The Feasibility of an Intraneural Auditory Prosthesis Stimulating Electrode Array

Quarterly Progress Report #12

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Abstract:

This is the twelfth quarterly progress report for this project. As will be seen below, our studies are not yet complete, and work is continuing over the next quarter to complete these studies. We report below, the progress we have made over the twelfth quarter.

1. Histological Studies

We have continued processing our ten chronically implanted cats for histological analysis of cochlear nerves. These cats were implanted for periods ranging from 6 months to two years with either untethered electrode arrays, or with electrodes arrays that had lead wires connected to a skull mounted connector. Although our tissue processing is incomplete at this stage, we have found a mixed response to chronic implantation of auditory nerve with the Utah Electrode Arrays. Implanted nerves generally show more tissue disruption than non-implanted, contralateral nerves from the same animal. However, in spite of this disruption, implanted nerves show normal looking auditory nerve fibers in the vicinity of the electrode tips, providing proof-of-concept that penetrating electrode arrays can be chronically implanted in auditory nerve for periods exceeding one year with only minimal impact on the auditory nerve.

2. Effects of electrical stimulation on cellular histopathology

We have concluded our experiments on chronic electrical stimulation of auditory cortex in five cat using our portable stimulator, and are in the midst of conducting immuno-histological analysis of the tissues. Preliminary immuno-histochemical studies of chronically implanted auditory cortex indicated the presence of gliosis around the electrode shanks that was extensive for some electrodes and minimal in others. We have monitored electrode impedances before, during and after the periods of stimulation, and found little, but no consistent changes produced by the current injections. We have designed a multi-channel VLSI stimulator chip that will allow further reduction in the size and weight of future versions of the portable stimulator.

3. Electrophysiological Studies

We have conducted sixteen more experiments on the mapping of the activity in the auditory cortex, evoked by electrical stimulation of the auditory nerve. We have investigated the effect of anesthesia level on the acoustically evoked activity patterns in auditory cortex, and found no significant differences in the patterns with halothane delivered at 0.75, 1.0, 1.25, and 1.5%. Our maps of the characteristic acoustic frequencies of primary auditory cortex have improved, and provide the highest resolution, most complete maps available. Our cortical activation patterns due to direct electrical stimulation of the auditory nerve are less complete. Our activation patterns to date have been evoked by stimulation through an average of 3.6 of the eleven potentially implanted electrodes. We found that increases in current levels injected into the auditory nerve produced increases in the regions of auditory cortex activation. We also found that stimulation of different electrodes implanted in the auditory nerve produced different patterns of activation of auditory cortex. These differential activation patterns demonstrate that selective activation of cortical regions can be achieved via direct electrical stimulation of the auditory nerve with an array of implanted electrodes.

WORK PERFORMED DURING REPORTING PERIOD

1. Histological Studies

One goal of the auditory nerve prosthesis project was the evaluation of the histological consequences of chronic implantation of a penetrating electrode array into the auditory nerve. We have chronically implanted 10 cats with 3 x 4 (12 electrode) Utah Electrode Arrays, allowed them to free roam in gang housing conditions, and have sacrificed them at periods from 6 to 24 months, post implant. We have processed 5 of these specimens to date. We have fixed the tissues via cardiac puncture, and have harvested the auditory nerves for histological processing consisting of dehydration, Spurr's plastic embedding, prestaining with 2% osmium in 0.1 M NaCacodylate buffer, 3 micron serial sectioning, and poststaining with toluidine blue in 1% sodium borate. We have harvested both implanted and unimplanted nerves (used as control tissues).

All aspects of tissue processing have proven to be more difficult than anticipated. Damage to some nerves was associated with the harvesting of implanted nerves. We attempted to produce minimal mechanical force on the nerve during removal of it and the implanted electrode array from its bony surroundings. As the nerve is quite curved and short (on the order of 2 mm), obtaining sections normal to the fiber axes was problematic. Our tissue embedding, in spite of an extended infiltration period, has also proven to be variable, and in the first two specimans, we did not have good preservation of the center of the nerve. However, in a number of samples, we were able to get fairly well infiltrated, fairly well stained sections.

Sections through unimplanted auditory nerve

An example at various magnifications of one unimplanted auditory nerve is shown in Figure 1.

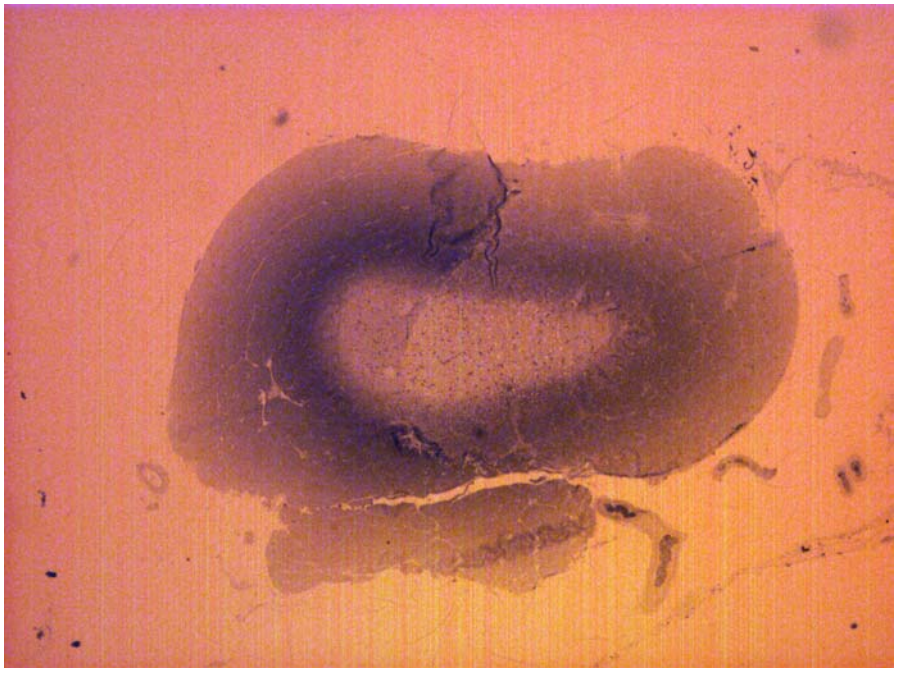

Figure 1a – Section of auditory nerve, contralateral to implant site, 4X.

