Eighth Quarterly Progress Report

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Feasibility of an Intra-Neural Auditory Prosthesis Stimulating Electrode Array

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1. Introduction

The objective of this research is to evaluate the feasibility of intra-neural stimulation for hearing replacement. We are stimulating the auditory nerve in cats with penetrating multi-channel electrode arrays and recording from the inferior colliculus (ICC) as a means of characterizing activation of the central auditory pathway.

2. Summary of activities for the quarter

In the present quarter, we conducted acute physiological experiments in four cats and we began human temporal bone studies in collaboration with otologic surgeons Alex Arts and Mark Wiet. The first peer-reviewed publication from this contract appeared online: Middlebrooks, JC, and Snyder, RL: Auditory prosthesis with a penetrating nerve array, JARO, DOI: 10.1007/s10162-007-0070-2, 2007. An invited presentation was given at the Mid-Winter Meeting of the ARO in Denver (February 12). The principal accomplishments of this quarter were the following:

- *Comparison of surgical approaches for placement of intra-neural stimulating arrays in humans.* In collaboration with Drs. Alex Arts and Mark Wiet, we have begun exploring the optimal surgical approaches to the auditory nerve in humans for placement of an intra-neural stimulating array. We participated with them in two human temporal-bone dissections and evaluated four potential approaches. We refer to these approaches as intra-cranial, infra-labyrinthine, juxta-labyrinthine, and trans-labyrinthine. The *intra-cranial* approach is a standard approach through the posterior fossa. Advantages of the intra-cranial approach are that it offers direct visualization of the 8th nerve, is relatively familiar to surgeons, can be performed on all patients, requires little or no drilling on the temporal bone, and circumvents the possible deleterious effects of drilling on residual hearing. Its disadvantages include loss of CSF, increased danger of menigitic infection, damage to the facial nerve, and possible cochlear ischemia due to vascular spasm. Other concerns are the difficulty in penetrating the free-floating, pulsating nerve with and electrode array at this location, difficulty in mechanical fixation of the array, and possible damage to the nerve due to pulsating motion of the nerve relative to a rigid intra-neural array. The *infra-labyrinthine* approach allows the nerve to be accessed and visualized within the more confined space of the medial internal auditory canal, but CSF loss, nerve pulsations and vascular spasm are still judged to be significant problems. Also, the infra-labyrinthine approach would be precluded in about ~1/3 of cases by the presence of the jugular bulb in the path of access to the nerve. The *juxta-labyrinthine* approach accesses the nerve ~2 mm distal to the cochlea. With this approach, the nerve can be directly visualized, CSF loss and vascular spasm are judged to be minimal, and direct damage to the cochlea is minimal, enhancing preservation of residual hearing. It remains to be determined whether the juxta-labyrinthine approach is feasible in all patients. Finally, the *trans-labyrinthine* approach accesses the nerve through the facial recess, involving a small perforation of the osseous spiral lamina. This approach is analogous to the lateral approach that we have been using in cats. Advantages are: visualization of the nerve, albeit somewhat limited; minimal loss of CSF; minimal mobility of the nerve; and minimal possibility of infection. This surgical approach is similar to the standard surgical approach for conventional cochlear implants and is therefore familiar to most otologists. The main disadvantage of this approach is that our consulting surgeons believe that it is the most likely to compromise any residual hearing. Using this approach in the cat, however, we have been

largely successful in conserving hearing, especially in the low- and middle-frequency ranges that are the ranges in which residual hearing is most likely to be found in candidates for auditory prosthesis. Hearing preservation is documented in the following paragraph.

