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Protective Effects of Patterned Electrical Stimulation on the Deafened Auditory System

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Abstract

This report examines the effects of intracochlear electrode separation, and mode of stimulation (bipolar or monopolar) on neural threshold and spatial selectivity in the inferior colliculus (IC) of the cat. Single and multi-unit recordings were made in 10 acutely deafened adult cats refered to as controls, in 5 neonatally deafened cats which were studied between 6 and 18 months of age and 6 neonatally deafened adult cats and 6 neonatally deafened cats which were studied at ages of 2.5 - 6.5 years. The neonatally deafened animals were examined histologically following the physiological experiment to assess their spiral ganglion cell survival. The group of animals studied at ages of less than 1.5 years had a mean spiral ganglion cell density of 42.7% of normal while the animals studied at greater than 1.5 years had a mean spiral ganglion cell density of 9.9% of normal. All animals were implanted with an intracochlear electrode consisting of a silicone rubber carrier and four or five stimulating contacts. The electrode configurations studied included 2 monopolar intracochlear electrode sites, radial bipolar, 1 mm longitudinally separated offset radial bipolar and 4-6 mm longitudinally separated bipolar stimulating pairs.

These results indicate that: (1) Monopolar thresholds are approximately 6 dB lower than the lowest bipolar thresholds in the same animals. (2) Varying longitudinal inter-electrode separation of bipolar contacts from 0.0 mm (radial), to 1.0 mm (offset radial), to 4-6 mm (longitudinal) did not systematically effect average IC threshold in either control animals or short term neonatally deafened animals. In contrast, the long term neonatally deafened animals (>1.5 yrs. of age) did show a systematic decrease in threshold with increased longitudinal contact separation. (3) Bipolar stimulation produces selectivity which is approximately 30% more restricted than monopolar stimulation for a given superthreshold level.

Of the combinations evaluated in this study the offset radial bipolar configuration appears to be the optimum electrode configuration for the greatest number of circumstances modeled. However, in consideration of the very large individual variability observed it is advantageous to maintain the ability to configure an implanted system to best fit each subject and to develop fitting strategies which make this possible in the clinical setting.

Introduction

In order to produce effective multichannel stimulation each channel of a cochlear implant must activate distinct populations of auditory neurons over a reasonable dynamic range. To produce such activation requires minimizing electrical field interactions in and around the electrode to tissue interface and maximizing the spatial selectivity of auditory nerve fiber excitation regardless of the stimulating strategy employed. To better understand the effects of some aspects of intracochlear electrode design, channel interaction and spatial selectivity we measured the spatial selectivity of several stimulating electrode configurations. To assess the role of neural survival on the spatial selectivity of intracochlear electrical stimulation we made these same measurements in both control and chronically deafened animals in which the degeneration of the auditory nerve array was also examined. These observations are directly relevant to the development of future intracochlear electrodes since they will provide a better understanding of some of the fundamental parameters which underlie the great variability in results seen among cochlear implant users.

The effective design of improved intracochlear electrodes must be based on accurate models of the interaction between the stimulating electrode and peripheral neurons. Historically, several approaches have been taken to measure or predict these complex interactions. These have included computer modeling of electrical fields within the cochlea and the resulting neural activity, animal-based physiological and behavioral studies, inference of spatial excitation patterns in human subjects, and attempts to correlate histological results obtained after death with performance measures made during cochlear implant use.

Computer Modeling

Computer modeling of the spatial characteristics of neural activation by intracochlear stimulation is based on mathematical predictions of electrical field strength within the scala tympani and surrounding cochlear structures. As a foundation for these models typical resistance values for perilymph, endolymph, bone and cochlear membranes have been well documented *in vitro* (Strelioff, 1973; Finley, 1989) and *in vivo* (Spelman et al., 1987; Suesserman, 1992). A mathematical model predicting the longitudinal flow of electrical currents in the cochlea was first described by Strelioff (Strelioff, 1973). Finley utilized finite element analysis (FEA) to model two (Finley et al., 1987) and three dimensional (Finley, 1989)spread of current within the cochlea from sources within the scala tympani. These studies suggested that electrode geometry is extremely important in determining the shape of potential fields surrounding peripheral axons and ganglion cells while tissue impedances are of secondary significance.

Although the finite element technique more accurately represented the anatomy of the cochlea and potential fields within the scala tympani it required lengthy computations. To minimize the number of computational tasks Suesserman (Suesserman et al., 1993) and Rodenheiser (Rodenhiser et al., 1995) developed lumped parameter models of longitudinal voltage gradients in the guinea pig cochlea. These models simulated several monopolar stimulus configurations including several series of monopolar contacts with varied phase orientation.

Although these models provided many insights, they made several predictions which conflict with observations using intracochlear electrical stimulation in animal and clinical studies. For example, Finley, et al(1990) predicted that thresholds for stimulation with radial bipolar electrodes would be lower than those for offset radial electrodes and that longitudinally spaced electrodes would have the highest threshold. However, Merzenich and White (1977) found that the neuronal threshold order for ICC neurons was opposite to these predicted values for similar electrode configurations (Merzenich et al., 1977). In addition, the FEA model (Finley et al., 1990) predicts that both offset radial and longitudinally separated electrode pairs will produce bimodal popluations of activated neurons. Corresponding patterns have not been observed in either the auditory nerve (van den Honert et al., 1987) or the inferior colliculus (Merzenich et al., 1979; Snyder et al., 1990) in cats stimulated with these electrode configurations. Third, lumped parameter modeling (Suesserman and Spelman, 1993) predicted a broad, but clearly tuned, population of neurons activated by a single monopole in the scala tympani. In contrast, no measurable tuning was seen in auditory nerve studies (van den Honert and Stypulkowski, 1987)with monopolar stimulation.