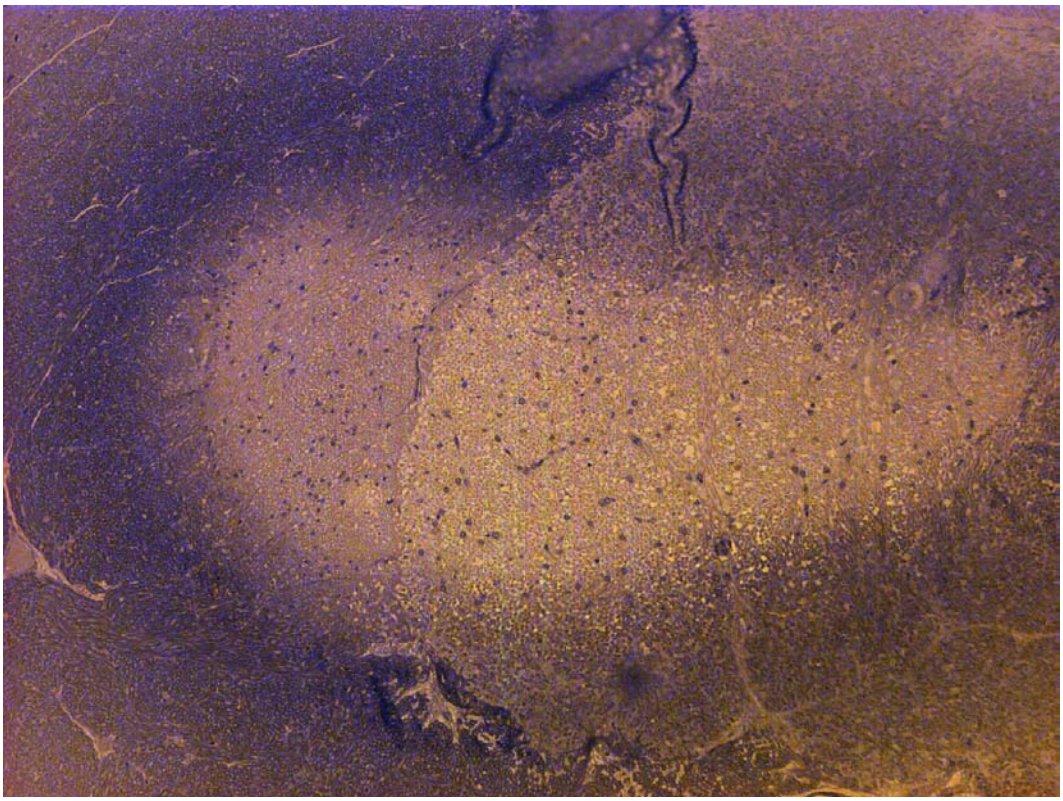

Figure 1b – Section of auditory nerve, contralateral to implant site, 10X

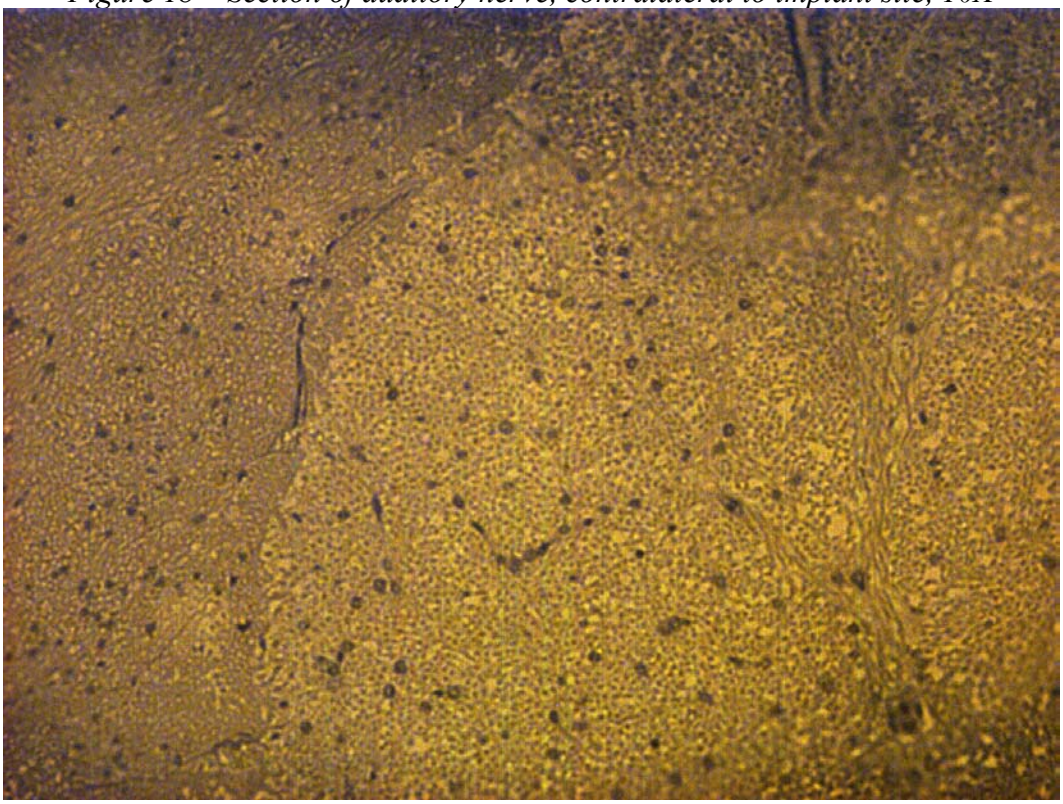

Figure 1c – Section of auditory nerve, contralateral to implant site, 20X.

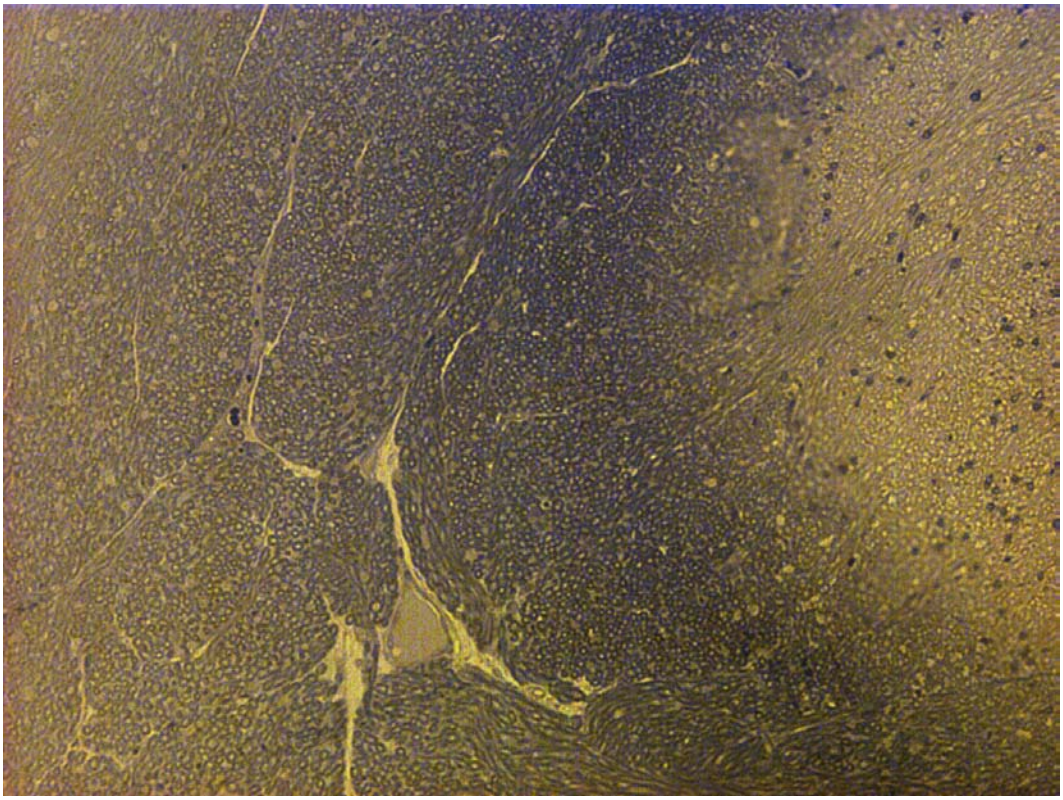

Figure 1d – Section of auditory nerve, contralateral to implant site, 10X.

As seen in these micrographs, the general organization of the tissue has been preserved, with normal, myelinated axons distributed throughout the nerve.

Sections through implanted auditory nerve

The results from our histological processing of our implanted nerves was also complicated due to the presence of the array in the implanted nerve. As the lead wires connecting the array were fully encapsulated in the surrounding bone, array removal from the bone often resulted in tissue disruption. However, in a number of animals, we were able to successfully remove the nerve with minimal harvesting insult. Examples of an implanted nerves from two implanted cats are shown in Figure 2. In these panels, we show results from two implanted nerves, but with sections through different electrode tracks. The panels show electrode tracks at various magnifications and with sections coaxial with the electrodes and oblique to the electrodes.

