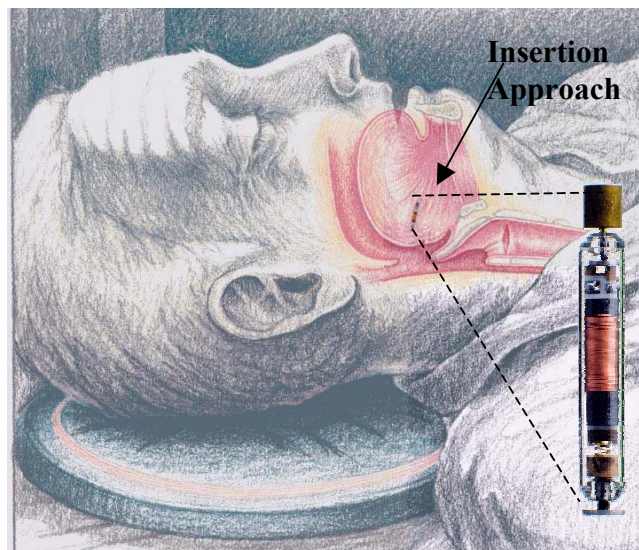


Fig. 1. Closure of the airway during sleep can be prevented by stimulating the tongue protrusor motor units, whose endplates are located near the midline at the posterior genioglossus. A single BION inserted into the posterior genioglossus can be powered and controlled by a transmitting coil located in the pillow.

II. SUBJECTS

A. Screening for Positional Obstructive Apnea

Subjects have been diagnosed at Saint John Sleep Disorders Center with moderate to severe OSA. We screen prospective participants for significant level of positional obstructive apnea (i.e. at least 50% more frequent on their back than on their side) because our current study aims to treat OSA due to tongue prolapse. In addition, enrolled participants must be generally healthy and have normal blood clotting time to qualify for this research study.

B. Patient with Positional Moderately Severe OSA

As of April, 2004, we had studied one patient with a history of heavy snoring and moderately OSA (Supine: 31 episodes/hr, Lateral: 7/hr). He had uvulopalatopharyngoplasty in 1996 with little relief. He has been reluctant to use prescribed high level of CPAP treatment (21cm of H₂O) because it is uncomfortable. He is 44 yrs of age, height of 182 cm and weighs 126 kg.

III. METHODOLOGY

A. Targeting Midline Posterior Genioglossus

Bipolar wire electrodes were strategically placed at the optimal stimulation site in the genioglossus [5]. A fine (27 gauge) hypodermic needle carrying electrodes (50 μ Pt90-Ir10 wires with Teflon insulation) bent back along the shank was inserted into the tongue muscle from under the chin along the midline. During insertion, trial electrical stimulation was used to evoke muscle contraction to guide the needle past the geniohyoid to reach the posterior genioglossus; this method was developed in preclinical studies in anesthetized pigs [4,5]. The desired target site was identified by eliciting tongue motion with relatively weak stimulation pulses. The needle was removed leaving the flexible wire electrodes in place for stimulation during the overnight session, as illustrated in Fig. 2. The ends of the wires were stripped of insulation for 2mm and separated longitudinally by the same distance as the electrodes of a BION. The needle is coated with Parylene, insulating it from the stimulating wire electrodes.

B. Stimulation Administered without Synchronization

We hypothesized that electrical stimulation does not have to synchronize with inspiration to prevent OSA [4,5]. Instead, repetitive intermittent electrical stimulation could be used to recover or maintain airway patency. In this method, we applied a brief train of electrical pulses during an ON period followed by no stimulation during an OFF period. This method of stimulation is repeated in continuous cycles at approximately the natural respiratory rhythm of the sleeping participant, obviating the need for a sensor to synchronize stimulation with breathing..

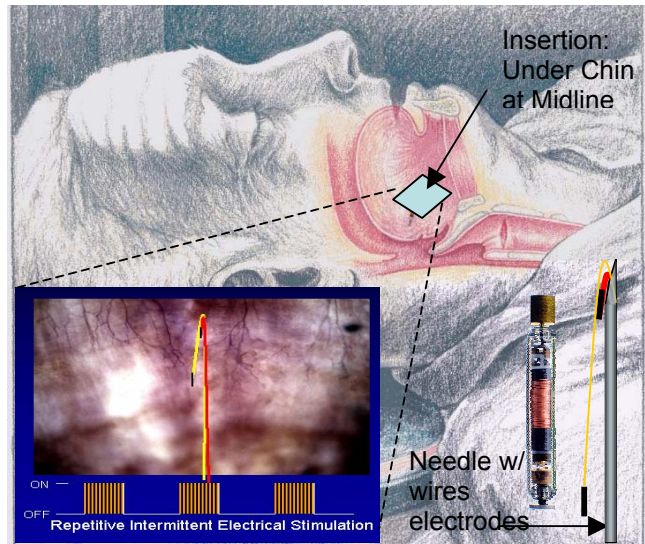


Fig. 2. Bipolar hooked wire electrodes inserted at midline of posterior genioglossus. *Right:* Bare tips of wire electrodes are separated at the same distance as the BION's electrodes. *Left:* Coronal/Horizontal section of wire electrodes in posterior genioglossus at midline. Repetitive intermittent electrical stimulation is used to activate motor endplates to produce the desired tongue movement.