To predict thresholds and response distributions for a specific population of peripheral neurons the results of electrical field models must be integrated with a model of neural excitation. The physiological parameters which define the initiation and propagation of action potentials have been discribed and mathematically modeled in detail with increasing complexity and accuracy (Frankenhaeuser et al., 1964; McNeal, 1976; Colombo et al., 1987; Parkins et al., 1987; Reilly et al., 1987; Frijns et al., 1994; Frijns et al., 1994) for review). In 1990 Finley presented the first combined model of auditory electrical stimulation. This model integrated FEA predictions of electrical field strength and computed the resulting distribution of activated fibers using a lumped-element neural response model. The model predicted the threshold and spatial distribution for dendrites stimulated with an electrode consisting of an insulating carrier and a bipolar set of contacts in either a radial, longitudinal, offset radial or longitudinal banded configuration. Model simulation with radial bipolar pairs, placed relatively close to the habenula, activated the most restricted set of neurons while stimulation with longitudinal banded pairs of electrode contacts, placed near the spiral ligament, produced the least selective activation pattern. The high degree of selectivity predicted for stimulation with a well placed radial electrode configuration is in accordance with the observations of Merzenich (Merzenich and White, 1977) van den Honert (1997) and Snyder (1990). Clopton et al. (Clopton et al., 1995) described simplified compartmental model predictions for spiral ganglion cell activation with monopolar, bipolar and quadrupolar stimulation (using adjacent out-of - phase electrodes to minimize current spread). In this study the model predicted that bipolar stimulation would produce the least selective pattern of activation followed by monopolar stimulation and quadrupolar stimulation producing the sharpest tuning.

A significantly improved integrated model was reported by Frijns (Frijns and Kate, 1994; Frijns, Mooij et al., 1994). In addition to response thresholds for dendrites, cell soma and central axons in a rotationally symmetrical geometry the neural response calculations in this model yield conduction velocities, strength duration curves, absolute and relative refractory periods and predicted frequency following behavior. Several predictions of this model are of particular interest. First, the model predicts a large increase, up to 20dB, in the bipolar stimulation threshold when peripheral dendrites are removed from the model. In contrast to this prediction Snyder (1990) found that cats which were neonatally deafened, and then studied physiologically after a mean interval of ≈42 weeks, actually had lower mean IC unit thresholds than the comparison control group. Previous studies have indicated that this group of deaf animals would have only a very small number of surviving peripheral processes. Second, the Frijns model predicts that spatial tuning would also degenerate with the loss of peripheral fibers. Again, the Snyder study showed no significant loss of tuning, as measured in the IC, in this chronically deafened group of animals compared to the control group. Third, this model predicts that significant stimulation of neurons in adjacent cochlear turns would occur at levels near threshold for the region immediately surrounding the stimulating electrode. Analogous multiple regions of representation have not been reported in mapping experiments in the auditory nerve or inferior colliculus.

Some of the differences between the predictions of these various modeling studies and between modeling and data from animal physiological experiments may be attributed to differences in the anatomy of the species modeled, i.e. human and guinea pig cochleae have been most frequently modeled while most physiological data has been generated in cats. Other sources of variation include the small number of animals used in some physiological experiments, the large variety of electrode designs which have been modeled and tested in animals and the lack of anatomical evaluation of animals studied physiologically. In this study we have attempted to eliminate several of these variables by measuring the responses to intracochlear electrical stimulation with several electrode configurations placed on a single, wholly implanted silicone rubber carrier which is similar in design to a clinically appied device. With this strategy we measured responses to each configuration in a single penetration of the inferior colliculus to generate data on both threshold and spatial distribution. By applying this strategy to three groups of animals representing three stages in the degeneration of the peripheral auditory nervous system we compared the effects of neural degeneration on these measures.

Animal Physiology and Behavioral Studies

Several animal studies have measured the effect of electrode position on the threshold and/or spatial distribution of neural responses to intracochlear stimulation or inferred response patterns using masking techniques. The electrically evoked auditory brainstem response (EABR) has been used to compare the efficacy of stimulation at the promontory, round window, scala tympani and scala vestibuli in guinea pigs (Marsh et al., 1981) and in cats (Lusted et al., 1984). The threshold and growth in response magnitude were measured for differnet interelectrode separations in animals of different, measured neural survival

(Vivion et al., 1981). Smith, et al. (Smith et al., 1994), measured EABR responses to several monopolar locations and to bipolar electrode pairs in the same animals. These studies concluded that the threshold for monopolar stimulation was usually lower than that for bipolar stimulation and that bipolar electrode pairs with greater interelectrode separation had lower thresholds than closely spaced electrodes. Two latter EABR studies (Shepherd et al., 1993; Xu et al., 1993) examined the effects of electrode position within the scala tympani in deafened cats. Shephard compared EABR threshold in surgical preparations which permitted the placement of a bipolar banded electrode near the spiral ganglion, adjacent to the habenula perforata, in the middle of the scala tympani volume and adjacent to the spiral ligament. They concluded that lowest thresholds were achieved when the electrode was placed immediately beneath the osseous spiral lamina and peripheral dendrites. These data generally concur with the modeling studies cited above.

