"A Cochlear Nucleus Auditory prosthesis based on microstimulation"

Contract No. **No. NO1-DC-1-2105**
Progress Report #7

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ABSTRACT

The objective of this project is to develop central auditory prostheses 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 calls for the development of arrays of silicon substrate electrodes, which should allow placement of many more electrode sites into the human ventral cochlear nucleus than is possible with discrete iridium microelectrodes. We are developing an array for implantation into the human cochlear nucleus which has 16 electrode sites distributed on 4 silicon shanks extending from an epoxy superstructure that is 2.4 mm in diameter.

The probe shanks are either 2 or 3 mm in length. The 3 mm probes are intended to span the full tonotopic gradient of the human ventral cochlear nucleus, while the 2 mm shanks are appropriate for implantation into the feline ventral cochlear nucleus. To date, two of the 2 mm arrays have been implanted into the posteroventral cochlear nucleus 2 young adult female cats. One implant failed, due to compression of the dorsal surface of the cochlear nucleus during insertion of the array, but a second array was implanted successfully, using a slightly modified technique. At 15 and at 24 days after implanting the array into cat CN142 we recorded, via an electrodes near the contralateral inferior colliculus, the averaged evoked responses from each of the electrodes sites in the PVCN. Although we have yet to conduct the histologic evaluation of the electrode sites of these cats, it appears that these sturdy and rather broad silicon probes can be inserted into the cochlear nucleus with minimal tissue damage. Thus, at 15 days after implantation, the thresholds of the responses evoked from the electrode sites on the rostral 2 shanks were 6 μA or less This is comparable to the threshold of the responses evoked in the PVCN by our chronically-implanted discrete iridium microelectrodes. Also, we were able to record action potentials from single and from several neurons near many of the electrodes sites, which is an indication that there is minimal scarring around the silicon shanks. The threshold of the AERs from all 8 sites on the caudal 2 shanks was very high and was less than 35 μA for only 2 of these sites (#3 and #7). The array was implanted near the caudal pole of the cochlear nucleus & we assume that the high thresholds of the AERs from the caudal shanks is due to the array having been implanted slightly caudal of its optimal position, so that the caudal shanks are outside of the central nucleus of the PVCN.

INTRODUCTION & METHODS

The objective of this project is to develop central auditory prostheses 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 calls for the development of arrays of silicon substrate electrodes, which should allow placement of many more electrode sites into the human cochlear nucleus than is possible with discrete iridium microelectrodes. We are developing an array for implantation into the human cochlear nucleus which has 16 electrode sites distributed on 4 silicon shanks extending from an epoxy superstructure that is 2.4 mm in diameter. This is the same footprint as our first- generation human arrays employing discrete iridium microelectrodes and is designed to be implanted using the same inserter tool. The silicon probes are fabricated at the University of Michigan under the direction of Ms. Jamille Hetke.

The probe shanks are either 2 or 3 mm in length. The 3 mm probes are intended to span the full tonotopic gradient of the human ventral cochlear nucleus. In the previous report (#6), we described the implantation of the 3 mm probes into the feline spinal cord using the handheld inserter tool. The 2 mm shanks are appropriate for implantation into the feline ventral cochlear nucleus.

