**10th Quarterly Progress Report**

**January 1, 2005 to March 31, 2005**

**Neural Prosthesis Program Contract N01-DC-02-1006**

**The Neurophysiological Effects of Simulated Auditory Prosthesis Stimulation**

# A Lithographically-defined Thin-Film Cochlear Implant Electrode for Research

**Submitted by:**

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**(in alphabetical order)**

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This quarterly progress report presents our progress in the 10th quarter of this contract. In this quarter, we completed fourteen physiology experiments that continued and extended our investigations of the interaction between auditory information channels. Specifics of these experiments, as well as other work completed during the quarter, are summarized briefly in the following sections. The final section preceding the appendices of this report outlines the experiments and other work we plan for the next quarter. Finally, the bulk of this report, collected in Appendix II, describes our design and fabrication of a new lithographically-defined thin-film cochlear implant electrode, and results from the first experiment using this new electrode.

(N.B. The work described in Appendix II comprises work that will be submitted for peer-reviewed publication in an archival journal within the next year. Authors will include S.J. Rebscher, M. Islam, R.L. Snyder, and B.H. Bonham. The working title for this manuscript is "A lithographically-defined thin-film cochlear implant electrode for research." Notification will be made in a future quarterly progress report when this manuscript has been accepted for publication.)

**Summary description of work over last quarter**

- We have completed fourteen neurophysiology experiments investigating channel interaction in the inferior colliculus (IC) and spiral ganglion. These experiments include:
    - Intracochlear measurements of electrically-evoked compound action potentials (intracochlear ECAP) in guinea pigs. This work was conducted in collaboration with Leo Litvak and Gene Friedman of Advanced Bionics Corp. The goal of these experiments is to compare the channel interactions inferred from measurements of neural responses in the inferior colliculus with the channel interactions inferred from intracochlear ECAP measurements. This comparison will establish a basis for physiological interpretation of ECAP measurements made in human cochlear implant users.
    - Continued investigation of the improvement in cochlear spatial (i.e., frequency) resolution that can be obtained by adjusting the remote current fraction (RCF). These experiments examine the extent of neuronal activation along the tonotopic axis elicited using a continuum of electrical stimulation that extends from monopolar configuration to tripolar configurations (ref. QPR #8).
    - Continued investigation of the interaction between interleaved electrical pulse trains that are presented contemporaneously on one or two independent cochlear implant channels.
    - Investigation of the differences in the spatial distribution of temporal response patterns of inferior colliculus neurons elicited by electrical pulse trains that differ in pulse rate. The pulse rates vary from 50 pps to 4000 pps and are delivered via intracochlear electrodes. These experiments extend our previous studies of the temporal response properties of inferior colliculus neurons and are conducted in part in collaboration with John Middlebrooks of the University of Michigan.
    - Continued investigation of electrical forward masking (i.e., interaction of electrical pulse trains that are presented sequentially on two independent cochlear implant channels). This work was conducted in part in collaboration with John Middlebrooks of the University of Michigan.
    - Continued investigation of interactions between electrically and acoustically evoked activity in the inferior colliculus. These experiments model effects of electrical stimulation in implant patients who retain some residual hearing. This work was conducted in collaboration with M. Vollmer of UCSF and J. Tillein of MedEl.
    - One experiment using the new lithographically-defined thin-film electrodes (described in Appendix II to this report).
- We have engaged E. Kishawi, of BioElectric Solutions, Inc. to design and fabricate electronic circuitry to

measure cochlear prosthesis inter- and intra-electrode impedances. This equipment will be used in a series of experiments designed to identify the extent to which electrode impedance can be used to estimate the proximity of cochlear implant electrodes to tissue during insertion. This position feedback should reduce the incidence of insertion trauma during prosthesis implantation. If successful, these measurements will also allow us to estimate the distance of the stimulating contacts from the wall of the scala tympani after electrode insertion, and consequently allow us to estimate the distance of the stimulating electrical contacts from the nearest neural elements.