In addition to the threshold data generated in EABR studies single and multi-unit recording in either the auditory nerve or in the inferior colliculus provides a relative measurement of the spatial response patterns to electrical stimuli and mapping studies have been conducted in cats at each of these locations. Because the tonotopic organization in the auditory nerve must be inferred by the characteristic frequency (CF) of each fiber using acoustic stimuli the acoustic function of animals used in these mapping experiments must be maintained. This precludes the use of deaf animal models which reflect the varied degeneration of the peripheral auditory system seen in deaf patients. As an alternative, the central nucleus of the inferior colliculus (ICC) is tonotopically organized in sheets or lamellae representing low frequency cochlear locations near the surface and high frequency locations in the depth of the nucleus. This well documented frequency gradient allows measurement of response selectivity when the response threshold is plotted against the microelectrode recording depth. Recording experiments in both the acoustic nerve (Hartmann et al., 1984; Parkins and Colombo, 1987; van den Honert and Stypulkowski, 1987) and the ICC (Merzenich, White et al., 1979) were in agreement with EABR studies reporting both lower response thresholds for monopolar electrical stimulation and more rapid growth of response magnitude than with bipolar stimuli. These studies also found that increasing the longitudinal separation between stimulating contacts increases the growth of response magnitude while decreasing the selectivity of activation. In this comparison van den Honert and Stypulkowski found that selectivity for longitudinally oriented electrode pairs with 1 mm separation was, on average, three times more broad than for radially oriented pairs. They oberserved no measureable tuning in most preparations using monopolar stimulation. These results for bipolar tuning are similar to those of Merzenich, et al, although the latter study did observe significant tuning in monopolar experiments albeit much more broad than even the greatest longitudinal sepration of 2.4 mm for a bipolar pair. Snyder, et al (Snyder, Rebscher et al., 1990), studied the spatial representation of intracochlear electrical stimulation in the ICC in control cats, neonatally deafened cats and neonatally deafened cats which had recieved electrical stimulation for up to four months. As in previous experiments these studies indicated that radial bipolar stimulation may produce very selective excitation in prior normal animals with central representation becoming less tuned as interelectrode spacing increased. This study also found that chronic electrical stimulation expands the ICC region representing the chronic stimulating location and that the spiral ganglion cells in this portion of Rosenthal's Canal were preferentially preserved (Leake et al., 1991). It is also notable that this study found no significant difference in spatial selectivity between control animals and unstimulated, neonatally deafened animals up to 1.3 years old. These results indicate that not only does the auditory system maintain its basic organizational structure after deafening but that frequency selectivity is not significantly degraded when a large number of neurons are lost through degenerative processes.

The results of behavioral experiments in primates (Pfingst et al., 1984; Pfingst et al., 1985; Pfingst et al., 1995) were similar to those of the physiological studies described above, i.e. these experiments indicated that threshold is lower for monopolar stimulation than for bipolar stimulation and is lower for increasing separation of bipolar stimulating elements. To measure spatial resolution animals were trained to discriminate between two sequential stimuli at two monopolar stimulation sites along an array of contacts. The animals were successful in this task even when the separation between test electrodes was reduced to 0.5 mm (Pfingst, Glass et al., 1985) and were most successful when the stimulus amplitude approached the upper limit of their operating range. Considering the rapid spread of excitation demonstrated for monopolar stimulation in the physiological studies cited above this result indicates that discrimination between two stimulus sites can be successfully accomplished in the presence of substantially overlapping representations, at least when these stimuli are separated in the temporal domain.

Human Psychophysics

Ideally, computer simulations and studies in appropriate animal models will yield a framework for understanding the results observed in human cochlear implant patients. In practice, the correlation between the results of basic research studies and clinical studies has been quite variable. For example, there is excellent agreement between predictions of the relationship of monopolar and bipolar thresholds in modeling studies (Colombo and Parkins, 1987), animal physiology and behavioral experiments (Merzenich and White, 1977) van den Honert, 1987 #76; Parkins, 1987 #212; Pfingst, 1995 #176] and clinical studies (Eddington et al., 1978; Shannon, 1983; Brown et al., 1996). However, these results and predictions are more conflicting when spatial selectivity is considered. A review of the basic science studies which have modeled or physiologically measured the selectivity of electrical stimulation in the scala tympani lead to the conclusion that broadly overlapping neural fields will produce high levels of confusion between electrode channels. One would expect that these confusions would be particularly prominent when using monopolar stimulation or laterally placed banded electrodes (Merzenich, White et al., 1979; van den Honert and Stypulkowski, 1987; Finley, Wilson et al., 1990). For example, van den Honert observed that monopolar stimulation resulted in a "lack of any spatial selectivity in the stimulation pattern" measured in the eigth nerve. In contrast to these observations, behavioral experiments (Pfingst, Morris et al., 1995) and clinical experience indicate that animals and most patients are able to discriminate the percepts from different electrode sites. In many cases these subjects were able to order these sites in correct tonotopic sequence (Eddington, Dobelle et al., 1978; Shannon, 1983; Tong et al., 1985; Townshend et al., 1987; Busby et al., 1996). Most of these patients attained this high level of discrimination using either monopolar or banded electrode configurations for which animal and modeling studies predict poor spatial selectivity. In addition, it appears that psychophysical discrimination abiltiy in cochlear implant patients can be even greater if deconvolution or "current focusing" techniques are employeed to either sharpen the tuning of multipolar channels or to generate "virtual channels" between two or more electrode sites (Townshend, Cotter et al., 1987; McDermott et al., 1994). In addition to being able to differentiate between stimulation sites, the cognitive processes involved in speech discrimination recognize the correct tonotopic order of frequency information coming into the system and performance is drastically reduced if this order is perturbed (Rabinowitz et al., 1995). It should be noted that one group of subjects which generally do poorly in electrode discrimination tasks and speech recognition are adults with prelingual deafness (Eddington, Dobelle et al., 1978; Busby et al., 1993).