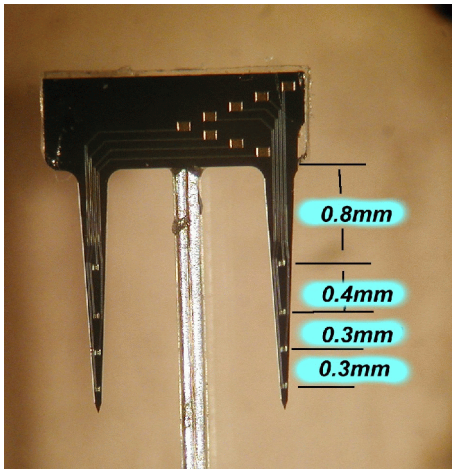

Figure 1

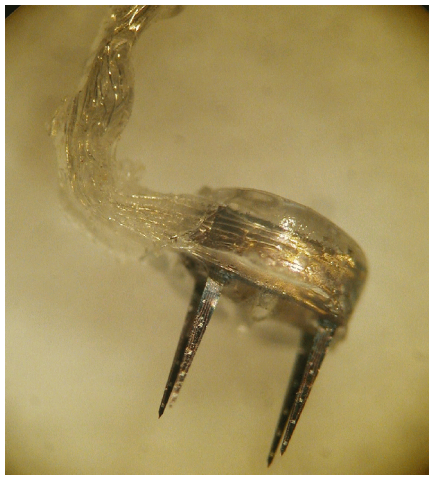
Figure 2

While awaiting delivery of the probes designed for the cochlear nucleus, we have developed a procedure for fabricating the arrays using probes designed for chronic implantation into the feline spinal cord (QPRs 2 & 3). The procedure for the cochlear nucleus arrays differs only slightly. Figure 1 shows a probe with 2 of the 2 mm shanks, each with four 2,000 μm² iridium electrode sites distributed between 0.8 and 1.7 mm below the horizontal spine. Figure 2 shows an array with 2 of the probes (4 shanks in 16 sites) extending from an epoxy superstructure which floats on the dorsal surface of the cochlear nucleus. The array cable is angled vertically, to accommodate the transcerebellar approach to the feline cochlear nucleus, as described below.

To date, two arrays have been implanted into 2 young adult female cats. The cats were anesthetized with Halothane and Nitrous Oxide, and the head fixed in a stereotaxic frame. The surgery was performed using aseptic technique. The scalp was opened in a midline incision, the attached muscles reflected, and a small craniectomy was made over the right occipital cortex. The recording electrode (a Teflon-insulated stainless steel wire with approximately 1 mm of insulation removed from the tip) was inserted by stereotaxis into the deep right inferior colliculus, in order to broadly sample inputs from the cochlear nucleus. The recording reference electrode was implanted dorsal to the right inferior colliculus. The depth of the recording electrode was adjusted so that the response evoked by a train of clicks delivered to the left ear was maximized. The leads from the recording and reference electrodes were then secured to the skull with bone cement. A second small craniectomy was made over the left lateral cerebellum just posterior to the tentorium. The rostro-lateral portion of the cerebellum was aspirated using small pipettes, to expose the dorsal

surface of the cochlear nucleus. The upper surface of the array's epoxy superstructure was positioned on the end of a vacuum wand mounted on a stereotaxic electrode carrier and, under visual control, the array was advanced into the dorsal surface of the cochlear nucleus. The array cable was fastened to the bone at the edge of the craniectomy using cyanoacrylate and the vacuum was released, leaving the array in place in the cochlear nucleus. The cavity was then filled with gelfoam and the craniectomy was sealed with bone cement.

The percutaneous connector supplying connections to the stimulating and recording electrodes was fixed to the skull using stainless steel screws and bone cement. The muscles and skin were closed in layers. The cats was then given appropriate postoperative care, including analgesics.

RESULTS

One implant failed, due to marked compression of the dorsal surface of the cochlear nucleus during insertion of the array. In cat CN142, more of the cerebellum caudal to the implant site was aspirated, to provide better visualization of the cochlear nucleus and of the array during insertion. For about 4-5 days after the surgery, the cat exhibited some evidence of nausea (anorexia, adipsia, excessive salivation). With supportive care, she recovered fully by day 7, with no apparent residual neurological deficits.