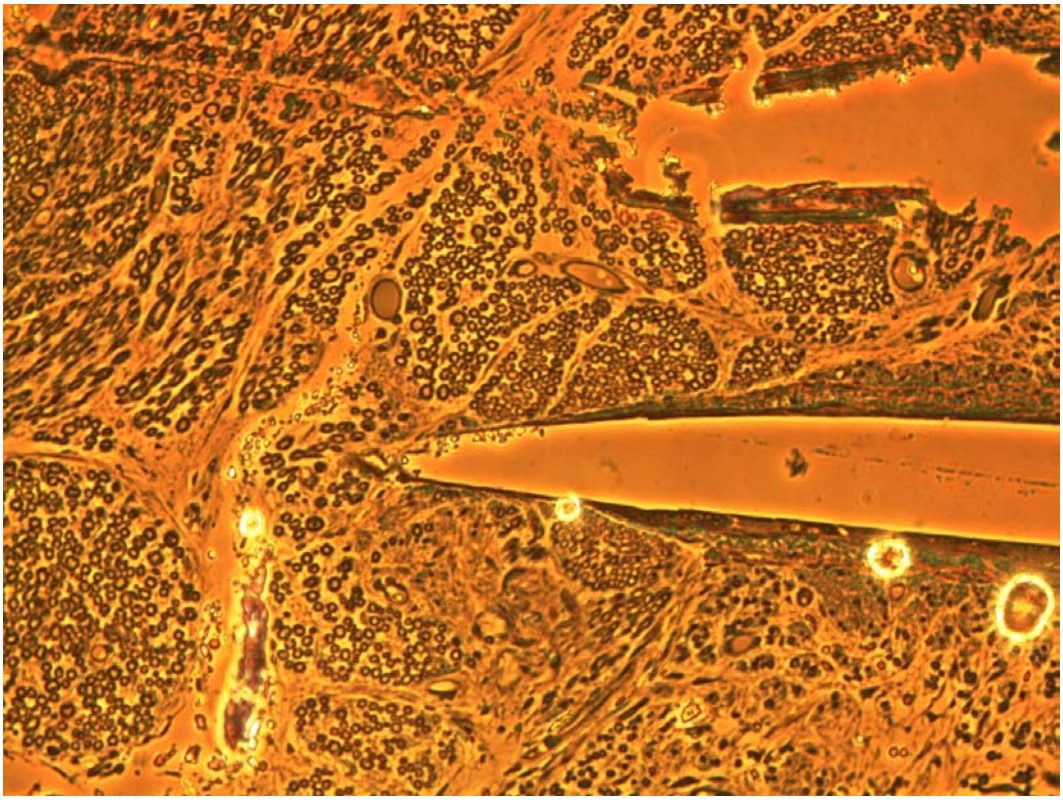

Figure 2a – Coaxial section of implanted nerves, showing electrode tip, 20X.

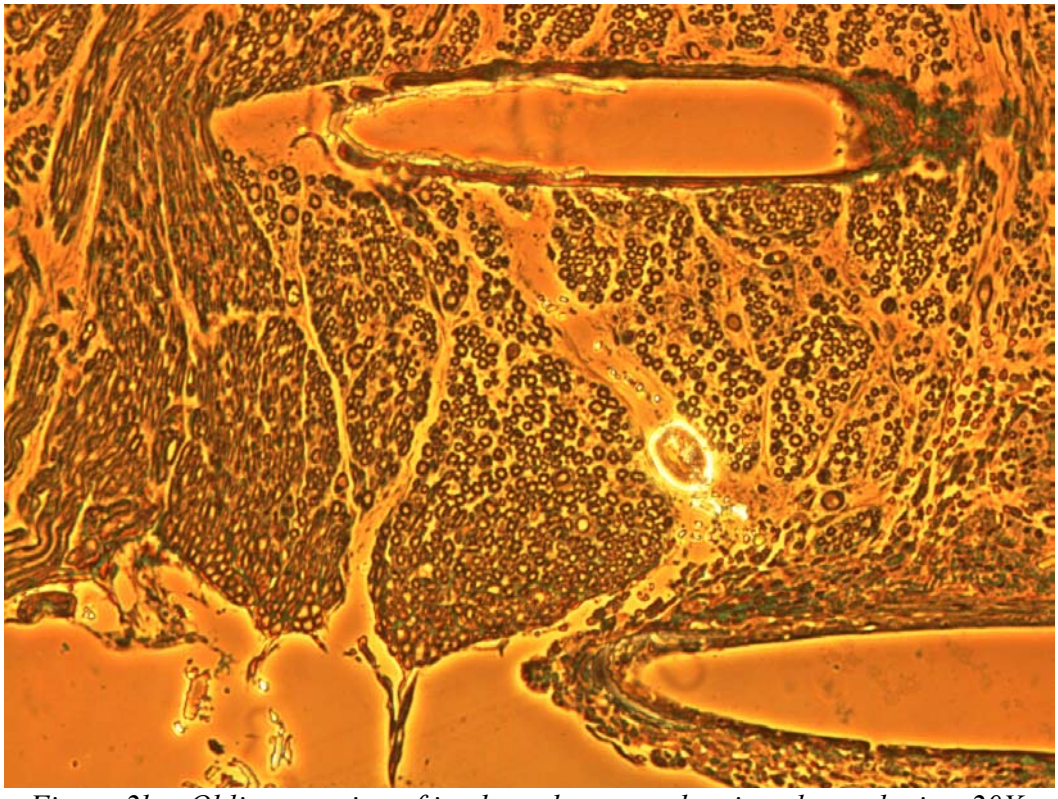

Figure 2b – Oblique section of implanted nerves, showing electrode tips, 20X.

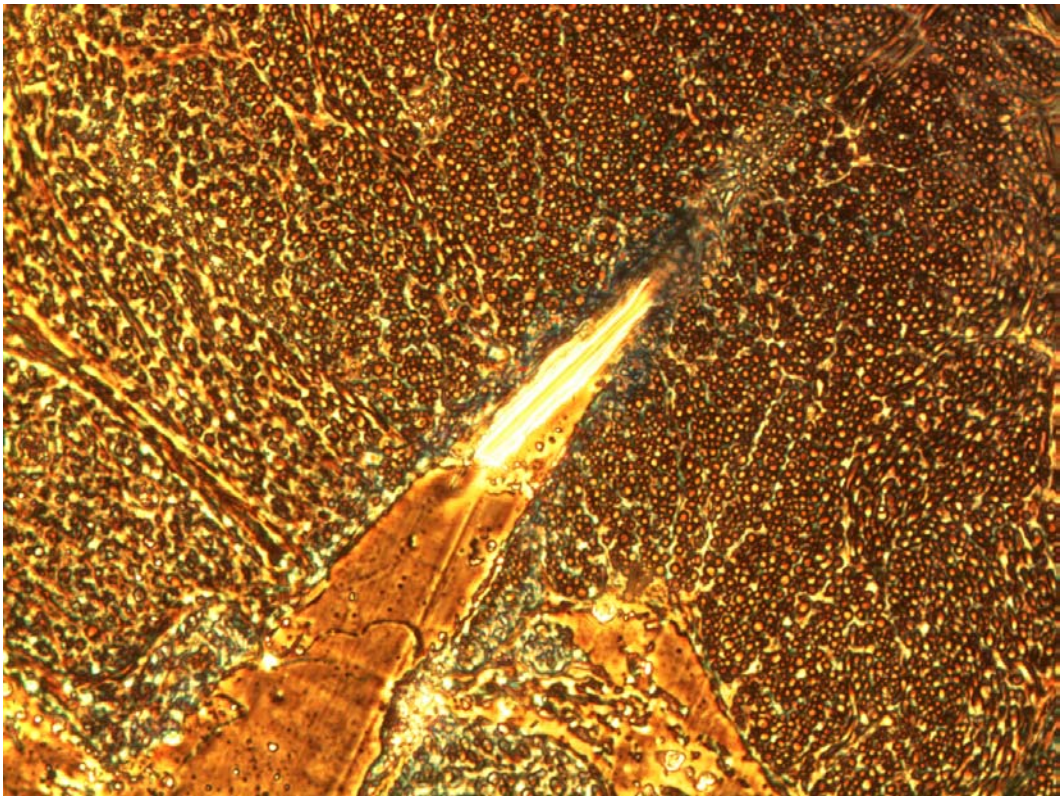

Figure 2c – Coaxial section of implanted nerves, showing electrode tips, 20X.