From an engineering perspective this ability to discriminate electrode sites may not mean that current electrode designs attain sufficient spatial selectivity for high level speech discrimination in many, or perhaps most, patients. All of these studies require subjects to compare two percepts presented sequentially. Thus, both the electrical and neural interactions which may occur between two channels were eliminated. Although the central nervous system is clearly able to differentiate between neural patterns which differ only at the fringes of the representation when presented nonsimultaneously, significant distortions may occur within these representations when signals are presented in simultaneous or overlapping sequence. For this reason it is still highly desirable to minimize the spread of electrical signals within the scala tympani.

Goals of this Study

In this study we have directly measured the response thresholds and spatial representation of intracochlear electrical stimulation in the tonotopically organized midbrain of the cat while manipulating the longitudinal separation of stimulating contacts on a silicone rubber carrier within the scala tympani. Our primary goal is to generate the data necessary to design improved intracochlear electrodes which will maximize channel independence and dynamic range while minimizing operating threshold for the greatest number of patients. These data will also be useful in evaluating the efficacy of computer modeling techniques and better understanding the processes involved in speech recognition with cochlear implants .

Table 1. *Animal Summary*

Cat Number	*Duration of Deafness (Months/Meth)*	*Duration of Implant (Weeks)*	*Electrode Type*	*Spiral Gang. Survival (% Normal) 90% of BM*	*EABR Thr. Bipolar 1,2 200μSec (μAmps)*	*ICC Thr. Bipolar 1,2 100Hz Sine (μAmps)*
			Acutely Deafened Control Animals			
105	1.5/AOAA	4 weeks	UCSF	≈	63	36
134	Kanamycin	Acute	UCSF	≈	50	45
138	Kanamycin	Acute	UCSF	≈	50	22
401	Intracochlear	Acute	UCSF	≈	50	63
655	Intracochlear	Acute	UCSF	≈	63	112
755	Intracochlear	Acute	UCSF	≈	NA	32
865	Intracochlear	Acute	UCSF	≈	63	32
242	Kanamycin	Acute	UCSF	≈	316	56
553	Kanamycin	Acute	Wing	≈	200	36
518	1/Kanamycin	Acute	Wing	≈	63	5
			Neonatally Deafened Animals (Less than 1.5 years of age)			
K11	8/neomycin	Acute	UCSF	NA	100	50
K26	14/neomycin	3 weeks	UCSF	23.5	200	50
K30	7/neomycin	20 weeks	UCSF	NA	100	40
K44	6/neomycin	Acute	UCSF	64.4	100	14
K46	9/neomycin	Acute	UCSF	40.3	100	14
			Long Term Neonatally Deafened Animals (More than 1.5 years of age)			
K03	31/neomycin	2 weeks	UCSF	13.1	398	126
K16	44/neomycin	Acute	UCSF	10.7	126	45
K24	30/neomycin	Acute	UCSF	7.2	251	50
K33	51/neomycin	1 week	UCSF	5.1	251	112
K51	78/neomycin	6 weeks	Wing	4.85	398	56
K73	41/neomycin	2 weeks	Wing	18.3	126	14

Methods

The deafening and implantation histories of the animals included in this study are presented in **Table 1**. The control group consisted of adult animals that were deafened acutely prior to the physiologic experiment. Four adults were deafened unilaterally by intracochlear injection of neomycin. Six adults were deafened with a single subcutaneous injection of Kanamycin (400mg/kg) followed by slow infusion of ethacrynic acid (10-25mg/kg) (Xu et al., 1990). One adult animal (#105) was deafened by a single subcutaneous injection of kanamycin (400mg/kg) followed by a single subcutaneous injection of aminooxyacetic acid (25mg/kg) (Leake et al., 1987). During the systemic deafening procedures auditory brainstem responses (ABR) were measured continuously until no responses were observed at a level of 105dB SPL. In most cases adult animals were deafened one to two weeks prior to the physiological experiment and implanted at the time of the experiment. In three cases the animals were deafened or implanted for longer periods prior to the final experiment as described in Table 1.

Neonatally deafened animals were given a single intramuscular injection of neomycin sulfate (50 or 60 mg/kg) daily beginning 24 hours after birth and continuing for 16 days. At 16 days of age the ABR for both right and left ears was recorded for .1ms click stimuli presented at a level of 105dB (SPL). If any auditory response was identified the administration of neomycin sulfate was continued until day 21 at which time the animal was retested. No ABR response was seen in this 21 day test for any of the animals in this study. These animals were maintained without complications for periods of up to 6.5 years prior to implantation and the final physiological experiment.