- We have fabricated four guinea pig cochlear implant electrodes for use in the studies described above. Three of these electrodes were of our traditional (wire and ball type) design. The fourth electrode used our new photolithographically-defined thin-film electrodes (described in Appendix II).
- We have provided silastic electrode carriers to P. Bhatti and J. Hetke of the University of Michigan. These space-filling carriers are designed for insertion into guinea pig cochleas. In addition, we have conducted two trial insertions of their silicon substrate thin-film stimulating electrodes. We dissected two cat cadaver heads and demonstrated the insertion characteristics of their electrodes into the scala tympani of the cochleas of these heads.
- We began our analysis of data from the physiology experiments described above, and have continued analysis of experiments that were completed during previous quarters.
- We have prepared and presented three posters and one invited talk describing our work on this contract. These were publicly presented in February at the Annual Midwinter Meeting of the Association for Research in Otolaryngology. In addition, one of us (RLS) was invited to present a summary of our work to the Biology Department at Utah State University.
- We have acquired a multi-channel input/output module (RX-8) from Tucker-Davis Technologies. This module will enhance our ability to present electrical stimulus pulse trains on multiple channels by improving temporal registration between channels. Prior to receiving this module, we used two TDT RP-2 processors to drive our current sources. For high-frequency pulse trains, clock skew between the two independent RP-2's limited the duration and minimum interval between pulses that could be used without pulse overlap. The RX-8 module uses a single internal clock for all output channels; consequently it eliminates clock skew between channels.
- Alexander Hetherington has joined our group as a Development Technician. Mr. Hetherington's contribution to this contract will include implant electrode fabrication, design and implementation of improved fabrication techniques, and fabrication of new hardware for electrode manufacture. This additional effort provided for electrode fabrication will improve the quality of our electrodes, increase the number of implant electrodes for our own experiments, and allow us to provide more implant electrodes for researchers at other institutions.

**Abstracts/Presentations**

*(Text of these abstracts is appended to this report. PDF files of the first two posters are available from the Epstein Lab server ftp://epstein.ucsf.edu/pub/Posters.)*

S.M. Bierer, R.L. Snyder, and B.H. Bonham. Inferior Colliculus Responses to Two-Channel Stimulation. Association for Research in Otolaryngology Midwinter Meeting, Feb 2005: 1019.

B.H. Bonham, R.L. Snyder, S. Corbett, T. Johnson, S.J. Rebscher, M. Carson, F. Spelman, and B. Clopton. Physiological Measures of Auditory Nerve Activation by Current Steering. Association for Research in Otolaryngology Midwinter Meeting, Feb 2005: 1025.

R.L. Snyder, B.H. Bonham, S.J Rebscher, and P.A. Leake. Patterns of Excitation in the Inferior Colliculus Produced by Intracochlear Electrical Stimulation in Cats and Guinea Pigs: Models of Cochlear Implant Stimulation.

Association for Research in Otolaryngology Midwinter Meeting, Feb 2005: 250.

M. Vollmer, J. Tillein, and B.H. Bonham. Forward masking in cat inferior colliculus using combined electric and acoustic stimulation of the cochlea. Association for Research in Otolaryngology Midwinter Meeting, Feb 2005: 1021.

## Travel

Steve Bierer, Ben Bonham, and Russell Snyder attended the annual meeting of the Association for Research in Otolaryngology in New Orleans during February.

Russell Snyder traveled to the University of Michigan in March. During the visit, he conducted experiments for this contract in collaboration with John Middlebrooks and consulted with Pamela Bhatti and Jamille Hetke to discuss their development of Silicon implant electrode arrays and cochlear insertion of those devices.

## Work planned for next quarter

During the next quarter:

