The Feasibility of an Intraneural Auditory Prosthesis Stimulating Electrode Array

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ABSTRACT:

Over this quarter we have accomplished the following tasks:

1. We have continued experimentation on mapping of neuronal activation patterns in AI resulting from acoustic stimulation of the ipsilateral ear, and by electrical stimulation of USEA's implanted acutely in auditory nerve.

2. We have begun a series of preliminary experiments using the University of Utah's new small animal CT scanner to explore its use in identifying the site of the UEA implants in chronically implanted cats.

3. We have completed fabrication of our microcomputer controlled, constant current, back-pack stimulators, and have evaluated the performance of the stimulators

4. We have chronically implanted 10 x 10 UEA's in AI of two additional cats and have begun 60 hour stimulation of these cats with our portable back-pack stimulators.

5. We have met with Dr. Fred Linthicum who advised us on histological procedures for studying auditory nerve pathology.

1. WORK PERFORMED DURING THIS REPORTING PERIOD.

1. We have continued experimentation on mapping of neuronal activation patterns in AI resulting from acoustic stimulation of the ipsilateral ear, and by electrical stimulation of USEA's implanted acutely in auditory nerve.

Our experiments on the mapping of AI are progressing, but at a slower rate than we had hoped. We have been training a new graduate student who is working on this project, and he has yet to fully master the complexities of the surgical approach and the stimulation/recording instrumentation (plus the monitoring and controlling of the cat's status). We have yet to fully record high quality acoustically and auditory nerve evoked activity maps from AI in the same cat. However, we are beginning to be able to make maps of the electrically evoked neural activity patterns from AI as shown in Fig. 1. The stimulation used in this particular experiment consisted of 50 uamp, 80 usec per phase, biphasic currents, with a return electrode located in the fascia near the implant site.

In this figure, we have plotted two sets of eleven maps of the neural activity recorded from AI. Each of the 22 maps shows the multi-unit responses recorded from each of the 100 electrodes in a 10 x 10 UEA that was implanted in AI. The eleven maps in the left group show the spontaneous responses recorded prior to electrical stimulation from each of the eleven active UEA electrodes implanted in the auditory nerve. The eleven maps on the right show the evoked responses recorded in the period from 10 to 30 ms after stimulation though each of the eleven electrodes implanted in the auditory nerve. Thus, each map represents the neural activity in a 20 ms bin. The activity at each recording site is indicated with the color bar.

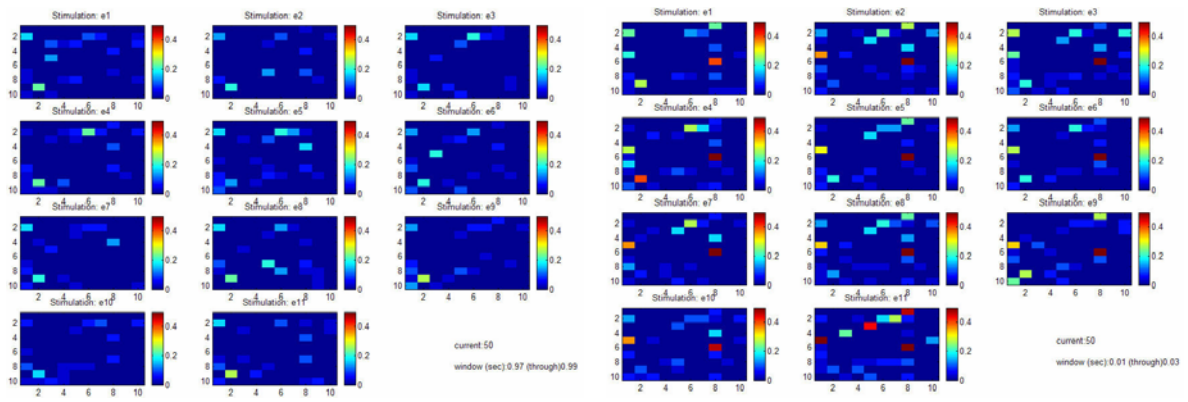

Fig. 1. Neural activation maps recorded in AI with a 10 x 10 UEA. Left – maps recorded in a 20 ms bin prior to electrical stimulation. Right – maps recorded from 10 to 30 ms after stimulation via each of the eleven electrodes implanted in the auditory nerve.