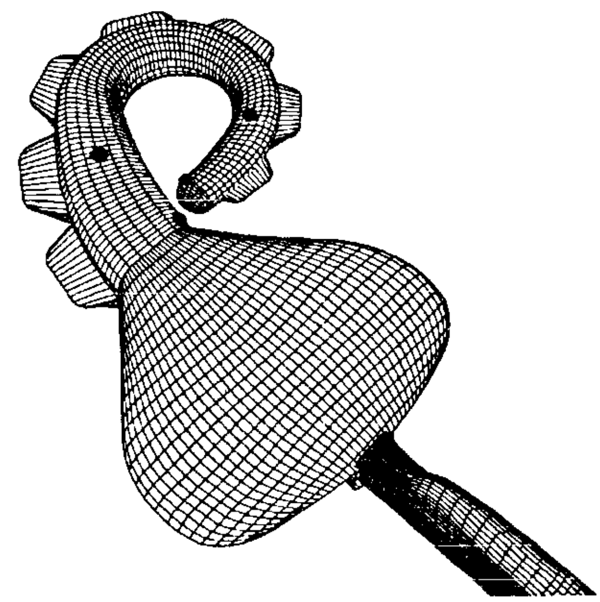


Figure 1. ***Four contact UCSF intracochlear "Wing" electrode.***

The left cochlea of each animal was implanted (see Leake, et al, 1991) with one of two multichannel intracochlear electrodes. The latest version of the UCSF cat electrode with positioning "wings" is shown in Figure 1 and detailed specifications for both electrode designs are shown in Table 2 and Figure 2. The electrode consists of an injection molded silicone rubber carrier which held five Pt:Ir electrode contacts 225μm diameter. This electrode tapers from slightly larger than 1 mm at the basal contact set to 0.5 mm at the tip. The enlarged "wing" section near the round window and the small fins along the more apical electrode body were designed to improve the position of the electrode carrier within the scala tympani and to partition the volume of conductive fluid adjacent to the electrode. The previous UCSF cat electrode consisted of a simple cylindrical carrier which tapered from 1.0 mm at the round window to 0.6 mm at the tip. The radial position of the electrode contacts was unchanged in the two designs.

Table 2. *Electrode Contact Position Data*

	Electrode Type UCSF	UCSF "Wing"
Number of Animals	n=17	n=4
	Distance Between Contacts	
Apical "Offset" Pair (Electrodes #1 and #2)	1.0 mm	1.0 mm
Apical (Electrode #1) to Basal (Electrode #4)	4.0 mm	6.0 mm
Total Electrode Length (Round Window to Tip)	7.0 mm	9.0 mm

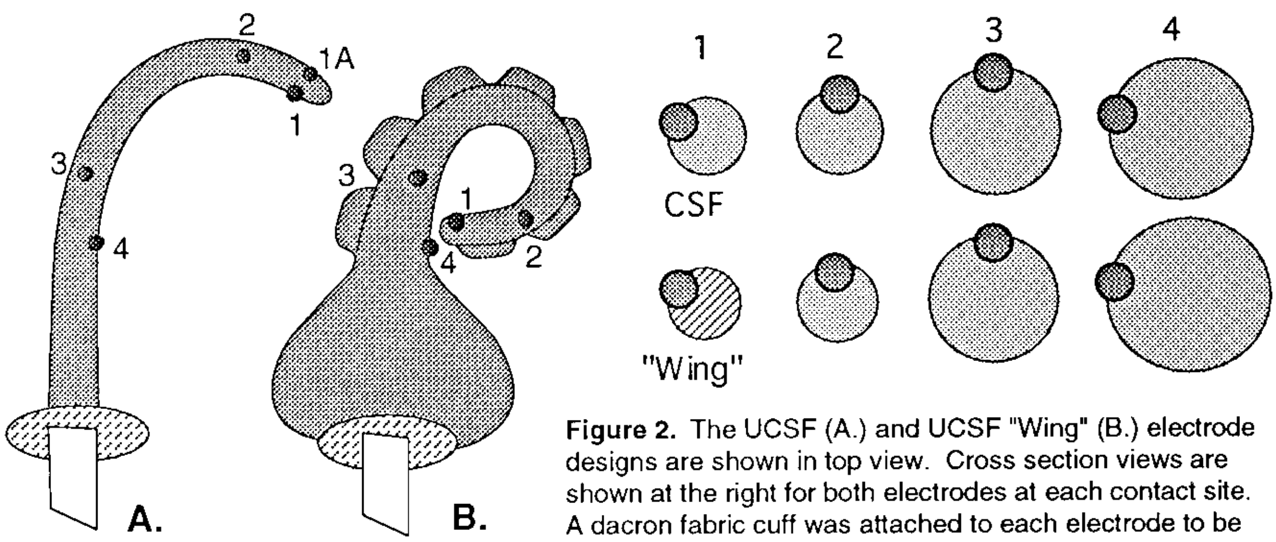
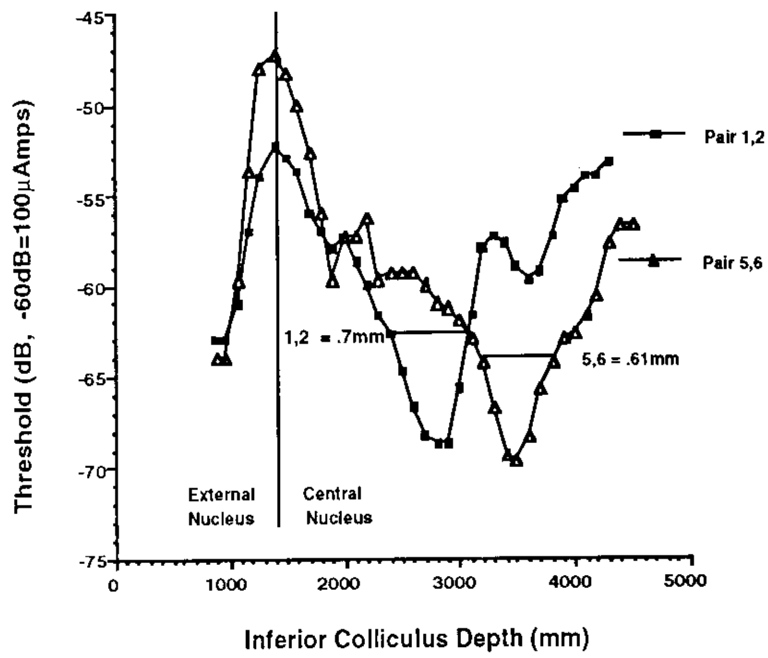


