Appendix E

Surgical Procedure

The neck was extended and neck and chest prepared and draped in sterile fashion. The neck incision was a classical cervicotomy for the submandibular space (4 to 5 cm) and followed the inferior border of the mandible in a natural skin crease. Thirteen surgical procedures were performed on the right side and one on the left (this patient had a history of breast cancer and had a Port-a-cath implanted on the right hemithorax). The cervical incision was carried down through the platysma muscle. Dissection was performed between the submandibular gland and the digastric muscle with identification of the posterior and anterior belly of the muscle at its intermediate tendon. Branches of the facial vein were ligated during the dissection, as deemed necessary.

The hypoglossal nerve was identified in Pirogoff's anterior triangle for thirteen patients and in Beclard's triangle for one patient, both in the submandibular triangle. A 2 cm section of the nerve was dissected circumferentially. Next, the electrode cuff was wrapped around the nerve. The cuff electrode was opened with anatomical forceps to pass the leading flap of the cuff under the nerve so that the cuff encircled the nerve with the electrode cable directed posteriorly. The next step was to gently press the nerve into the cuff and allow the cuff to close and surround the nerve.

The leading flap was pulled over the electrode cuff and rotated so the electrode cable was on the superficial surface. Two loops of the lead were made and held in place by passing absorbable suture through the soft tissue in the posterior digastric muscle area and in the infrahyoid space area. These loops acted as a strain relief and protected the cuff from being pulled away from the nerve during healing. The suture around the lead was left loose, so that it could not damage the lead.

The chest incision (4 cm) followed a horizontal line 2 cm beneath the clavicle. Dissection for the placement of the IPG was done superficial to the fascia pectoralis plane, with a depth from the skin of 0.5 – 2 cm. Care must be taken to avoid the superior edge of the IPG being at the level of the incision.

Then the lead was tunneled from the chest to the submandibular incision. The electrode connector was firmly inserted into the inline connector of the IPG until it was fully seated. The connector was secured with a torque-limiting wrench by tightening the setscrew of the inline connector against the locking collar of the electrode connector.

The IPG was turned on and electrode impedance values and tongue movements were measured for all six contacts, one by one (while the wounds were still open).

The wounds were irrigated and haemostasis assured at the end of the procedure. The incisions were closed in layers with absorbable suture for the subcutaneous plane and non-absorbable sutures for the skin. A drain was left in place for 24 hours and patients were observed in the hospital overnight.

Device and Stimulation Details

The aura6000 system consists of an implantable pulse generator (IPG), a hermetically sealed titanium cancontaining the battery and the stimulation system (hardware & software) placed in a subcutaneous pocket in the upper chest, and a multi-contact electrode with an 8mm soft silicone cuff housing six independent contacts (also called a lead), subcutaneously tunnelled and connected to the IPG. The electrode cuff is rolled over the main trunk of the hypoglossal nerve near the middle tendon of the digastric muscle, below and anterior with respect to the maxillary angle. Thus, the six contacts are radially in contact with the nerve and can activate different fibers of the nerve (see Figure 1). Stimulation is sequentially cycled from one contact to

the next, so that the nerve is continuously stimulated (i.e. during both inspiration and expiration, with a tonic rather than phasic type activation) throughout the night but a given nerve fibre is never under continuous stimulation. The IPG is controlled through a remote control device (RCC). The RCC also acts as a charger with charging coil placed over the IPG. Charging the system used in this study required approximately one hour per day. The IPG is activated at bedtime, and stimulation begins after a clinician-programmable delay (most were at 45 minutes), stimulating for 7 hours, or less if the patient stops the IPG.

During titration in awake patients, stimulation started with 100 to 300 μAmp at 200 μs cathodic phase duration at a frequency of 1 and 25 pulses per second to determine sensory and motor thresholds and to choose the best contacts. During therapy, stimulation was cycled between each of the selected contacts, one at a time. Stimulation for a contact would ramp up in 2 s from a sub-threshold value to the programmed amplitude, remain on at the plateau level for a fixed period of time (generally 60 s), then ramp down to the sub-threshold value in 2 s and then terminate. After this the next contact would ramp up, remain on for its plateau duration and then ramp down, and so forth for the remaining selected contacts. At least two contacts would be selected so that nerve fibers activated were stimulated at no more than 50% duty cycle. After the last programmed contact had completed its stimulation pulses the first contact in the series would be activated and this cycle would be continued throughout the night until the end of the therapy period.

The stimulation system is probably more complex than those used in previous studies, since the THN system allows independently controlling the current to each contact, the stimulation frequency, the cathodic phase duration, the number of contacts and whether contacts are activated alone or in combination. In the present study currents from 300 to 1500 μA, stimulation frequencies between 30 and 45 Hz and cathodic phase durations from 200 to 250 μsec were used. Two to 4 contacts were active per patient.

Table E-1

Listing of adverse events

Adverse events	**Number of events**	**Event Description**	**Number of Subjects**
Procedure related events			
Serious AE	1	Defective connector at surgery	1
Simple AE	2	Transient Hemilingual Paresis	2
	1	Transient dysphagia	1
Therapy Related Events			
Serious AE	4	Broken Lead, Defective IPG	3
Simple AE	11	Too strong or too weak sensations, Twiddlers Syndrome	7
Technical AE	45	RCC or Charging Coil malfunction	13