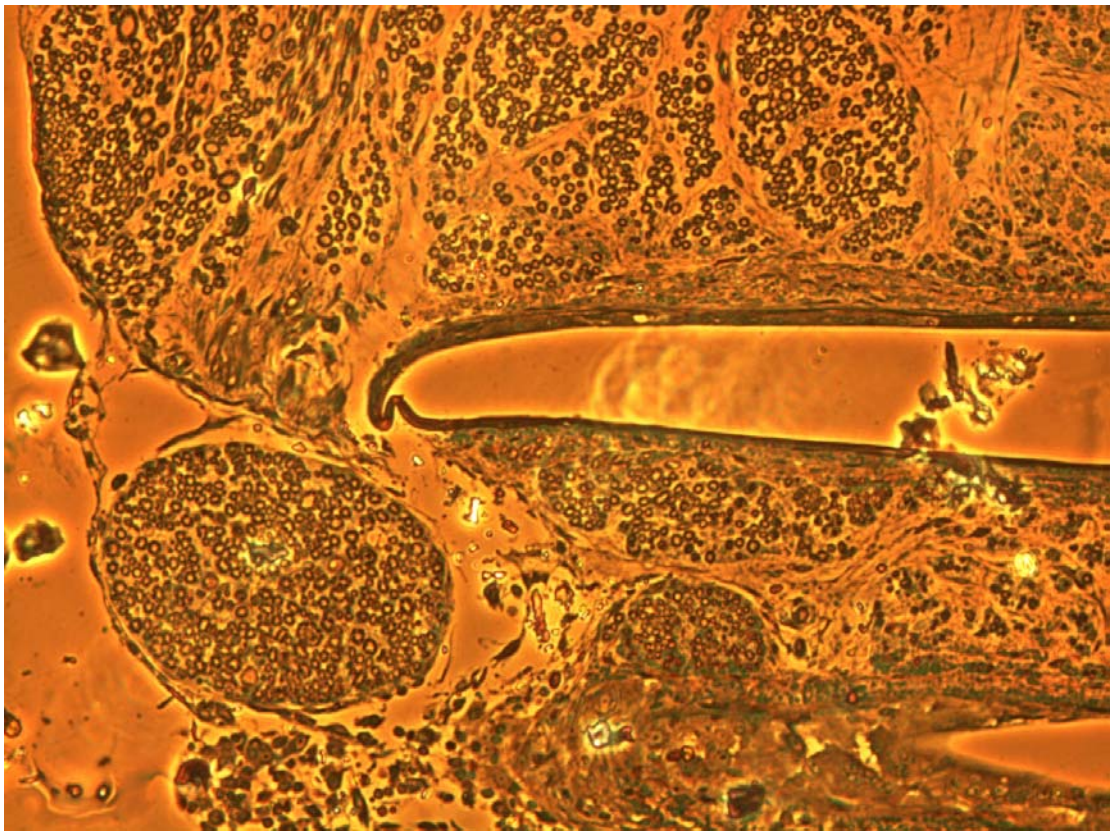

Figure 2d – Section of implanted nerves, showing electrode tips, 20X.

In the five samples of implanted auditory nerves we have processed to date, there was evidence of auditory nerve disruption due to the implantation process (or possibly due to the tissue harvesting procedure). In all five samples, the number of auditory nerve fibers has been reduced, and there has been significant gliosis in the region of the implant. However, in spite of this implant induced pathology, we were able to find normal appearing fascicles, and normally myelinated axons in regions of the nerve around the electrode tips. The micrographs in these panels provide a good summary of the effects of chronic implantation. Quite normal appearing axons are seen near the tips and along the sides of the electrodes. However, as seen in the figures, adjacent to the sides of the electrode, further away from the tip there is an apparent localized cellular response to the electrode, possibly consisting of microglia. Because of the possibility that micromotion occurred between the array and the nerve during the harvesting of the tissues, an alternative explanation of the lack of cellular response near the tip of the electrode is that the electrodes were pushed further into the nerve during harvesting.

While our final conclusions regarding the histopathological response to electrode implantation must wait until we have finished processing the remaining 5 samples, the preliminary evidence from these five cats suggests that very long term chronic implantation of penetrating electrodes into the auditory nerve can damage a significant number of axons, but that a large subset of axons remain that could be stimulated with current injections via the implanted electrode array.

2. Effects of electrical stimulation of auditory cortex on cellular histopathology

Our contract required that we perform histological analysis of auditory nerve that had been chronically stimulated for a total of 60 hours. Our initial focus in stimulation experiments was the auditory cortex for the following reasons. The cerebral cortex is much less complex than the anatomical organization of the auditory nerve. We can implant 100 electrodes in the cerebral cortex, providing greater control tissues than could be obtained from the relatively small number of electrodes that are implanted in the auditory nerve. We have no anatomical data on the effect of chronic current injections on any neural tissues. Finally, we needed to validate the backpack stimulation system. Based upon a positive, controlled study of the effects of chronic current injections into cerebral cortical tissue, we could then proceed to stimulation of the auditory nerve.

In order to accomplish chronic electrical stimulation, we have designed and built chronic 'backpack' multi-channel stimulators, chronic backpacks to carry the stimulators, developed a lead wire system to convey stimulus signals to the implanted array, implanted the auditory cortex of four cats with 10 x 10 Utah Electrode Arrays, stimulated three of these animals for 60 hours each, and have sacrificed the animals for histological evaluation. As we were also interested in understanding the consequences of 'tethering' produced by the lead wires connecting the array to the skull mounted connector, each implant contained an identical 10 x 10 electrode array (with lead wires) that was implanted in the contralateral hemisphere, but that was unstimulated. Cats were allowed complete recovery from all aspects of the implantation procedure before they underwent chronic stimulation. This recovery period was from 6 to 8 weeks.

The backpack stimulator was designed to provide 11 channels of constant current stimulation. Three of the channels were designed to provide 100 microamp pulses, three provided 75

microamp pulses, three provided 50 microamp pulses, and 2 provided 25 microamp pulses. Thus, eleven of the 100 electrodes implanted in auditory cortex were stimulated, allowing the remaining 89 electrodes to act as non-stimulated control electrodes. The 100 Hz stimuli were biphasic, 200 microsecond duration, with no interphase period. The backpack stimulators worked flawlessly throughout all stimulations.

We had planned to perform the stimulation of the cats all at the same period. However, the interconnection between the backpack stimulator and the skull mounted connectors proved to be an attractor of the cat's attention, and the implanted cats would usually manage to disconnect themselves if they were not attended. Thus, all periods of stimulation were conducted in a serial fashion, and done under constant, direct supervision. When the cats were supervised, they did not attend the interconnection and the period of stimulation could be completed without incident. In the final three cats that were stimulated, there was no behavioral evidence of any discomfort or startle due to the electrical stimulation.