At 15 and 24 days after implantation of the array, cat CN142 was anesthetized lightly with Propofol and the responses evoked from each of the microelectrodes in the right PVCN were recorded via the electrode below the left inferior colliculus. 1024 successive responses were averaged to obtain each averaged evoked response (AER, Figure 4). Because of its short (~ 1 ms) latency after the stimulus, the 1st component of the AER is assumed to represent neuronal activity evoked directly in the neurons projecting from the PVCN to the inferior colliculus, while the second component may represent neuronal activity that is evoked transsynaptically. The stimulus was cathodic-first, charge-balanced pulse pairs, each phase 150 μs in duration. The response growth functions, which represent the recruitment of the neural elements surrounding the microelectrode, were generated for each stimulating electrode site in the PVCN, by plotting the amplitude of the first component of each of the AERs evoked from the site, against the amplitude of the "probe" stimulus that evoked the AER. The amplitude of the first component of the AER was measured from the peak of the positivity to the trough of the subsequent negativity (Figure 4)

Figure 3 is the diagram of the microelectrode array that was implanted into the posteroventral cochlear nucleus of cat CN142, showing the location of the 16 microelectrode sites. Sites #2 and #11 were electrically open. Figure 4A,B shows the AERs that were evoked from microelectrode sites #1 and #5 in the PVCN. The amplitude of the 150 μs/ph cathodic-first current pulse pairs is printed near the right edge of each trace. For reference, Figure 5 shows the AER evoked by a train of acoustic clicks delivered to the left ear. The mean sound pressure was approximately 55 dB, based on previous calibrations using a Bruel & Kjaer 4176 omnidirectional microphone and a B&K 2235 sound level meter..

Figure 6 shows the response growth functions (RGFs) evoked from 11 of the electrode sites. These RGF's were computed from the amplitude of the first component of the AERs, as described above. For the 7 functional sites on the 2 rostral shanks, the AER thresholds were close to 6 μA at 15 and at 24 days after implantation. Figure 7A &B show the RGFs from the rostral-lateral shanks, and Figure 7C &D shows the RGFs from the rostral- medial shanks. The threshold of the responses from all 8 of the caudal sites was very high and was below 35 μA only for sites #3 and #7. These electrodes were near the caudal pole of the CN.

We were able to record action potentials from neurons in the PVCN, via all of the rostral electrode sites. Figure 8 shows 3 samples recorded from electrode #1 (dorsal in the PVCN) and 3 samples from electrode #9 (ventral in the PVCN) in response to an acoustic stimulus (quiet clapping of hands at a distance of about 2 meters).

DISCUSSION

Our objective is to create a clinical device which must be handled and loaded into the inserter tool by the surgeon, and also must penetrate the tough glial limitans overlying the human cochlear nucleus. Thus the silicon probes used in this study were designed with relatively broad shanks, in order to increase their strength. As described in our last report (#6), we were able to insert arrays containing the 3-mm probes into the feline spinal cord (our model for the human brainstem) several times without fracturing the probes. Although we have yet to conduct the histologic evaluation of the electrode sites of the cats described in the present report, it appears that these silicon probes can be inserted into the cochlear nucleus with minimal tissue damage. Thus, at 15 days after implantation, the threshold of the responses evoked from 7 electrode sites on the rostral 2 shanks of the array in cat CN143 were 6 μA or less (The electrical connection to one site was open). This is comparable to the threshold of the responses evoked in the PVCN by our chronically-implanted discrete iridium microelectrodes (McCreery et al., 1997, 2000). Also, we were able to record single unit activity from all 7 of these rostral sites, and even from most of the caudal sites, which is an indication that there is minimal scarring around the shanks. The threshold of the AERs from all 8 sites on the caudal 2 shanks was very high and was less than 35 μA for only 2 of these sites (#3 and #7). The array was implanted near the caudal pole of the cochlear nucleus & it is likely that the high thresholds of the AERs from the caudal shanks is due to the array having been implanted slightly caudal of its optimal position, so that the caudal shanks are outside of the central nucleus of the PVCN. A less likely explanation is that both of these shanks inflicted significant tissue injury during insertion. The issue will be resolved by the histologic evaluation of the implant site.