Figure 2. The UCSF (A.) and UCSF "Wing" (B.) electrode designs are shown in top view. Cross section views are shown at the right for both electrodes at each contact site. A dacron fabric cuff was attached to each electrode to be secured to the temporal bone near the round window.

The methods used in the electrophysiological experiments conducted with these animals have been described previously (Snyder et al., 1990; Snyder et al., 1991; Snyder et al., 1995) . In brief, animals were sedated with ketamine (22mg/kg) and acepromazine (2mg/kg), the animals were shaved and an IV catheter was inserted in the cephalic vein. Sodium pentobarbital (40-60mg/kg) was administered intravenously (I.V.) to induce an areflexic level of anesthesia. The animal's head was mounted in a mouth-bar head holder and each animal was continuously monitored and maintained fully anesthetized throughout the experiment. A craniotomy was performed to access the middle cranial fossa, and a portion of the tentorium was removed to expose the right inferior colliculus.

Figure 3. Normal Cat #CH553 Penetration 2



All stimuli were capacitively coupled and electrically isolated in a custom low noise electrical isolator (Vurek et al., 1981). Electrical stimuli were switched between the four intrachochlear electrodes with a custom switching array. The level for each stimulus was set using an audio attenuator (Hewlett Packard Co., Santa Clara, CA). All experiments were performed in an electrically shielded acoustic enclosure. Neural signals were recorded using a primary amplifier (gain = 1,000, Bandpass=100Hz-3KHz, Princeton Applied Research, Princeton, NJ or World Precision Instruments, Sarasota, FL) within the enclosure and a secondary amplifier (gain = 100, Tektronix, Inc. Portland, OR). Analog signals were digitized with an analog to digital converter (National Instruments, Austin, TX) controlled by custom software in a PC DOS environment. EABR responses were recorded differentially for 500 or 1,000 biphasic alternating polarity electrical stimuli (200μS/ph) using scalp electrodes placed over the ipsilateral bulla (reference), at the vertex of the skull (active) and over the contralateral bulla (ground). Recordings from the inferior colliculus were made using tungsten microelectrodes (≈1Mohm impedance, BAK Electronics, Germantown, MD) and a 100Hz continuous sinusoidal mapping stimulus. The trajectories of these electrodes were oriented in the coronal plane, 45° off the sagital plane so that they traverse the IC approximately perpendicular to its tonotopic organization. Response thresholds for each stimulating electrode combination at 100μm intrevals along the recording penetration trajectory were determined audiovisually. In cases where single units were successfully discriminated from multiunit activity single neuron responses were recorded as perstimulus time histograms. Multi and single unit response thresholds were plotted as a function of IC depth to generate a "spatial tuning curve" (STC) which allows the pattern of distributed activity across the auditory nerve array to be inferred. A typical plot for one penetration is shown in Figure 3. Peak to peak current measurements are reported in dB with -60 dB= 100 μAmps. To compare the relative selectivity of responses to either different electrode configurations or within different animal groups we measure the width of each STC at a level of 6 dB above threshold as shown in Figure 3. Only the central nucleus of the IC was used for these comparisons becuase the tonotopic organization of the auditory system is represented with higher resolution in this nucleus. In analyzing the data from these experiments all statistical comparisons within a given animal group were made between measurements of responses to different electrode combinations during the same penetration through the IC. This procedure eliminates the variation which may occur when one electrode configuration measured in an IC penetration is compared to a different configuration measured in a second penetration or in another animal. Thus, this measure of relative selectivity is compared for each electrode configuration in a single penetration. Because both the goals of this study and the techniques used in these experiments evolved throughout the duration of this investigation some electrode configurations were not tested in all animals. Most notably, the radial and monopolar conditions were not tested in the neonatally deafened animals studied at less than 1.5 years of age.