- We will integrate the new TDT RX-8 multi-channel I/O module with our existing equipment and configure experiment software to use it.
- We will continue the series of experiments examining the interaction of interleaved electrical pulse trains presented on one and two cochlear implant channels.
- We will fabricate and characterize additional thin-film cochlear electrodes. These electrodes will be used in experiments designed to investigate the relationship between the radial position of stimulating contacts within the scala tympani to the spatial (frequency) extent of activation of the spiral ganglion.
- John Middlebrooks will visit UCSF to continue a series of experiments investigating interaction of sequentially-presented pulse trains on cochlear implant channels (electrical forward masking).
- Leo Litvak of Advanced Bionics Corp will visit UCSF to continue a series of experiments comparing measures of channel interaction inferred from neural activity recorded in inferior colliculus to measures inferred from electrical activity recorded using intracochlear electrodes.
- We will continue analysis of data recorded in experiments during the current and previous reporting periods.
- We will begin a series of experiments examining the relationship of intracochlear electrode impedance to proximity of the electrode to cochlear tissue.
- We will begin a series of experiments designed to examine the relationship between the distance from electrode contacts to the modiolus and the specificity of spiral ganglion activation (determined by IC responses).
- We will prepare several presentation abstracts describing our work for the 2005 Conference on Implantable Prostheses. This meeting will be held in Asilomar during mid-summer.

**Appendix I - Abstracts of work presented at the Annual Midwinter Meeting of the Association for Research in Otolaryngology, February 2005**

Abstract **555**, Date **1:00 pm, Wednesday, February 23, 2005 (24 hours)**
Session **T15: Cochlear Implant Physiology**

Inferior Colliculus Responses to Two-Channel Cochlear Implant Stimulation

**Steven Bierer, Ben H. Bonham, Russell Snyder*

For normal hearing listeners, the perception of one tone can be suppressed by the presence of another. With cochlear implant listeners, a similar phenomenon occurs, albeit one that does not involve the suppressive mechanisms of the auditory periphery. We explored the nature of central mechanisms of suppression by stimulating with intracochlear electrodes and recording neural activity across the central nucleus of the inferior colliculus (ICC). Single and multi-unit activity from the ICC of the anesthetized guinea pig was recorded with a 16-channel electrode spanning the cochleotopic representation. First, single- and two-tone acoustic responses were obtained. With the recording electrode fixed in place, the guinea pig was then deafened and an 8-electrode cochlear implant was inserted into the scala tympani. Pulse trains were presented as bipolar pairs between neighboring electrodes (BP+0) or between alternating electrodes (BP+1). Two-channel stimulation was achieved by interleaving pulse trains from different bipolar pairs, with one channel varying in cochleotopic location and intensity and the other fixed. With the 1-channel stimulation, the extent of activation across the ICC was fairly restricted and reflected its cochleotopic organization. Each recording site, therefore, could be characterized by its best stimulus channel. For some recording sites, activity evoked by the best channel could be suppressed by stimulation on a second channel. The suppression was often greatest when the stimulation channels were adjacent (BP+0) or overlapping (BP+1). This finding is consistent with acoustic studies demonstrating lateral suppressive sidebands. At low rates of stimulation (50 pps), when responses to the two stimulation channels were well separated in time, the occurrence of pulses from the fixed channel could suppress responses to the other channel, even when the fixed channel itself produced only a modest response.

Abstract **1273**, Date **1:00 pm, Wednesday, February 23, 2005 (24 hours)**
Session **T15: Cochlear Implant Physiology**

Physiological Measures of Auditory Nerve Activation by Current Steering

**Ben H. Bonham, Russell Snyder, Scott Corbett, Tim Johnson, Steve Rebscher*

Current cochlear implants (CIs) employ a modest number (16-22) of electrodes to stimulate a small number (4-8) of discrete regions of the auditory nerve (AN) array. In CI patients, stimulation of individual electrodes (as monopoles) or adjacent/nearby electrode pairs (as bipoles) restricts the number of independently addressable regions of the AN array to at most the number of individual electrodes. Thus, CI stimulation using either of these paradigms results in stimulation of a small number of independent channels. In contrast, the normal ear can arguably be considered to have as many independent (though overlapping) acoustic channels as there are inner hair cells (~3500). There is currently no commercially implemented solution that increases the number of CI channels by increasing the number of physical electrodes (and consequently decreasing the spacing between electrodes). An alternative method that can be used to increase the number of independent CI channels is to change the way current is directed into the spiral ganglion by dividing, or steering, current among a local group of electrodes. This method can be employed with two effects. First, by sharing stimulus current between nearby (adjacent) electrodes, "virtual" electrodes can be created that lie between physical electrodes. Second, spread of activation of the AN can be decreased by shaping the field potential using countercurrent applied to adjacent electrodes. By measuring spread of activation along the tonotopic axis of the inferior colliculus, we have demonstrated that suitable division of stimulating current among a local group of electrodes can, but does not always, stimulate multiple independent, though overlapping, regions of the AN array. We have also demonstrated that injection of countercurrent into adjacent electrodes (i.e., partly tripolar stimulation) can, but does not always, reduce the spread of AN activation by a single implant electrode. (Sponsored by NIDCD #N01-DC-02-1006)