Because of the time required to complete these sequential stimulations, we have not yet completed the histological analysis of the stimulated tissues as of this quarterly report. We expect to complete the histological analysis over the course of the next three months. We present below a tabulation of the impedance values for stimulated electrodes, measured before, during and after implantation and stimulation.

Cat ID	Implant Date	Period of Stimulation	Impedance range at implant	Mean Impedance Prior to stimulation	Mean Impedance at explant
F03_069	11/30/03	No stimulation	Animal pulled out	Connector system	During recovery
F03_051	12/17/03	1/27/04-2/6/04	18K-92K	51K	30K
F03_068	1/22/04	3/16/04-4/6/04	30K-180K	57K	49K
F04-02	2/25/04	4/12/04-4/22/04	27K-70K	57K	47K

As has been shown in other chronically implanted tissues, the impedance of the implanted arrays varied post-implant. Also, consistent with other studies, the impedance changes are quite variable, with some electrodes increasing then decreasing impedance. The impedance changes, monitored at various times post-implant are shown in Figures 3.

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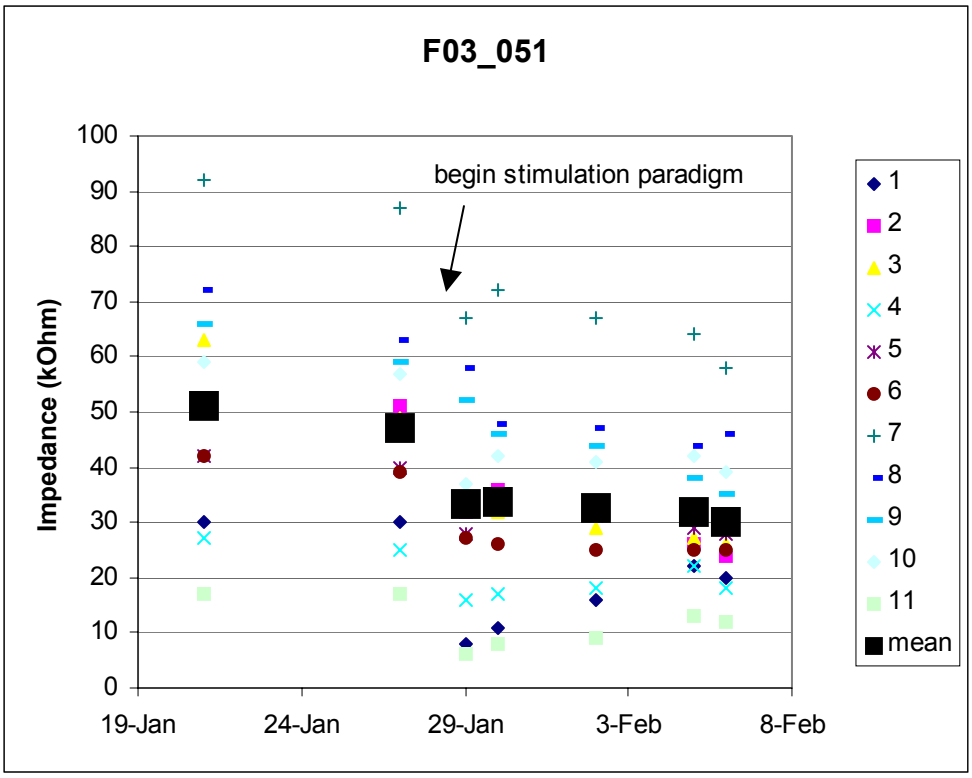
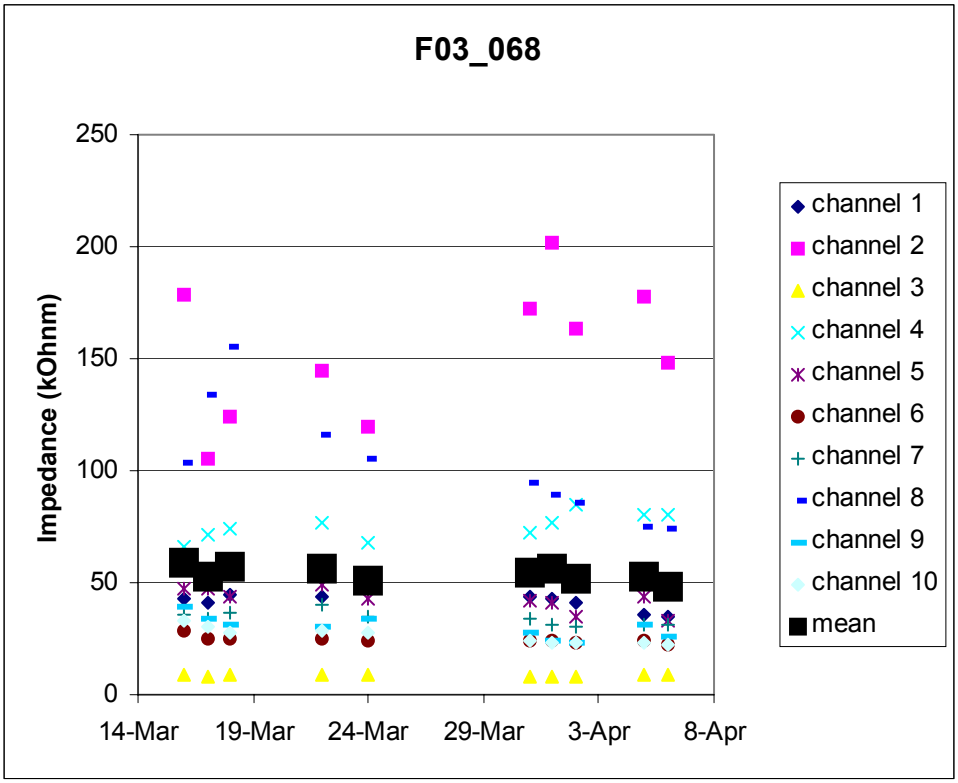

F03_051
Impedance (kOhm)
100
90
80
70
60
50
40
30
20
10
0
19-Jan
24-Jan
29-Jan
3-Feb
8-Feb
begin stimulation paradigm
1
2
3
4
5
6
7
8
9
10
11
mean


F03_068
Impedance (kOhnm)
250
200
150
100
50
0
14-Mar
19-Mar
24-Mar
29-Mar
3-Apr
8-Apr
channel 1
channel 2
channel 3
channel 4
channel 5
channel 6
channel 7
channel 8
channel 9
channel 10
mean