Results

Spiral Ganglion Survival

Eight of the ten control animals in this study were deafened immediately prior to the physiology experiment. For this reason the control group of animals are considered to have normal neural survival and were not histologically examined. For each neonatally deafened animal the cell density was measured and expressed as a percentage of normal cell density (Leake, Hradek et al., 1991)(see Table 1). The mean spiral ganglion survival for the neonatally deafened animals examined at less than 1.5 years was 42.7%. The mean survival for animals in the long deafened group (greater than 1.5 year survival) was 9.9%. Figure 4 illustrates representative spiral ganglion sections for each group of animals. The pathological condition of these deafened cochleae should be considered in evaluating the threshold and spatial tuning of responses to electrical stimulation in these animals. It is important to note the presence of peripheral fibers in the osseous spiral lamina in the aniamls deafened for less than 1.5 years compared to the long deafened group which shows a complete loss of these fibers.

Theshold and Spatial Selectivity

Control Animals - Table 3 summarizes the average minimum ICC response thresholds for monopolar, radial bipolar, offset radial bipolar and longitudinal bipolar electrode configurations measured in the acutely deafened, control animals. In this group the mean threshold to monopolar stimulation (-74.9 dB, 18μAmps) is lower than the threshold to all bipolar configurations. In these comparisons responses to the basal electrode pair (3,4) were not compared because of the difference in the scala tympani positioning of this basal pair due to the presence of the positioning "wing" in some animals.

Figure 4. Typical spiral ganglion sections from each of the three animal groups are illustrated in this figure.

A. This micrograph illustrates a normal adult cat cochlea. Ganglion cells (SpG) are clearly visible in Rosenthal's canal and many peripheral nerve fibers (N) can be seen passing through the osseous spiral lamina (OSL).

B. Neonatally deafened animals which were studied at less than 1.5 years of age showed significant loss of spiral ganglion cells. The average spiral ganglion cell density for this group was 42.7% of normal. The number of peripheral fibers was also reduced in these animals.

C. The long term deafened animals (>1.5 urs.) showed severe degeneration of spiral ganglion cell and complete loss of peripheral fibers. The mean spiral ganglion cell density for this group of animals was 9.9% of normal.

Table 3. *Control Animals*
Threshold: Longitudinal Separation

Stimulus Sites	*Number of Animals*	*Long. Separation (mm c to c)*	*Mean Threshold (dB)*	*P Value: Comparison w/ Pair 1,2*
1 Monopolar	n=8	-	-75.8±9.3	p= .001
2 Monopolar	n=8	-	-74.0±9.5	p= .03
1,1a: Radial	n=6	-	-68.6±10.0	p= .3
1,2: Offset	n=10	1.0	-67.5±8.0	-
1,4: Longitudinal	n=13	4.0 or 5.0	-68.1±10.2	p= .17

The Student's paired T test was used for statistical comparisons of thresholds for each stimulating combination as presented in Table 3. Comparisons having a P value less than .05 were considered significant. Since all combinations were not tested in all IC penetrations, these comparisons have been restricted to include only penetrations in which both conditions could be compared directly. These paired comparisons show a significant difference between the monopolar condition (contact #1 or #2) and the bipolar offset radial (pair 1,2) configuration. In contrast, there was no significant difference between the thresholds for the three bipolar configurations in this group of animals.

Table 4 summarizes the spatial tuning data for monopolar and bipolar stimulus configurations in the control animal group. Although individual penetrations in some animals demonstrate quite narrow tuning for monopolar stimulation the mean STC width is ≈40% greater with monopolar stimulation than with either closely spaced bipolar pair. There was no significant difference in selectivity measured with the three bipolar congfigurations.

Table 4. *Control Animals - Spatial Tuning*

Stimulus Sites	*Number of* Animals	*Longitudinal Separation* (mm c to c)	*Mean STC Width* (mm)	*P Value Comparison w/ Pair 1,2*
1 Monopolar	n=8	-	1.20±.67	p= .005
2 Monopolar	n=8	-	1.30±.63	p= .04
1,1a: Radial	n=6	0.0	0.86±.54	p= .26
1,2: Offset	n=10	1.0	0.78±.19	-
1,4: Longitudinal	n=13	4.0 or 5.0	0.97±.37	p= .29

Figure 5 illustrates two examples of STC plots which compare minimum threshold and spatial selectivity with each electrode configuration tested. The difference in threshold between monopolar and offset radial bipolar stimulation is illustrated in Figure 5A. The similarity between thresholds, and the differences seen in spatial tuning in some cases, for the three conditions of bipolar stimulation are shown in Figure 5B.