Abstract **540**, Date **8:00 am - 11:20 am, Monday, February 21, 2005**
Session **: F: The Brain's View of the Cochlear Implant**

Patterns of Excitation in the Inferior Colliculus Produced by Intracochlear Electrical Stimulation in Cats and Guinea Pigs: Models of Cochlear Implant Stimulation

**Russell Snyder, Ben H. Bonham, Steve Rebscher, Patricia A. Leake*

Contemporary human cochlear implants (CIs) use intracochlear electrodes with several electrical contacts to activate the auditory nerve array. The contacts of these devices are distributed along the cochlear spiral, and activation of each pair of contacts (consisting of an active and one or more return contacts) is thought to excite a restricted, unique and tonotopically appropriate population of auditory nerve fibers. Psychophysical and clinical studies indicate that these devices allow open-set speech reception in many users. Our studies seek to understand mechanisms that underlie this performance by focusing on the many factors that influence the spatial (spectral) and temporal distribution of neural activity evoked across the tonotopic organization of the central nucleus of the inferior colliculus. Among these factors are: the orientation and separation of the active and return contacts in a pair, the mode of stimulation (monopolar, bipolar and tripolar), the rate and amplitude of the electrical pulses, the recent activation history of the neuronal populations (forward masking), and the number of populations activated at any one time (simultaneous masking with two-channel stimulation). We will review the results of our multichannel intracochlear electrical stimulation experiments in deaf animal models. These models are designed to accurately reflect CI stimulation in humans. We will compare the patterns of activation produced by electrical stimulation with those evoked by acoustic stimuli in these animal models. NIDCD NO1-DC-02-1006, NO-1-DC-03-1006

Abstract **221**, Date **1:00 pm, Wednesday, February 23, 2005 (24 hours)**
Session **T15: Cochlear Implant Physiology**

Forward Masking in Cat Inferior Colliculus Using Combined Electric and Acoustic Stimulation of the Cochlea

**Maike Vollmer, Jochen Tillein, Ben H. Bonham*

Combined electric and acoustic stimulation (EAS) has been applied successfully to cochlear implant users with residual low frequency hearing. Using a forward masking paradigm, we examined the spectro-spatial interactions of EAS on inferior colliculus (IC) neurons. Anesthetized normal hearing cats were implanted with a scala tympani electrode array. An earphone was sealed to the auditory meatus for acoustic stimulation. Neural activity was recorded simultaneously at 16 sites along the tonotopic gradient of the central nucleus of the IC. A 20-ms electric probe was preceded by a 50-ms acoustic masker. Probe and masker were systematically varied in intensity and frequency. At low intensities, electric probe frequencies >1 kHz evoked activity at primary IC locations that corresponded to the probe frequency. This activity was masked when the electric probe was preceded by acoustic stimuli at the same frequency. At higher intensities, the electric probe evoked additional activity at a secondary IC location corresponding to the cochlear site of the stimulating electrode. This activity was masked by acoustic frequencies that corresponded to the same cochlear site. Strength of masking was generally increased by increasing masker intensity. Similar masking effects occurred when the electric probe was replaced by an acoustic probe (two-tone masking) at either the frequency of the electric probe or a frequency corresponding to the cochlear site of

electrical stimulation. The results indicate that EAS produces complex spatial interactions in the central auditory system. The extent of these interactions is dependent on the intensities and spectral characteristics of both electric and acoustic stimulus components. The results also suggest that electric stimulation evokes low-threshold acoustic-like electrophonic responses as well as high-threshold direct activation of the auditory nerve.
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