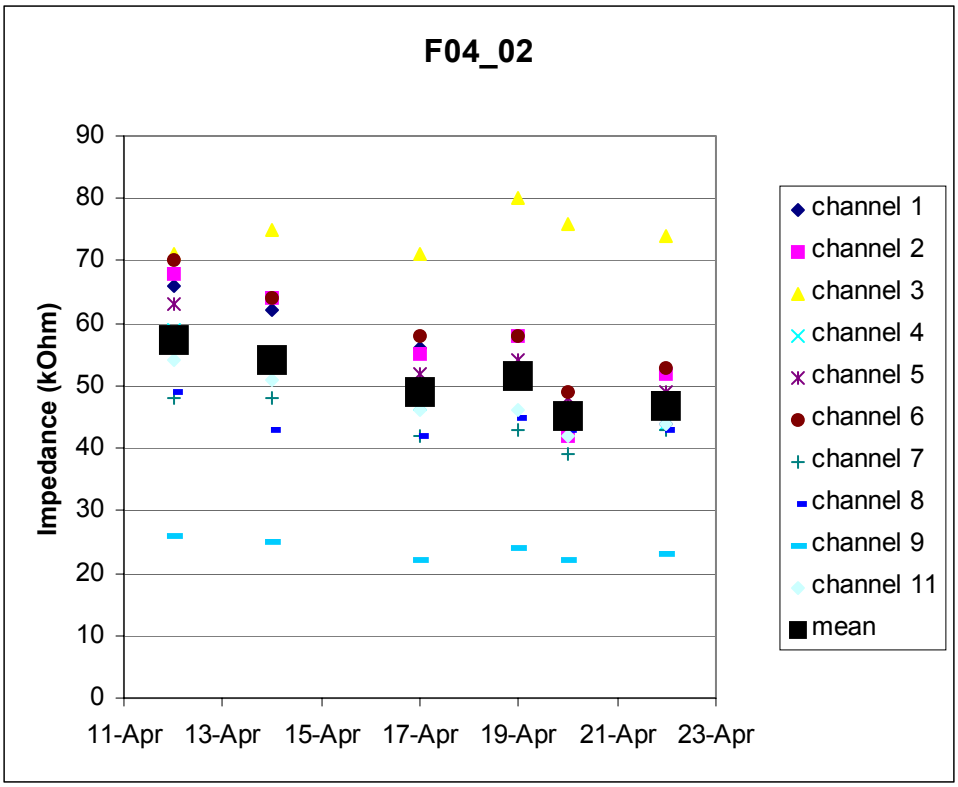


Figure 3 – Impedances of stimulated electrodes at various post-stimulation times.

3. Electrophysiological Studies

A main goal of this contract was to demonstrate the selectivity of auditory nerve stimulation achievable with direct stimulation of the auditory nerve via an array of implanted electrodes. We have done this with overlap experiments using electrically evoked auditory brainstem responses as our index of independence. These experiments, described in a number of previous quarterly progress reports, have shown that currents passed via pairs of electrodes implanted in the auditory nerve excite independent subpopulations of auditory nerve fibers. To better understand the issue of stimulation selectivity, we have attempted to map the neuronal activation patterns in auditory cortex evoked by stimulation via the electrodes implanted in the auditory nerve. Comparison of the acoustically evoked maps with the electrically evoked maps will allow us to ascertain if stimuli delivered via individual auditory nerve electrodes activate localized patterns of cortical activity, and if each auditory nerve electrode activates a unique cortical activation pattern. Over the past quarter, we have conducted sixteen more of such experiments, these experiments are summarized in the table below. Because of the effort we have expended in recording from auditory cortex over the last two years of this contract, we have decided to focus efforts on AI (rather than IC) over this twelfth quarter.

Exp date	Exp #	eABRs	Acoustic Evoked Pattern	Electrical Evoked Pattern	Notes
4/28/2004	34	2 or 3	**Good**	Poor	
4/23/2004	33	3 working	60 Hz contamination	Poor	
4/13/2004	32	N/A	**Good (70%)**		Right ear infected
4/6/2004	31	3 working	60 Hz contamination	**Yes**	
4/2/2004	30	3 working	N/A	**Yes**	No eABRs on right ear, hence the implantation was done on the left ear
3/31/2004	29	*			Brain edema
3/26/2004	28	*			Brain vessel was impinged and caused some hemhorrage
3/23/2004	27	*	**Excellent**		Anesthetic Expt.
3/18/2004	26	6 working	**		
3/12/2004	25	5 working	N/A		No eABRs on right ear, hence the implantation was done on the left ear
3/9/2004	24	*	**		
3/5/2004	23	*	**		
2/26/2004	22	3 working	Only 10 channels good	Yes, but on only a few channels	
2/19/2004	21	3 working	**Excellent**	**Yes**, but not well controlled intensities	
2/12/2004	20	N/A	Some but Poor		This exp was designed for acoustic stimuli
2/3/2004	19	*	**		

(*) Auditory nerve might be damaged from drilling temporal bone, or to poor UEA implantation.
(**) The tips of the 10x10 array might not reach layer 3 or 4 of AI.

The protocol used in these experiments was as follows. We first recorded acoustically evoked ABR's to evaluate the quality of the animal's auditory pathways. We then implanted a 3 x 4 electrode array in the auditory nerve using the trans-bullar surgical access we have described in previous quarterly reports, and measured eABR's evoked with each implanted electrode. This allowed us to evaluate the quality of the auditory nerve implantation. As indicated in the above table, in experiments where we were able to record eABRs we typically were able to record eABR's evoked by stimulation via 3 to 4 of the implanted auditory nerve electrodes (the remaining electrodes were unable to evoke eABRs with currents up to the 170 microamp limit we imposed). The implanted array and lead wires were cemented in the auditory nerve with bone cement, the bulla was filled with silicone to immobilize the lead wires, and the connector was sutured to the skin near the implant site. The animal was then turned over, the auditory cortex contralateral to the implanted nerve was exposed, and a 10 x 10 electrode array implanted in the cortex. We then performed acoustic stimulation of the implanted ear to demonstrate functionality of the nerve and to map the characteristic frequencies of auditory cortex. This was followed by mapping of auditory cortex using electrical stimulation with currents passed through each of the functioning auditory nerve electrodes.

In our research plan, we had proposed to implant 3 x 4 Utah Slanted Electrode Arrays (USEAs) in the auditory nerve. However, based upon our anatomical studies, it became clear that the region of the nerve that was to be implanted was highly curved, and that a USEA might not provide the desired access to most fibers in the nerve (the curved nerve might result in many or most of the USEA electrodes being implanted in a single functional plane in the nerve. For this reason, we decided to implant conventional, 1 mm long, 3 x 4 equal length Utah Electrode Arrays (UEAs) in the nerve. We believed that this would increase the likelihood that the electrodes would not reside in a single functional plane. All experiments conducted in this quarter were thus 3 x 4 UEAs.

As indicated in this table, it has proven to be difficult to record both acoustically evoked responses and electrically evoked responses in the same experiment. In some experiments we were able to make excellent, high spatial resolution acoustic maps of the auditory cortex but we were unable to achieve quality electrically evoked maps. In other experiments, we were able to make electrically evoked maps, but our acoustically evoked maps were unsuccessful.

Acoustically evoked cortical activation patterns.

Figure 4a shows an example of the tuning curve generated from responses recorded from one electrode. Acoustic stimuli consisted of 50 msec shaped tone bursts, presented once per second in a totally random sequence (all frequencies and intensities were presented before the sequence was repeated). The abscissa plots frequency from 1 to 30 kHz, on a logarithmic scale. The ordinate plots the intensity of the acoustic stimulus in 8 logarithmic steps, from just below threshold for the most sensitive neurons recorded to 1000 times this threshold (a 60dB range of intensities). The color of each pixel reflects the magnitude of the neural response evoked by each particular frequency and loudness (with blue representing no responses in the interval 0 to 25 msec, and red indicating the maximal response in this interval). Each tone was delivered from 20 to 30 times, PSTH's were averaged, and the tuning curves were generated from this averaged data. The tuning curve in Figure 4a shows a prominent characteristic frequency at about 12 kHz, and a secondary, less sensitive peak at about 1.8 kHz that appears when the stimulus is quite loud. In many of our acoustic cortical maps, we see units recorded at a number of electrodes that manifest such multi-peaked tuning curves.

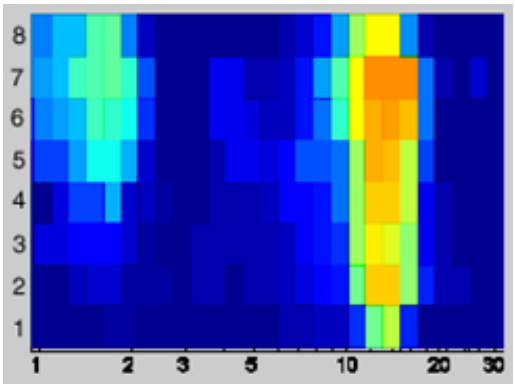


Figure 4a – Tuning curves generated from responses recorded in auditory cortex to acoustic stimulation of the contralateral ear (on the side opposite to that implanted with an array implanted in the auditory nerve). Ordinate plots stimulus intensity (log scale, 0 to 60 dB), and abscissa plots frequency in kHz.