- *Lateral approach to the auditory nerve with preservation of hearing.* In four cats, we attempted to preserve normal acoustical hearing while implanting a penetrating intra-neural stimulating array using a lateral approach through the osseous spiral lamina. We monitored the status of hearing throughout the procedure by recording thresholds in the ICC for tones presented at one-octave intervals from 0.5 to 32 kHz. We observed negligible change in thresholds at any frequency as the tympanic bulla was opened to expose the cochlea. Opening of the round window membrane and enlarging of the round window margin resulted in a 19-dB elevation in threshold, averaged across 4 cats at 8, 16, and 32 kHz, with negligible elevation in threshold at lower frequencies. In one cats, insertion of the stimulating probe into the nerve damaged the nerve, resulting in loss of acoustic responses at 8 kHz and above and unusually high thresholds for electrical stimulation. In the other 3 cats, threshold elevations ranged from 14 to 50 dB at 8 kHz, 0 to 22 dB at 16 kHz, and 8-28 dB at 32 kHz. Thresholds at lower frequencies (measured at 0.5, 1, 2, and 4 kHz) were essentially unchanged. In one of the cats, we recorded through the intra-neural array responses to acoustic stimulation. Several recording channels showed vigorous multi-unit responses, with sharp V-shaped tuning curves centered at ~20 kHz.
- *Transmission of temporal fine structure from the electrically stimulated auditory nerve to the ICC.* In three animals, we evaluated the transmission of temporal fine structure from intra-scalar and intra-neural stimulating electrodes to the ICC by monitoring ICC phase locking to unmodulated electrical pulse trains. We measured the ICC responses to 20 repetitions of a 300-ms electrical pulse train at each of a range of pulse rates and computed the vector strength of the response and the Rayleigh criterion for significant phase locking at the criterion of $p<.001$. The "limiting pulse rate" was the highest pulse rate at which significant phase locking was observed. Limiting pulse rates were higher for intra-neural stimulation than for monopolar stimulation with a conventional cochlear implant. For instance, about 45% of responsive ICC neurons phase locked to 300-pulse-per-second (pps) pulse trains presented through intra-neural electrodes, whereas only about 20% of neurons responded to that rate through a cochlear implant. About 35% phase locked to 500 pps through intra-neural electrodes compared to only 5% through the cochlear implant. There was a clear relation between phase-locking and the CF of ICC units: units that phase-locked to 500 pps and higher tended to have CFs < 2 kHz (measured with tones prior to deafening). We hypothesized that the dearth of ICC neurons phase locked to high pulse rates presented through a cochlear implant might reflect the lack of direct cochlear-implant stimulation of low frequency regions of the auditory nerve. We tested that hypothesis by exposing the cochlear apex and stimulating with a ball electrode placed on the spiral lamina, thus effecting intra-scalar stimulation of very low-CF neurons originating high in the cochlear apex. Stimulation at that site produced high-rate phase locking in low-frequency regions of the ICC, thus filling in the intra-scalar distribution right on top of the intra-neural distribution. Two-pulse temporal integration for the ball electrode site was similar to that obtained with intra-scalar electrode, showing time constants about double that obtained with intra-neural stimulation. Our tentative conclusion is that the superior phase locking produced by intra-neural stimulation is due almost entirely to its direct access to fibers from the apical cochlea, not from any other special property of intra-neural stimulation.

- *Transmission of envelope information from the electrically stimulated auditory nerve to the ICC.* In two animals, we measured phase locking of ICC neurons to amplitude-modulated electrical pulse trains delivered through penetrating intra-neural electrodes using the lateral approach. Carrier pulse rates were 508, 1017, 2035, or 4069 pps. Modulation frequencies ranged from 21 to 127 Hz; the maximum modulation frequency was set to ¼ of the 508-pps carrier frequency. We explored modulation depths ranging from -40 dB (re 100% modulation) to -5 dB; that is, 1% to 56% modulation. We used a signal detection procedure to determine the minimum modulation depth that could be distinguished from no modulation on the basis of phase locking of ICC neurons on single trials. The results were parallel in some respects to the results of tests of transmission of temporal fine structure. That is, modulation sensitivity tended to be greater for low-frequency regions of the ICC than for high-frequency regions, and sensitivity was greater for intra-neural stimulation than for scala tympani stimulation. Again, the comparison of modulation sensitivity between intra-neural and intra-scalar stimulation was confounded by lack of access to low-frequency fibers with scala tympani stimulation. Preliminary analysis of data obtained for modulated stimuli presented through the apical ball electrodes show great sensitivity to modulation.

3. Plans for next quarter:

- Document dissections of human temporal bones to refine the juxta-labyrinthine and trans-labyrinthine approaches.
- Conduct physiological experiments in 4 cats, using a lateral approach to the nerve. Confirm observations on the following topics with the goal of obtaining data sufficient for publication:
  - Preservation of hearing during placement of an intra-neural stimulating array, including recording through the intra-neural electrodes of auditory-nerve responses to tones.
  - Studies of transmission of fine-structure and envelope information, comparing high- vs low-CF pathways with intra-neural stimulation and comparing intra-neural vs intra-scalar stimulation at corresponding CF regions.
  - Test modulation sensitivity for intra-neural and intra-scalar stimulation at low and high carrier pulse rates. Test the hypothesis that modulation sensitivity decreases at carrier rates at which substantial temporal integration takes place.