While the effects of electrical stimulation of the auditory nerve are subtle in this experiment (we regard this as a pilot experiment), three observations seem clear: 1) there is a localized increase in neural activity in AI due to the stimulation via the electrodes in the auditory nerve, 2) this activity peaks over the time frame of 10-30 ms post stimulation, and 3) the AI activity profile evoked by stimulation via each electrode implanted in the auditory nerve differs to various degrees. We stress that the data illustrated in Fig. 1 must be regarded as very preliminary, and we look forward to expanding upon these findings in future experiments as our experimental technique improves.

2. We have begun a series of preliminary experiments using the University of Utah's new small animal CT scanner to explore its use in identifying the site of the UEA implants in chronically implanted cats.

While we have enjoyed success in acute implantation of the UEA into the auditory nerve, histological evaluation of the implantation site has been particularly challenging. This is a consequence of the complex location of the auditory nerve that has undergone array implantation. The entire nerve except the surgical opening required for array implantation, is encased in temporal bone. In chronic implants, this surgical opening is fully (or partially) filled with bone cement. Decalcification of the bone is a slow process, and, once decalcified, the removal of the implanted array can result in additional tissue insult and displacement of the tissue in the demineralized bone. To circumvent these problems associated with conventional histological approaches, we have used plain film radiography, conventional CT imaging, and MRI imaging to visualize the electrode placements, hoping that these approaches would provide us with sufficiently good visualization of the auditory nerve and the implanted array to validate the nature of the implantation. We have found that these techniques lacked sufficient resolution to permit good visualization of implanted array and the implant site, and retain the context of the anatomy in the vicinity of the implant site.

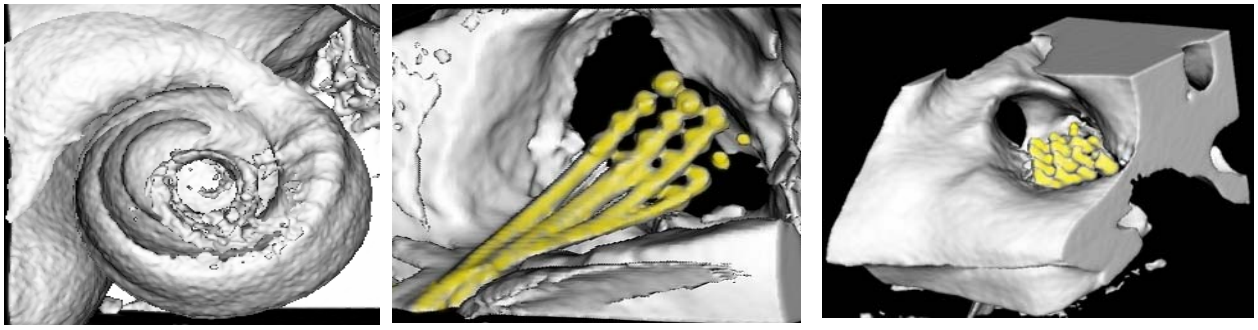

Fig. 2. 3-D rendered mages of the implant site obtained with the University of Utah's new EVS-RS9 small animal, computed tomography (CT) scanner at 27 um resolution. Left panel shows the cochlea. Center panel shows the rear side of the electrode array with its bond pads and lead wires emerging from the opening in the modiolus. Right panel shows the electrode side of the array, penetrating into the nerve, seen through the internal auditory meatus. In the right two panels, the array and lead wires have been colored to facilitate recognition.

All of these problems are greatly mitigated by the recent installation of an EVS-RS9 small animal, computed tomography (CT) scanner for use with sacrificed or live animals. As this scanner has an ultimate resolution of 27 microns, we were hopeful that it would allow 3-D visualization of the cochlear anatomy and the implanted electrode array. Examples of the resolution that is possible with this new scanner are shown above. The left panel of Fig. 2 shows a 3D reconstruction of the cochlea of a fixed cat. All turns of the cochlea can be easily seen. The center panel shows a scan focusing on the back side of the implanted electrode array with its attached lead wires. As seen in this panel, the silicon in the arrays lack sufficient contrast to be easily visualized, as do the implanted nerve tissues. A bottom view of the same electrode array is seen in right panel. It is clear from these latter two scanned images that this electrode array, implanted in the cat for over six months, has been well implanted in the auditory nerve, and that the resolution of the scanner allows visualization of individual lead wires (25 microns diameter). We have only recently begun to work with this scanner, and the images seen above are the first images to come from this new machine. We expect that subsequent experimentation will result in even higher contrast images. However, of particular import is the fact that we have been able to resolve the shanks of implanted electrodes and the metalized tips, but the contrast of these images was too poor for reproduction in this progress report (the metalized tips and shank diameters are, of course, beneath the limits of resolution, but their atomic structure appears to provide a detectable signal). We will use this new small animal scanner to examine the location of all chronically implanted arrays at the time of sacrifice.