IV. RESULTS

A. Reached Posterior Genioglossus

The needle was inserted at approximately 20° angle to the mandibular floor. During the insertion, the patient reported a sting from the needle with referred pain along the right side of the face and into the ear. At approximately 6 cm depth (see Fig. 3), the geniohyoid contracted at threshold of 0.6mA (200 μ sec pulse width and 2 pulses/second). The posterior genioglossus contraction occurred at about 10 cm depth with threshold of 1.8mA. After removing the needle, there was some residual aching and then a slightly sore throat that gradually resolved. No bleeding or swelling occurred during or after the insertion procedure.

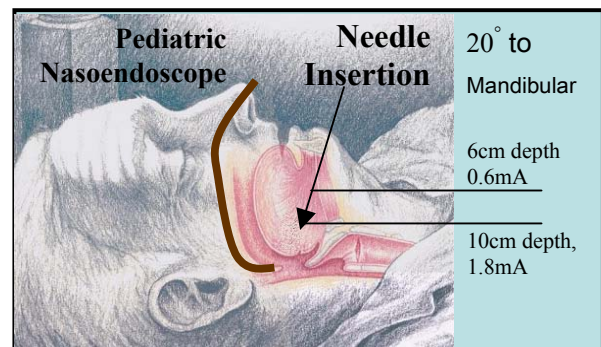


Fig. 3. *Right:* Depth of wire electrodes inserted and minimum currents to elicit muscle contraction. *Left:* Nasoendoscope inserted to observe effect of posterior genioglossus stimulation.

B. Effects of Stimulation

Stimulation initially produced a startle response even at very low levels (1.0mA, 10 pulses/second (PPS) and 200 μ sec pulse width). The patient denied pain but seemed alarmed by the spontaneous motion of the tongue. Repeated stimulation resulted in gradual habituation so that increasing levels of stimulation above motor threshold were well-tolerated. Even at the highest levels used (3.8mA and 10 PPS), the resulting motion of the tongue was, in fact, barely visible from the front of the mouth. A pediatric endoscope was passed nasally to view the back of the oropharynx; stimulation produced a small contraction and anterior displacement confined to the base of the tongue. Stimulation at levels well above motor threshold (3.0mA and 20 PPS) during the night did not wake the subject. Stimulation in the morning at levels (4.5mA and 20 PPS) well above the threshold that originally startled the participant were not even perceived by the participant.

C. Repetitive Intermittent Stimulation Aborts Hypopnea

We were not able to assess the effects of repetitive intermittent neuromuscular stimulation on OSA adequately. The participant had many fewer episodes of apnea during the night than when he was diagnosed. The few obstructive sleep apneas that occurred did not provide enough opportunity to properly evaluate the effects of stimulation. However, stimulation with parameters of 3.0 mA, 200 μ sec pulse width, 20 PPS, and duty cycle of 30% or more were well tolerated and seemed to be effective in preventing the development of hypopnea. Figure 4 captured a repeating hypopnea aborted shortly after the onset of neuromuscular stimulation using the parameters just described. No sleep was interrupted by neuromuscular stimulation.

V. DISCUSSION

The moderate sharp pain experienced during insertion of the needle is consistent with the referred pain to the chorda tympani that occurs commonly during dental anesthesia of the tongue. While tolerable with the fine needle, it may be necessary to use a short term local anesthesia of the sensory (but not motor) innervation of the tongue during implantation of the somewhat larger BION. The response to electrical stimulation is quite interesting. The startle response is not related to pain but rather to perceived motion of a highly mobile genioglossus with a high density of mechanoreceptors. It habituates rapidly and similarly to the awareness of a chip in a tooth once it is clear that it doesn't pose a risk to normal oral function.

The study design calls for up to 12 patients to be studied overnight with percutaneous wire electrodes. When we are confident that the stimulation is well tolerated and effective at preventing and relieving episodes of complete obstructive apnea, we will proceed to definitive implantation of BIONS.

VI. CONCLUSION

The results are preliminary but encouraging. Bipolar hooked wire electrodes were inserted into the target site without difficulty. Stimulation in midline posterior genioglossus produced selective tongue base protrusion. Stimulation does not disrupt sleep. Brief experience using neuromuscular stimulation without synchronizing with breathing (repetitive intermittent electrical stimulation) in posterior genioglossus suggests that it may be useful to prevent development of hypopnea and OSA.

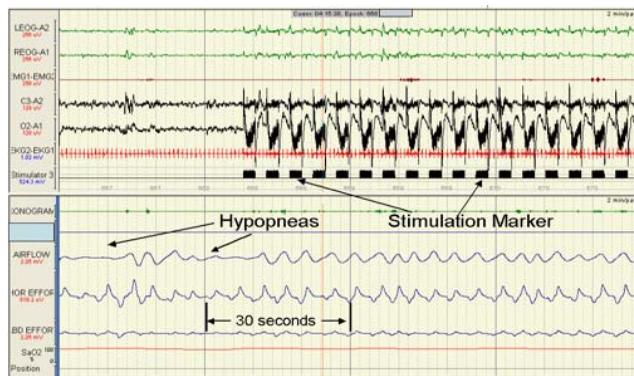


Fig. 4: Screen capture of polysomnogram, illustrating the arrest of developing hypopneas at the onset of neuromuscular stimulation.

ACKNOWLEDGMENT

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