"A Cochlear Nucleus Auditory prosthesis based on microstimulation"

Contract No. **No. NO1-DC-1-2105**

Progress Report # 2

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SUMMARY

The overall goal of this project is to develop a central auditory prosthesis based on an array of microelectrodes implanted into the ventral cochlear nucleus, in order to restore hearing to patients in whom the auditory nerve has been destroyed bilaterally. Our contract's work scope includes the development of a 16-site microstimulation array based on silicon substrate probes. Implantation of any microstimulating array into the human cochlear nucleus can be accomplished only with a hand-held inserter tool, and the requirement that the tool must be supported in the surgeon's hand dictates that the electrode insertion occur at high speed. Previously, we have fabricated 3-dimensional arrays from silicon microprobes designed and produced at the University of Michigan, and we have implanted these into the feline spinal cord for 30 days, using our high-speed inserter tool. These early arrays did contain design deficiencies which resulted in many of the fragile probe shanks being damaged during fabrication and also resulted in poor alignment of the rather flexible probe shanks in the finished arrays. However, these experiments did demonstrate that silicon probes can be inserted into the brain or spinal cord at high speed without inducing interstitial hemorrhaging and with remarkably little tissue injury.

We have developed a new procedure for fabricating 3-dimensional microstimulating arrays from 2-dimensional planar silicon substrate probes. The process includes a provision to reinforce the critical junction between the probe shanks and the supporting spine (the location at which these probe tend to fracture during high-speed insertion into the spinal cord). We have used the living feline lumbar and sacral spinal cord as a model for the human auditory brainstem, since both are covered by a thickened pial membrane. We implanted one of our new arrays into a cats's spinal cord, at high velocity (approximately 2m/sec). After three insertions, the probes had not fractured or chipped. This suggests that our design is sound, and we will next evaluate an array of the probes designed specifically for the cochlear nucleus.

RESULTS

Our contract's work scope includes the development of a 16-site microstimulation array based on multisite silicon substrate probes. Development of a silicon microstimulation array also is included in the workscope of our contract to develop techniques for microstimulation of the sacral spinal cord, so the work described in this section was supported by both projects.

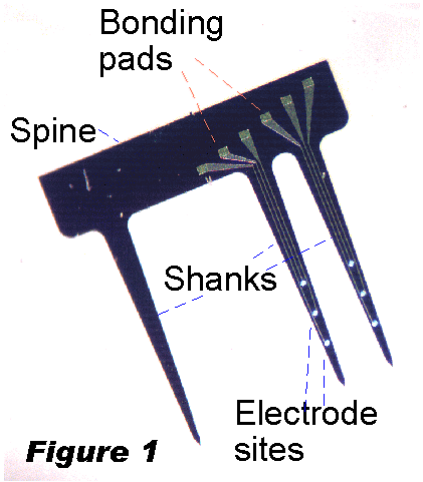

Figure 1

Figure 1 shows a probe that was designed for our program by Jamile Hetke at the University of Michigan. It is intended to be implanted into the feline sacral spinal cord. We have incorporated these probes into arrays which we have implanted into the feline spinal cord for 30 days, using our high-speed inserter tool. As noted below, these early arrays contained serious deficiencies. However, the experiments did demonstrate that these rather broad silicon shanks can be inserted into the spinal cord at high speed without inducing interstitial hemorrhaging and with remarkably little tissue injury.

Figure 2 shows a sketch of the probe that will be incorporated into the arrays for implantation into the cochlear nucleus. These probes will be included in a subsequent mask set produced at the U of M. In the interim, we are using the probes designed by Ms. Hetke for the spinal cord (Figure 1). The shanks are of the same length and aspect ratio as those proposed for the cochlear nucleus, although the overall configuration of the array is somewhat different.