While the scanner can be used in living animals, respiratory and cardiac based motion of the anesthetized animals limit the resolution capability of the scanner. Further, the scanner was designed for rats and mice. However, its 9.5 cm bore is sufficiently large to accommodate the decapitated head of an experimental cat. Thus, it is realistic only to consider its use in fixed or fresh feline heads.

3. We have completed fabrication of our microcomputer controlled, constant current, back-pack stimulators, and have evaluated the performance of the stimulators.

Because high channel-count, portable, wearable stimulators were not commercially available, we have developed a number of prototype backpack stimulators for chronic electrical stimulation via implanted Utah arrays. We had originally proposed a wireless telemetered stimulator that would require no user intervention to download stimulation voltages to a computer remotely located from the freely roaming, implanted animal. The complexity of this design and its limited battery life resulted in its being rejected from implementation. We also built a simple, microcontroller based stimulator that had an analog output stage. This design achieved constant current stimulation only by virtue of its operating with high power supply voltages, and the use of current limiting resistances in series with each stimulated electrode. This circuit did not provide adequate current constancy when the electrode resistance changed so this design was also rejected.

We finally developed an 11-channel constant-current stimulator (Fig. 3) that is capable of delivering 100 ua (3 channels), 75 ua (3 channels), 50 ua (3 channels) and 25 ua (2 channels) biphasic pulses at programmable duration and latencies. We designed the printed circuit board so that it could be fitted into a plastic housing that could be attached to a "back-pack" apparatus and worn chronically by a cat implanted with a microelectrode array. Presently, the stimulator is programmed to pulse for 16.0 hours then turn off for 8.0 hours before starting again. These times are programmable. Four of these stimulators have been manufactured as of July, 2003.

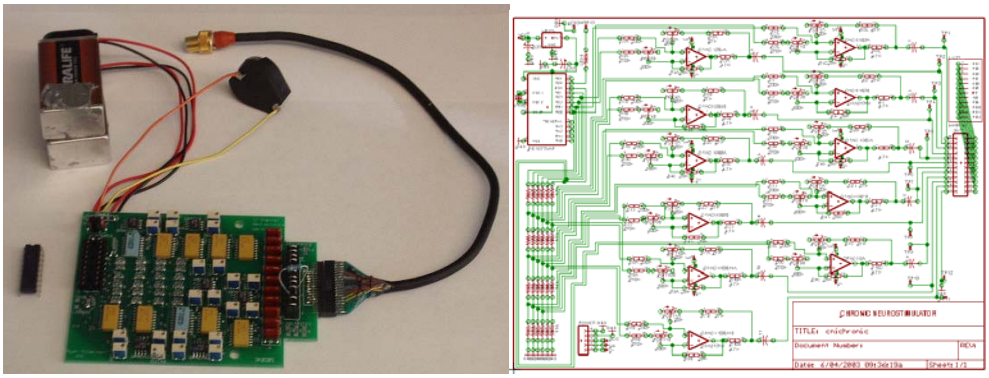

Fig. 3: Photograph of 11-channel constant current stimulator with batteries and connector and stimulator schematic.

Six volts from coin-type lithium batteries is reduced to 4V using a voltage regulator to power a PIC. The PIC has been programmed to send 3 pairs of symmetrically interleaved, 200 us pulses down resistor-divider networks. Eleven gain-identical improved Howland-type current pumps sense the voltages at different points of the resistor-divider networks for the voltage to current conversion. A similar application of this type of circuit was used by Pletto and Van Doren for constant current electrocutaneous stimulation. The operational amplifiers are powered by two 9V Ultralife lithium batteries. A 0.022 uF capacitor follows each Howland to block transmission of any DC current.