Since we have only a single recording electrode in the inferior colliculus, we have not been able to determine the capacity of these electrode arrays to access the tonotopic organization of the ventral cochlear nucleus. Just before the cat is to be sacrificed for histologic evaluation, we will perform a terminal acute experiment in which we will measure and compare the amplitude of the AERs evoked at various depths along the dorsoventral-ventromedial axis of the central nucleus of the IC, to determine how the different electrode sites activate different parts of the tonotopic gradient in the PVCN (McCreery et al., 1998). However, it is noteworthy that even at the maximum stimulus amplitude of 35 μA, the AERs from adjacent electrode sites were not of the same amplitude, indicating that there was not complete spatial overlap of the effective stimulus from these adjacent electrodes (Figure 7). It is also noteworthy that the amplitude of the AER evoked from a single electrode site at this maximum stimulus amplitude (35 μA) was comparable to the amplitude of the response evoked by an acoustic click of approximately 5 decibels delivered to the ipsilateral ear.

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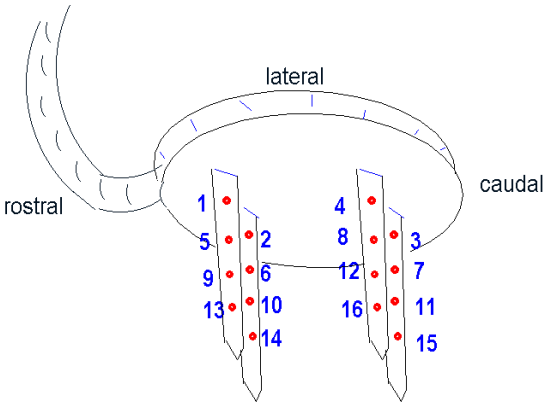