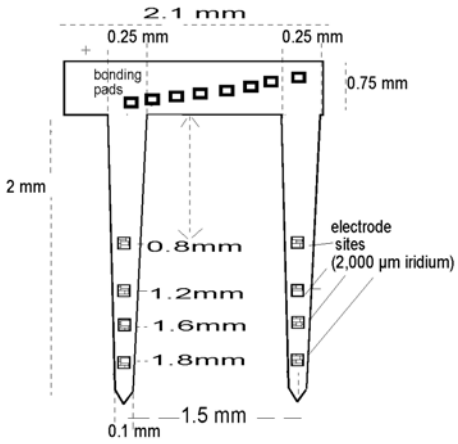

Figure 2

We have previously described a procedure for attaching platinum-iridium lead wires to the probes' bonding pads and then insulating the pad region with silicone elastomer. The probe spines then must be encapsulated into an epoxy superstructure to yield a three-dimensional array which can be implanted with a handheld inserter tool (e.g., Figure 6 below). Previously, we have fabricated arrays of the probes depicted in Figure 1, by inserting the shanks through a silicon rubber membrane in the bottom of a convex mold cavity and then filling the mold with Epoxy. This yielded arrays with a superstructure

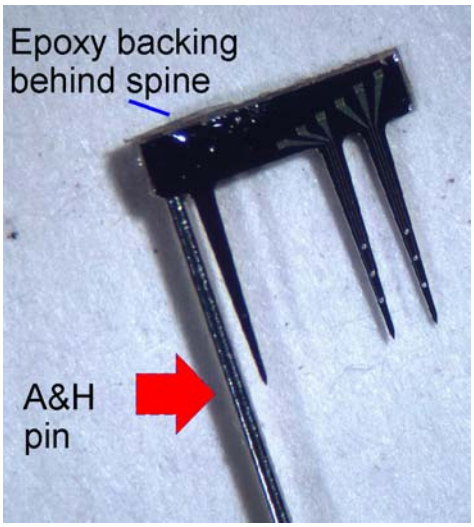

Figure 3

whose convex underside could conform to the curvature of the spinal cord or brain. However, this approach resulted in many probe shanks being damaged during fabrication and also yielded poor alignment of the shanks. We have therefore completely redesigned the procedure for fabricating the array.

In the new procedure, the 3-dimensional array is assembled from 2-dimensional "flag" subassemblies (Figure 3). To produce the flags, an alignment and handling pin (A&H pin; a straight segment of 0.2 mm stainless steel wire approximately 5 cm in length), is taped to a microscope slide. A small quantity of EpoTek 301 epoxy is partially polymerized to a viscous liquid, by heating at 60/C for 25 minutes. A droplet of this "gel" is applied to the terminal 1 mm of the A&H pin, in order to attach the probe spine to the pin. While the gel is semi-solid, gentle pressure is applied to the top of the spine with a slender wooden splinter, to insure uniform contact between the spine and the pin, and thus placing the shanks in the plane of the pin. The probe's shanks are then aligned with the axis of the pin, with the aid of a "Whipple grid" microscope reticule. The epoxy is then polymerized completely at 60/C. Next, a film of partly polymerized EpoTek gel is applied to a glass microscope slide, extending to the edge of the slide. The probe spine is allowed to float on the film with the features facing upwards and the probe shanks extending out beyond the edge of the slide so that their rear surfaces do not contact the gel (Figure 4). The short segment of the A&H pin that is attached to the probe's spine is allowed to sink into the gel film so that it will be completely encapsulated. After the EpoTek film has fully polymerized, it is trimmed around the perimeter of the probe spine using an excimer laser at 248 nm. Finally, the "flag" subassembly is freed from the glass slide by sliding a razor blade under it. The probes' spines now have a sturdy epoxy backing with a flat rear surface (Figure 5) that provides the necessary support

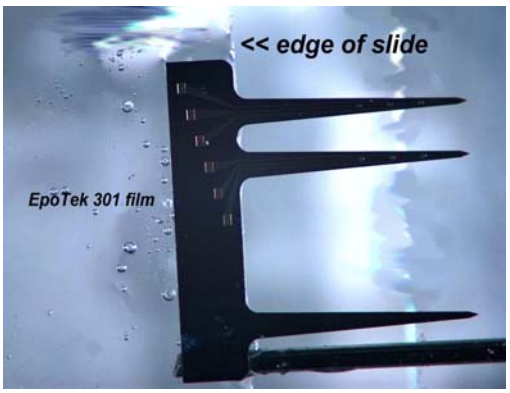

Figure 4

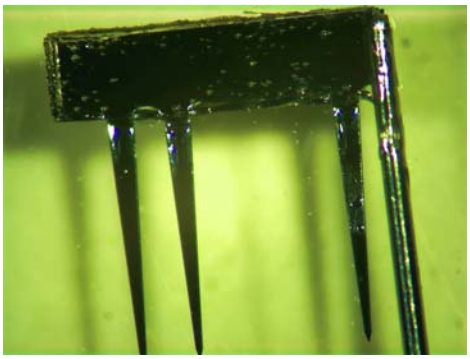

Figure 5

for the silicon spine during bonding of the lead wires to the pads.