Figure 4a shows the tuning curve from a single electrode. In the time required to acquire sufficient data to generate such a curve, we record responses from all 100 implanted electrodes, and we can use this parallel recorded data to generate 100 such tuning curves as shown in Figure 4b.

Effect of anesthesia level on activation patterns.

Based upon our experience in visual cortex, we were concerned that the depth of anesthesia may significantly influence the activation patterns of the neurons in auditory cortex. We therefore conducted an experiment wherein we varied the halothane level from 0.75, 1.0, 1.25 and 1.5% in an increasing and then decreasing sequence of concentrations. We allowed a 30 min period of equilibration between each change in anesthetic level. Following this equilibration period, we measured the activation patterns evoked by acoustic stimulation. Unlike the situation we have seen in the visual cortex, there were no obvious effects on the cortical activation patterns when changing the anesthetic level over these values. Based upon these findings, we have used a 1.25 % halothane level in all experiments. This anesthetic level provided a sufficiently deep anesthetic plane that ensured the animal would not regain consciousness throughout the entire experiment.

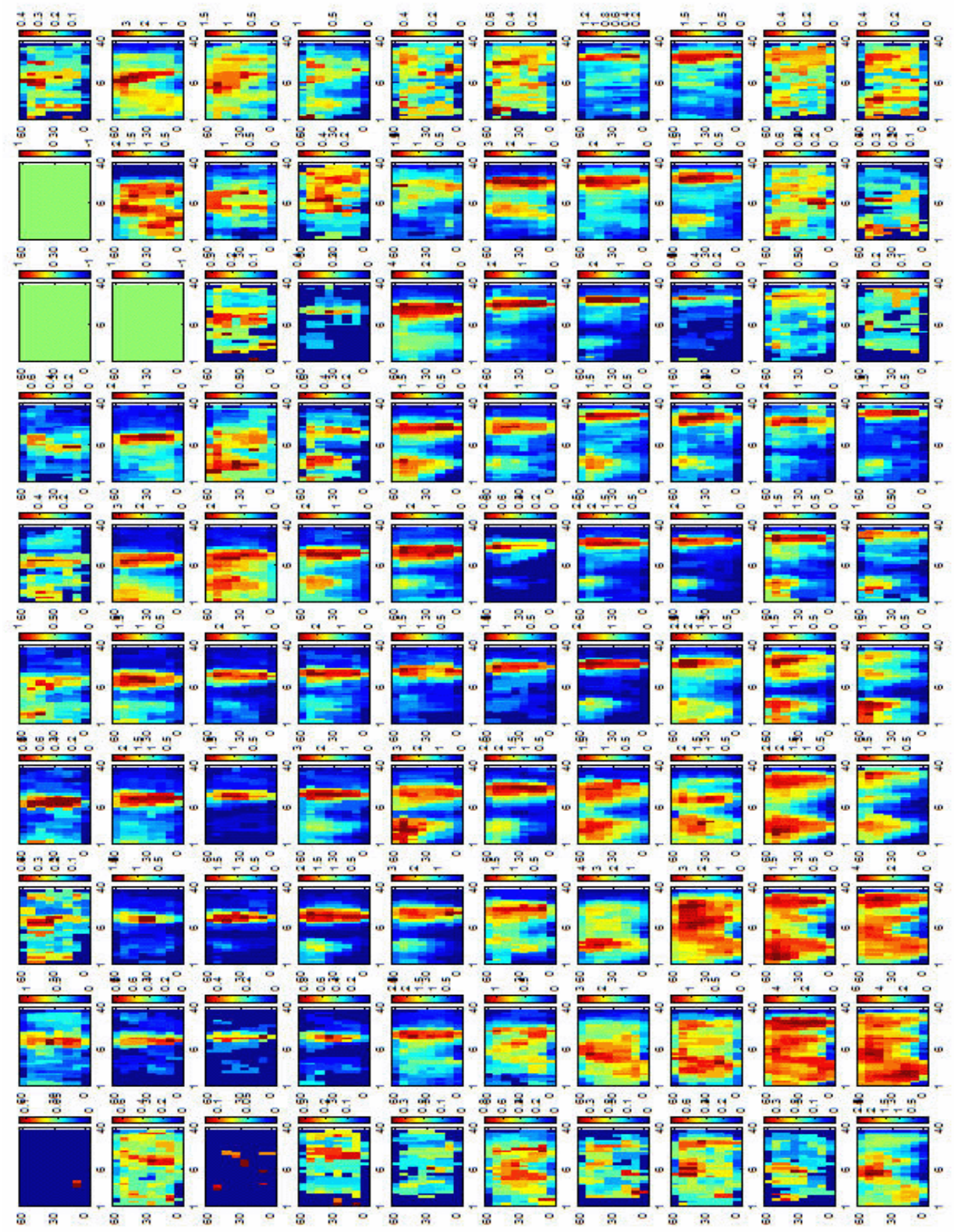


Figure 4b – Acoustically evoked tuning curves recorded with 10 x 10 array implanted in auditory cortex. Note that three of the electrodes in the array were broken (green boxes).

Electrically evoked cortical activity patterns.

The effects on the activation patterns in auditory cortex of current injections into auditory nerve were studied in 6 successful experiments, but always with less than the eleven potentially usable electrodes implanted into the nerve. Cortical activity maps evoked with auditory nerve stimulation were studied on each implanted electrode only if the electrode was able to evoke an eABR with current levels less than 170 uamps. Electrical stimuli consisted of biphasic, 80 microsecond pulses, with no interphase interval, delivered at a rate of around 1 pulse/sec. For electrical stimulation, each stimulus current level was delivered 18 times, and the evoked responses were averaged to create the cortical activation patterns. An example of the activation pattern produced by passing currents of 30, 50, and 80 uamps via a functional electrode is shown in Figure 5.

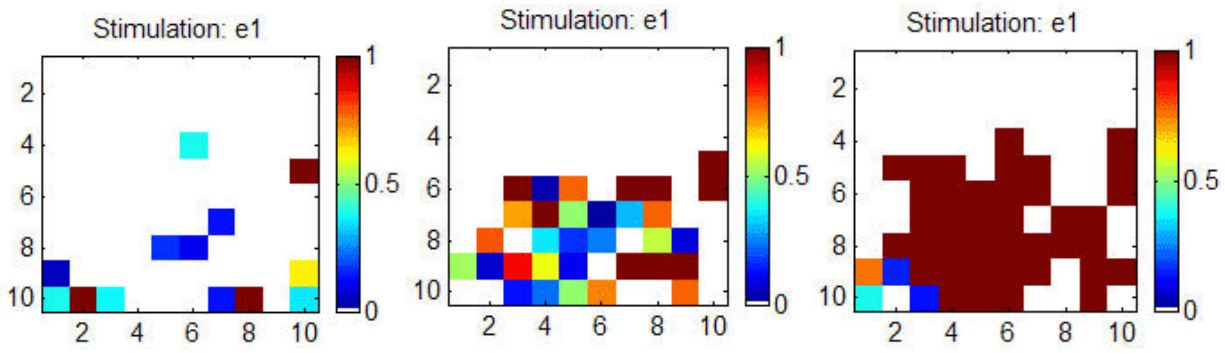


Figure 5 – The left, center, and right panels illustrate the cortical activation patterns evoked with stimulation of 30, 50, and 80 microamp stimuli passed through an electrode implanted in the auditory nerve. The numbers on the left and bottom of each panel represent row and column numbers of the implanted cortical array (electrode 1 is the upper left, and electrode 100 is the lower right). Normalized cortical activity is indicated in the color bar (note that electrode 50 was spontaneously active even in the absence of stimulation).