Figure 3

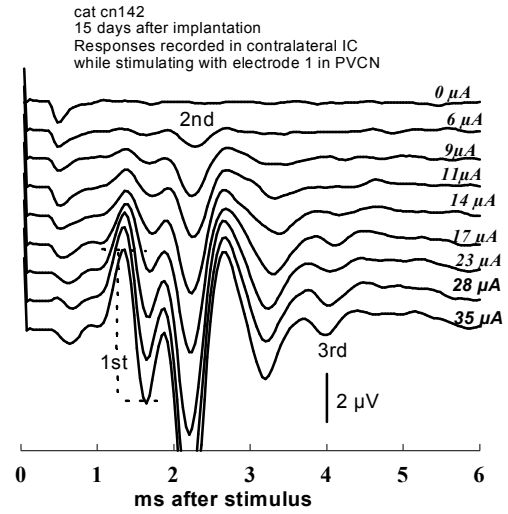

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Figure 4A

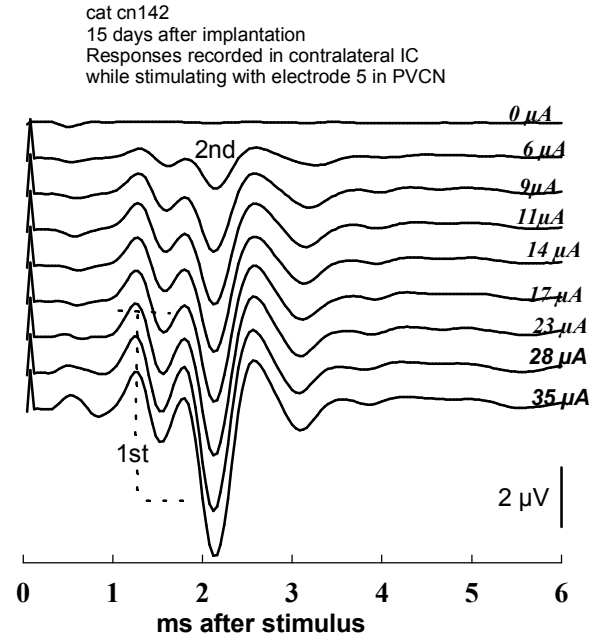

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Figure 4B

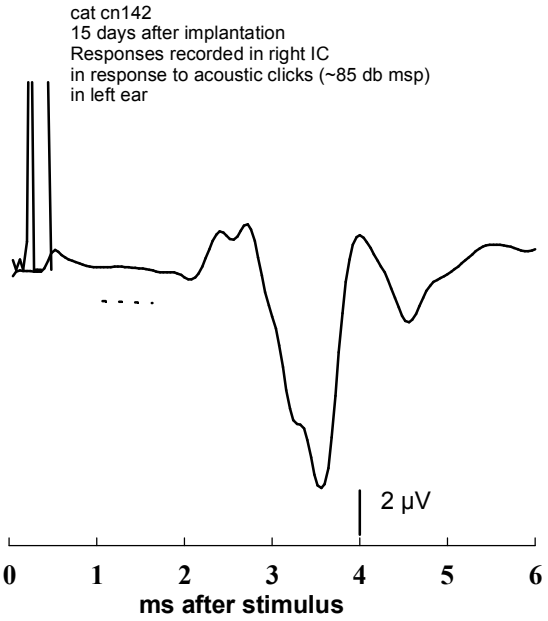

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Figure 5