For the human cochlear nucleus, the array must be implanted using an inserter tool that is held in the surgeon's hands, and this necessitates that the insertion occur at high speed. Insertion at high speed (1 m/sec or greater) may not necessarily be the optimal means of inserting these rather fragile probes, but this is the only mode of implantation that is practical with a hand-held tool that will access the human cochlear nucleus though the restricted opening afforded by the translabyrinthine approach to the human brainstem. During insertion into the brain at high speed, the unreinforced shanks will fracture at the junction between the shank and the spine. In order to distribute the strain in this region of the probe, we have formed tapered buttresses by placing a droplet of uncured EpoTek 301 at the base of each shank (Figure 6). The unpolymerized epoxy forms a meniscus at the corners between the epoxy backing and the shank, and maintains its shape as the epoxy cures.

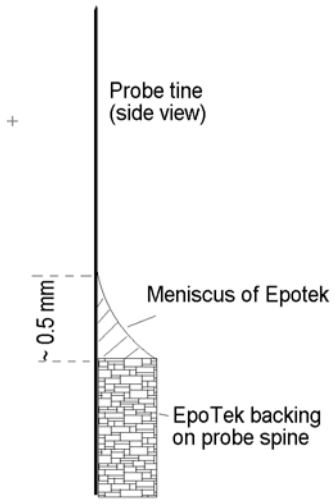

Figure 6

After the leads have been welded to the bonding pads, the probe spine is insulated with Type A silicone elastomer. We have soaked-tested these junctions in saline for up to 90 days, and the leakage resistance has remained greater than 1 Meg-ohm

Next, the free ends of the A&H pins are placed into metal guide tubes attached to a micromanipulator, so that two or more of the flag subassemblies can be lowered into a mold cavity with the probe shanks and the A&H pins pointing upwards and the shanks aligned (Figure 7). The flag subassemblies are sufficiently rigid so that the thin-film silicon spines do not become warped and the shanks are not misaligned as the lead wires are positioned within the cable channel extending from the end of the mold cavity. The cable channel is sealed around the lead wires with Type A silicone elastomer, and the mold cavity is filled with uncured EpoTek 301 epoxy. When the EpoTek is polymerized, the micromanipulator is retracted, leaving the A&H pins protruding from the casting. The pins are freed from the epoxy by rotating and

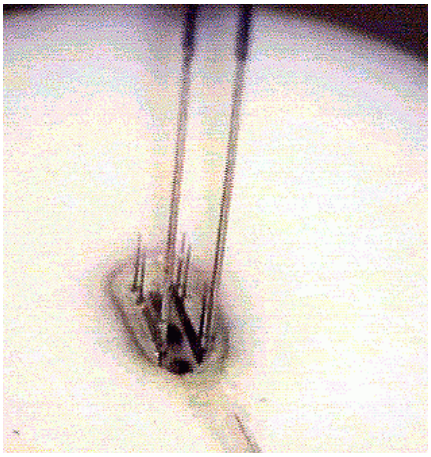

Figure 7

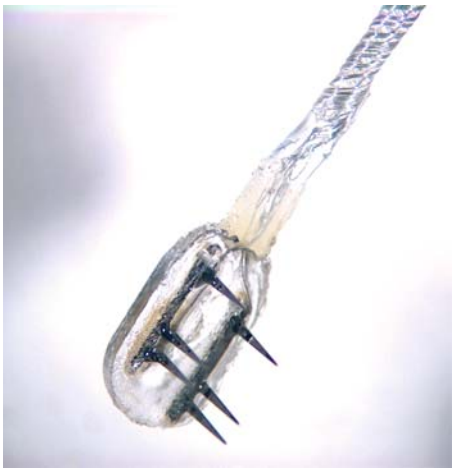

Figure 8

then retracting them. The array is then ejected from the mold by a trio of ejector pins. Finally, the platinum leads are spiraled around a segment of silicone tubing and coated with low durometer silicone elastomer to form a helical cable. A custom cable-winding device is used for this operation.