In this experiment, the 30 microamp stimulus evoked a cortical map that was only a little more complex than that evoked by 10 microamp stimulation, suggesting that 30 microamps was very near the threshold for this electrode. When the stimulation was increased to 50 microamps (center panel in Figure 5), a larger region of auditory cortex was activated with strongest responses recorded with cortical electrodes 53, 57, 58, 64, 87, 88, and 89. When the stimulation was increased to 80 microamps, a much larger cortical region was activated, consistent with spreading of auditory nerve fiber excitation due to this relatively large level of stimulation. An even greater spread in cortical activation was observed with 100 microamp stimulus currents. Current ranges of these values, when passed through auditory nerve electrodes that did not evoke eABR's did not evoke the graded sequence of responses like those shown in Figure 5, supporting our claim that the responses of Figure 5 reflect a graded and localized recruitment of auditory nerve fibers with increasing stimulus intensity.

In this same experiment, two other electrodes implanted in the auditory nerve also had low thresholds, and manifested a similar growth in cortical activation with increased stimulus strength. However, the superthreshold cortical activation patterns differed from that evoked by stimulation of electrode 1 and shown in Figure 5. We compare in Figure 6 the superthreshold

cortical activation patterns obtained by stimulation of auditory nerve electrodes 1, 2 and 3.

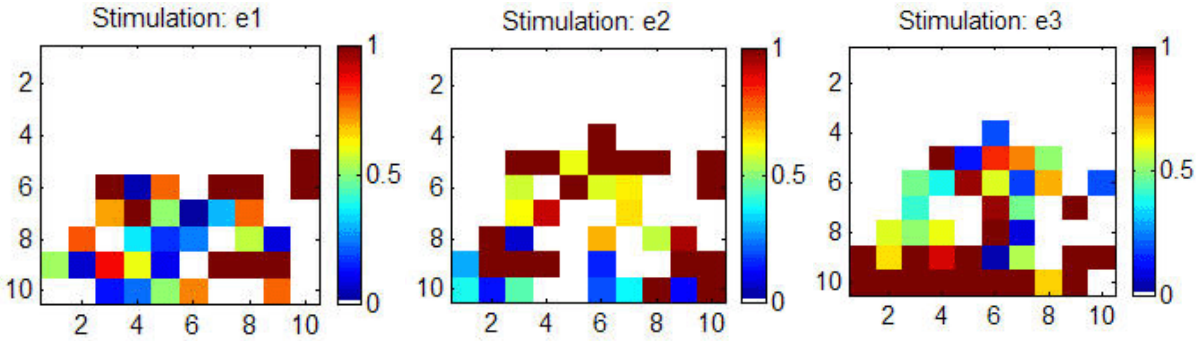


Figure 6 – Left, Center and right panels illustrate cortical activation patterns evoked by electrical stimulation via electrodes 1, 2, and 3 that were implanted in the auditory nerve. Currents of 50, 80, and 50 microamps were passed through electrodes 1, 2, and 3 to evoke these activation patterns.

As can be seen in figure 6, somewhat unique patterns of cortical activation were evoked by currents passed through these three different electrodes. We have tabulated below the cortical electrodes that were maximally activated by currents passed via these electrodes.

Electrode 1: 53, 57, 58, 64, 87, 88, and **89**

Electrode 2: 36, 43, **44**, 46, 47, 48, **55**, 60, 72, 82, **83**, 84, **89**, **90**, 98, 100

Electrode 3: **44**, **55**, 66, 69, 76, 81, **83**, 85, **89**, **90**, 91, 92, 93, 94, 95, 96, 97, 99

The large number of electrodes that recorded evoked activity in Figure 6 indicates that the stimulation of electrodes 2 and 3 were well above threshold, and that stimulation of electrode 1 was closer to threshold. **However, in spite of this super threshold stimulation, the only cortical electrode that recorded activation evoked by stimulation from all three auditory nerve electrodes was electrode 89**. Further, in the superthreshold stimulation via electrodes 2 and 3, only cortical electrodes 44, 55, 83, 89, and 90 showed common excitation. The time required to conduct these experiments, and our desire to explore the dynamic range of the cortical response to auditory nerve stimulation required this 'low resolution' view of the dynamic range. We believe that auditory nerve excitation closer to threshold would generate cortical activation maps manifesting even greater selectivity. This provides our best evidence to date supporting the selective activation of auditory cortex by direct stimulation of the auditory nerve.

3. PUBLICATIONS AND PRESENTATIONS

No publications were submitted, nor presentations made during this quarter.

4. DISCUSSION

The experiments we have done to date provide a mixed picture of direct auditory nerve stimulation via an array of implanted electrodes as a means to restore hearing. The histological studies we have performed on cats chronically implanted with the Utah Electrode Array clearly demonstrate some disruption of the nerve, compared to contralateral, unimplanted nerves. However, in spite of this disruption, the implanted nerves still have large numbers of auditory nerve fibers, many of which are in close apposition to the tips of the implanted electrodes. This suggests that these auditory nerve fibers could be expected to be excited by current injections via the implanted electrodes. The nerve disruption could be caused by many factors that have not been investigated in this study. The presence of any foreign body in neural tissues will evoke an immune response, resulting in the production of a fibrotic mass surrounding the implanted material. The extent of the fibrosis will be greater or less, depending upon the nature of the materials. The nerve disruption could be caused by the rapid electrode insertion. It is likely that the complex surgical access could also provide significant tissue insult in the process of exposing the nerve, as could the tethering forces produced by the implanted lead wires. Further experimentation would be required to determine which of these factors is most critical in the production of the pathology induced by the implantation.

Another positive result was the stability of the impedances of the electrodes during the 60 hours of current stimulation. We used a range of current stimulation levels that we expect would be wider than what we would expect would be required to evoke auditory tonal perceptions, so we look forward to see if these currents induced any pathological tissue responses around the site of current injections. The large number of control electrodes (89) will provide additional data on the pathology induced by the electrodes themselves (insertion and materials). We also will have three additional control arrays implanted in the contralateral hemisphere that were tethered, but which underwent no current stimulation. These experiments, and our experience obtained in histological evaluations of implanted auditory nerves will set the stage for the chronic auditory nerve stimulation experiments that we were unable to perform over this contract period.

Finally, our experiments on stimulation selectivity provide encouraging results suggesting that direct electrical stimulation of the auditory nerve with penetrating electrodes will evoke a set of unique tonal percepts. This conclusion is supported by our overlap experiments that showed that currents passed through individual electrodes excite small, independent populations of auditory nerve fibers. The auditory cortex mapping experiments described in this progress report further support the view that currents passed through individual auditory nerve electrodes excite localized and independent regions of auditory cortex. These experiments will require further refinements: we look forward to having more functional electrodes exciting auditory nerve, and to exploring the cortical activation profiles with more, and more closely spaced current levels. We hope to explore the region around threshold stimulation with a greater number of current levels, which should allow us to better specify the tonal percepts expected with stimulation via each electrode implanted in auditory nerve.

Our general conclusion is that feasibility of direct auditory nerve stimulation via electrode arrays implanted in auditory nerve has been demonstrated by these experiments. The current levels required to evoke eABRs, and cortical activation was shown to be as low as 1 to 10 microamps. The electrodes can be chronically implanted in the nerve for periods up to 2 years, with large numbers of normal appearing auditory nerve fibers remaining around the implanted electrodes. Finally, auditory nerve stimulation appears to excite localized regions of auditory cortex, which

presumably would evoke unique tonal percepts. These conclusions support the continuation of research in an auditory nerve based auditory prosthesis.