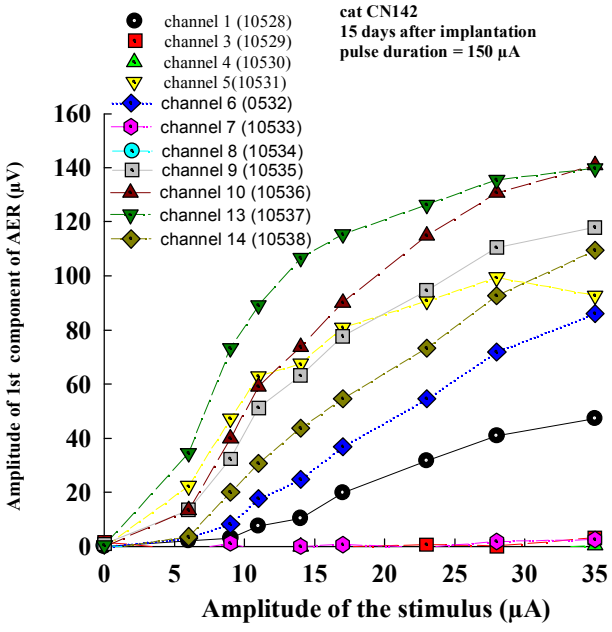

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Figure 6

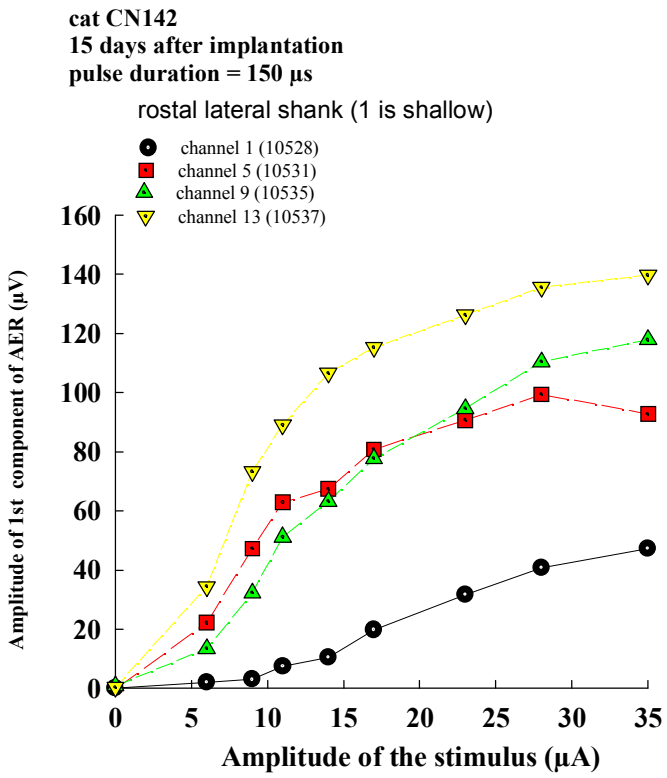


Figure 7A

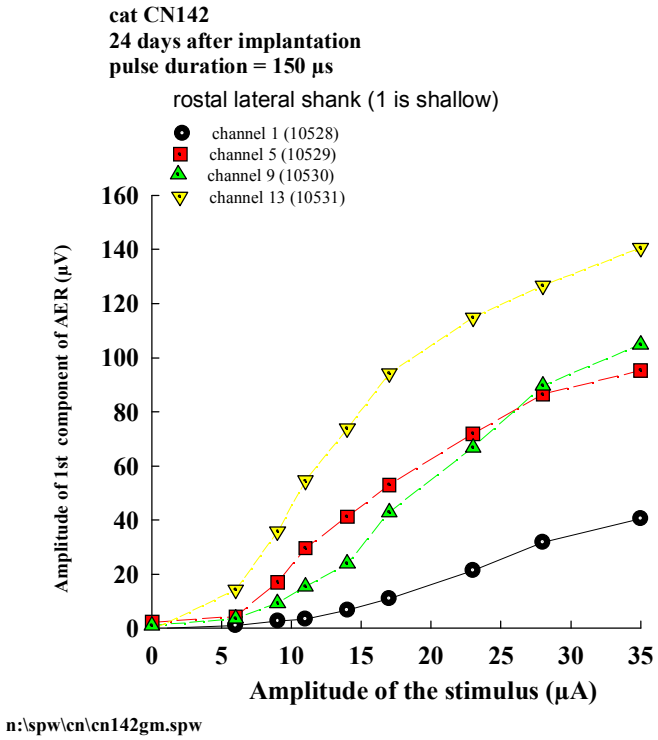


Figure 7B

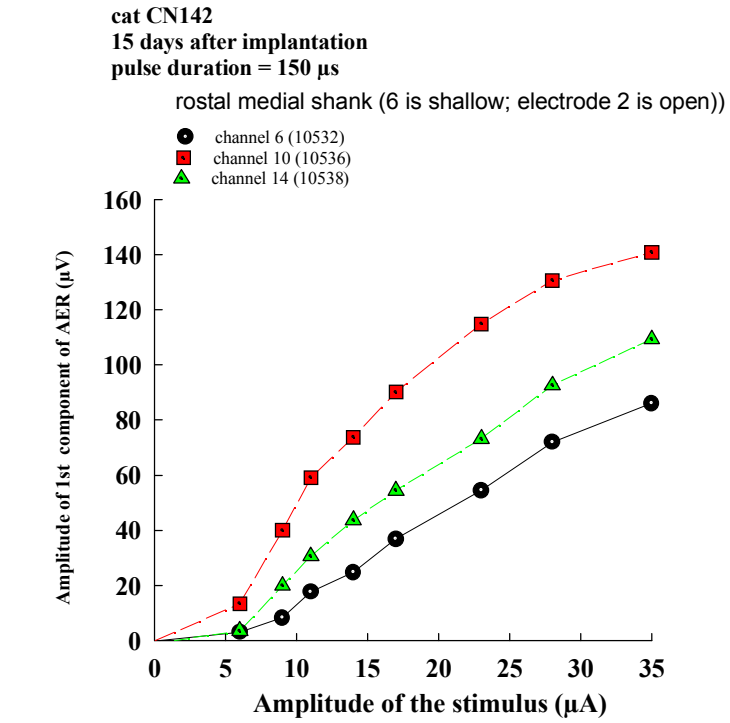


Figure 7C