A complete array with a helical cable is shown in Figure 8. The procedure outlined above is moderately labor-intensive and requires some faculty with microfabrication procedures. However, it is a reliable means of producing three-dimensional silicon substrate arrays which can be inserted into the brain at high speed. The most difficult and time-consuming operation is fabricating and bonding the lead wire subassemblies.

We have used the living feline lumbosacral spinal cord as a model for the human auditory brainstem, since both are covered by a thickened pial membrane. In an acute experiment, an array with 2 probes (6 shanks) was inserted three times into the sacral spinal cord of an anesthetized cat, at a velocity of approximately 2m/sec using the high-speed inserter tool. Figure 9A shows the array within the barrel of the tool, and Figure 9B shows the array after implantation. After the third insertion all six shanks were undamaged and their tips were not chipped (Figure 10). This suggests that our design is sound, and we will next evaluate an array of the probes designed specifically for the cochlear nucleus (Figure 2), when they become available from the University of Michigan. These arrays will be implanted into the feline spinal cord, and if they prove to be sufficiently durable, and if tissue injury is minimal, they will be implanted into the feline cochlear nucleus.

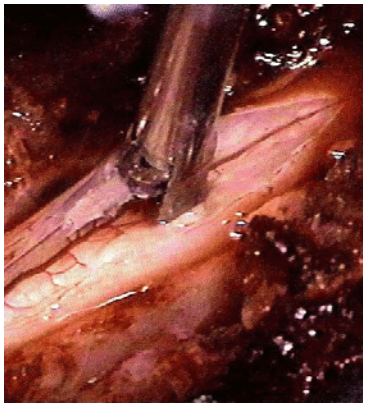

Figure 9A

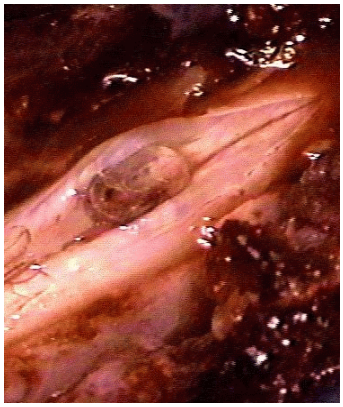

Figure 9B

Figure 10

One remaining problem is how to tether the shanks so that if they do fracture, the detached fragment does not migrate through the brain. We have found that an epoxy backing will delaminate from the shanks after 30 days *in vivo*, so this type of backing is not a reliable method of restraint. One possible solution is to encapsulate the probes with 3-4 ：m of Parylene-C, after the lead wires have been attached and the bonding area has been encapsulated in silicone elastomer. The Parylene can then be photo-ablated from the electrode sites using our excimer laser. We do not expect that the Parylene will strengthen the shanks significantly, but it should anchor any shanks that do fracture. We will investigate this approach during the next quarter. An unresolved problem is how best to validate that the Parylene will indeed anchor a fractured shank; if the shanks are fracture intentionally before implantation, they cannot be inserted into the brain.

Construction of 16 channel tel-stimulator

Another task in our work scope is to upgrade our 4-channel telemetrically-controlled backpack stimulator so that 16 electrode sites can be pulsed independently. We have designed a 12-channel controlled-current stimulator board which will reside within the cover plate of the backpack of the existing system and will not add to the pack's volume or weight. As of this writing, the printed circuit board has been fabricated, and 4 of the 12 channels have been tested. During the present quarter, the assembly of the board will be completed and integrated into our backpack stimulator.

Fabrication of the human arrays

The microelectrode arrays for the first human implantations are being assembled in Sydney, Australia by Cochlear Ltd using discrete iridium microelectrodes fabricated at HMRI. At HMRI, we fabricate the electrodes, insulate the shafts, and expose and activate the electrode tips. In Sydney, they are incorporating these into arrays, using the specifications developed at HMRI and HEI. During the past quarter, we have shipped 74 electrodes to Sydney. Presently, they are fabricating test units and conducting soak tests.

We also have produced a video as an aid to instructing surgeons in the loading and handling of the inserter tool.