The following is a list of important specifications regarding the stimulator, batteries, connector, and housing:

Dimensions: 5.6 x 3.3 x 1.4 inches
Mass: 240 grams

Batteries: 2, 9V Ultralife Lithium, 2, 3V CR2032 Lithium
Battery life: >1 week (16 hours of stimulation per day)
Stimulation parameters: 3 channels 100 ua, 3 channels 75 ua, 3 channels 50 ua, 2 channels 25 ua. Programmable pulse times, durations, latencies.

Fig 4 shows in vitro data taken for channel one (100 ua) of the stimulator connected to a Utah Electrode Array immersed in saline. For load variances of 0 ohms to 100Kohms, the current injected is 100 ua +/- 5 ua for this channel.

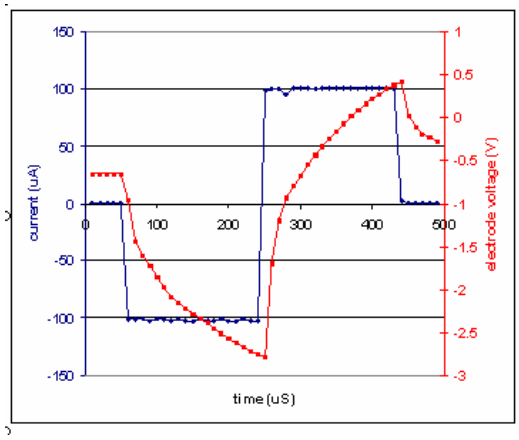

Fig. 4. Waveforms showing 100 ua current (black trace) and voltage (red trace) produced by current injection via UEA.

4. We have chronically implanted 10 x 10 UEA's in AI of two additional cats and have begun 60 hour stimulation of these cats with our portable back-pack stimulators.

Before using our backpack stimulators on electrode arrays chronically implanted in the cat auditory nerve, we are testing out the instrumentation by chronically stimulating cat AI. We are starting in AI because of the relative ease of surgical access to AI, and because histological analysis of AI is much easier than such analysis in auditory nerve.

We have implanted six animals to date and stimulated and have performed a histological analysis on one of these animals. Shown in the table below is an update of the progress we have made in our chronic stimulation experiments.

Cat	Implant Date	Notes
F02-096	Feb 20, 2003	Animal stimulated for 60+ hours with voltage waveform stimulator. Histology inconclusive
F03-023	May 2, 2003	Ti pedestal broke loose from skull twice. Numerous wires broken. No stimulation/histology performed
F03-038	July 11, 2003	Presently being stimulated
F03-039	July 11, 2003	Presently being stimulated

F03-040	July 22, 2003	Recovering from surgery. Will be stimulated
F03-036	July 29, 2003	Animal too small to support pedestal. Surgery terminated. Animal recovering

5. We have met with Dr. Fred Linthicum who advised us on histological procedures for studying auditory nerve pathology.

As we have described above, we have found the histological evaluation of auditory nerves that have been implanted with Utah arrays a difficult procedure due to the thick temporal bone that completely surrounds the entire nerve. Our temporal bone anatomy has been done by a researcher at the Salt Lake City, Veterans Administration Hospital, but he is not highly experienced in temporal bone processing. During this past quarter, we had a visit from Dr. Fred Linthicum of the House Ear Institute, who provide a critique of the techniques we have used in the past, and those that will be used by Dr. Patrick Tresco if our competing continuation proposal is approved. Dr. Linthicum found that our present techniques were typical of those he has used, but he was laudatory of the techniques that Dr. Tresco will be using in our future histological work.

2. PLANS FOR THE NEXT REPORTING PERIOD.

We will focus on the following components of the proposed work.

1. We will continue to map excitation patterns in AI in response to stimulation of the auditory nerve with implanted UEA's.

2. We will extend our fiber excitation independence experiments to stimulation via Utah Slanted Electrode Arrays.

3. We will chronically implant UEA's in the A1 of 5 more cats and evaluate the consequences of 64 hour stimulation using H&E and GFAP staining.

4. We will begin analysis of the implant sites of all sacrificed, implanted cats with the new high resolution, small animal scanner.

3. PUBLICATIONS AND PRESENTATIONS

No new publications have issued over this quarter.

4. LITERATURE CITED

Poletto, C.J. and Van Doren, C.L., A high voltage, constant current stimulator for electrocutaneous stimulation through small electrodes. IEEE Trans Biomed Eng, Vol. 46, 8, 929-936, Aug 1999.