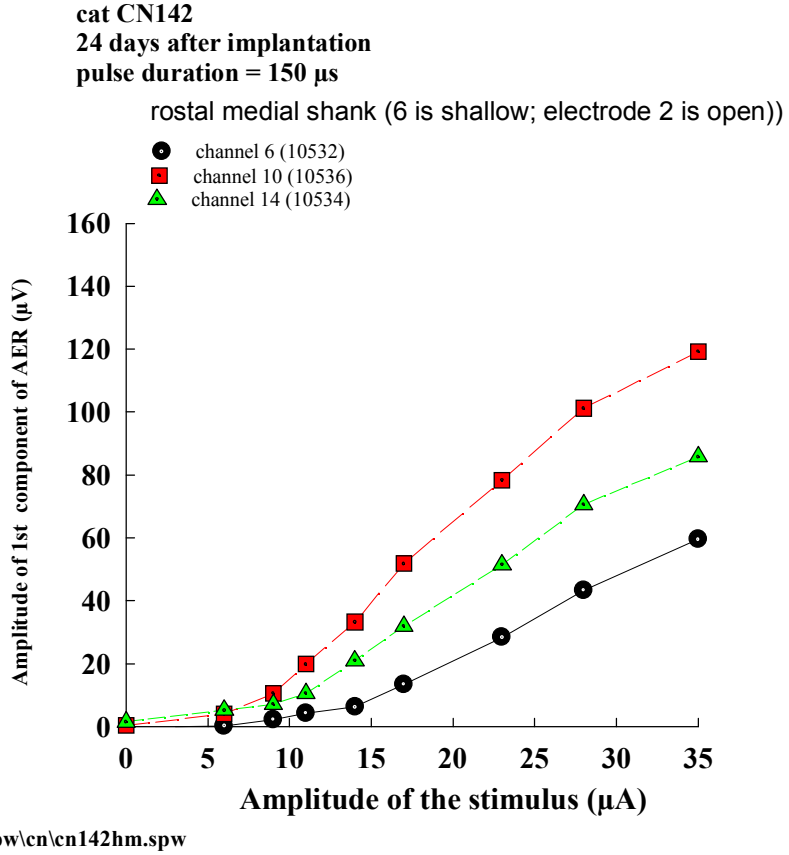
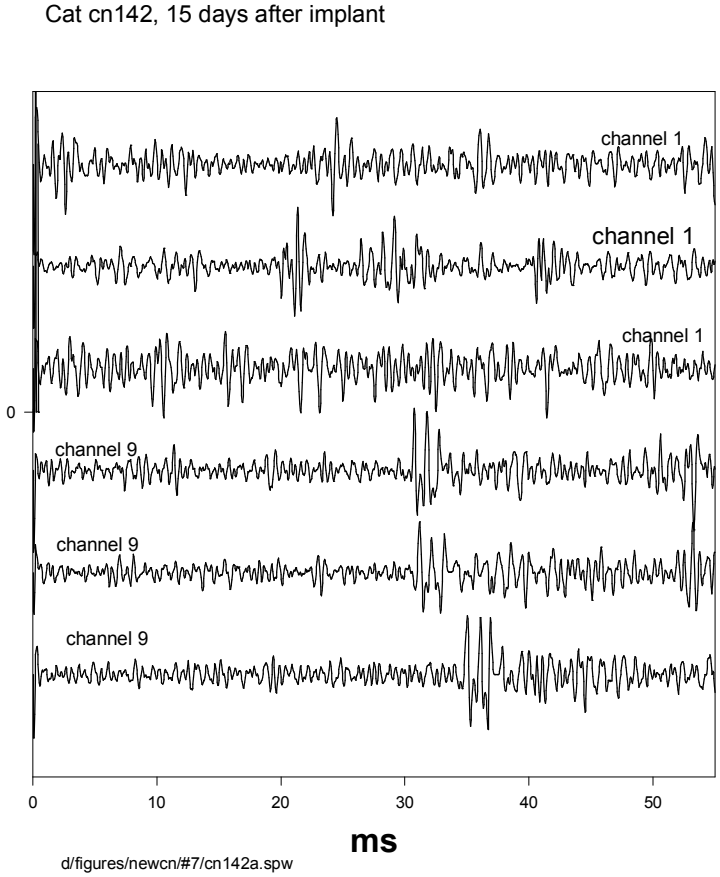


Figure 7D


Cat cn142, 15 days after implant
channel 1
channel 1
channel 1
0
channel 9
channel 9
channel 9
0
10
20
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50
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Figure 8