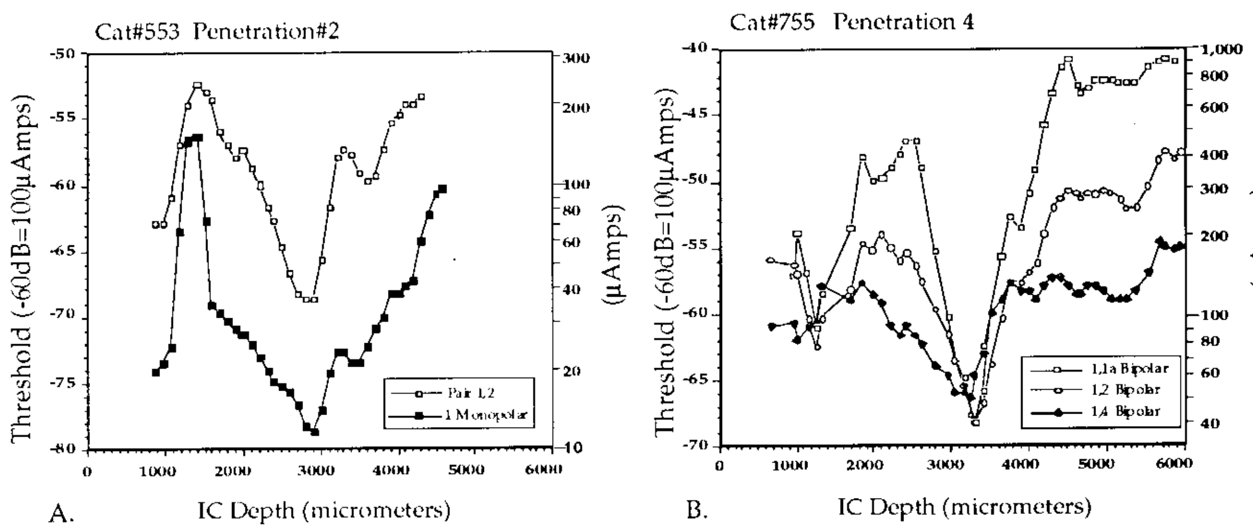


Figure 5. The spatial distribution of responses in the ICC are illustrated for monopolar and bipolar configurations in Figure 5A and for radial, offset radial and longitudinal bipolar configurations in Figure 5B.

Neonatally Deafened Animals (<1.5 years) - Minimum ICC thresholds for bipolar stimulation in these neonatally deafened animals are shown in Table 5. The monopolar and radial bipolar configurations were not tested in this group of animals. In paired comparisons there was no significant difference between the threshold for offset radial and longitudinal configurations in this group of animals.

Table 5. *Neonatally Deafened Animals (<1.5 years) Threshold*

Stimulus Sites	*Number of Animals*	*Long. Separation (mm c to c)*	*Mean Threshold (dB)*	*P Value Comparison w/ Pair 1,2*
1,2: Offset	n=5	1.0	-69.2±8.0	-
1,4: Longitudinal	n=3	4.0 or 5.0	-67.4±10.1	p=.20

Table 6 summarizes the spatial tuning data for neonatally deafened animals studied at an age of less than 1.5 years. Although the response threshold was not significantly different for offset radial versus longitudinal bipolar stimulation in this group the spatial selectivity of responses was significantly greater for the offset radial configuration. It is also interesting to note that the variation between animals (as indicated by the standard deviation of the data for each configuration) was also much greater for the longitudinal configuration. This difference was also seen in the control group data summarized in Table 4.

Table 6. *Neonatally Deafened Animals (<1.5 years) Spatial Tuning*

Stimulus Sites	*Number of Animals*	*Long. Separation (mm c to c)*	*Mean STC Width (mm)*	*P Value Comparison w/ Pair 1,2*
1,2: Offset	n=5	1.0	0.73±.09	-
1,4: Longitudinal	n=3	4.0 or 5.0	1.17±.33	p= .03

Long Term Neonatally Deafened Animals (>1.5 years) - In contrast to either the control group or the neonatally deafened animals studied at less than 1.5 years the thresholds for the long deafened animals were significantly different for each stimulus configuration evaluated (Table 7). The thresholds for bipolar stimulation were directly related to longitudinal electrode separation, i.e. in paired comparisons the threshold for the offset radial pair (separation of 1.0 mm) was ≈5 dB lower than that for the radial configuration and the threshold for the longitudinal configuration (4.0 or 5.0 mm separation) was again ≈5 dB lower than that for the offset radial configuration.

Table 7. *Long Term Deafened Animals (>1.5 years) Threshold: Longitudinal Separation*

Stimulus Sites	*Number of Animals*	*Long. Separation (mm c to c)*	*Mean Threshold (dB)*	*P Value Comparison w/ Pair 1,2*
1 Monopolar	n=4	-	-73.0±10.4	p= .005
2 Monopolar	n=4	-	-73.3±9.1	p= .02
1,1a: Radial	n=4	-	-61.6±9.9	p= .001
1,2: Offset	n=6	1.0	-64.9±7.1	-
1,4: Longitudinal	n=6	4.0 or 5.0	-68.3±8.7	p= .03

In general, the spatial selectivity of ICC responses was reduced in this group of long deafened animals(Table 8). However, there was no significant difference between the width of spatial tuning curves derived with any the five electrode configurations tested.

Table8. *Long Term Deafened Animals (>1.5 yrs.)*
Spatial Tuning

Stimulus Sites	*Number of* Animals	*Longitudinal Separation* (mm c to c)	*Mean STC Width* (mm)	*P Value Comparison w/ Pair 1,2*
1 Monopolar	n=4	-	1.97±.77	p= .15
2 Monopolar	n=4	-	1.85±.48	p= .25
1,1a: Radial	n=4	0.0	1.76±.99	p= .37
1,2: Offset	n=6	1.0	1.35±.58	-
1,4: Longitudinal	n=6	4.0 or 5.0	1.66±.94	p= .10

Comparisons Between Animal Groups - Changes in Spatial Selectivity and Threshold Over Time

In addition to these direct comparisons between electrode configurations within each group of animals we have compared both threshold and spatial tuning between the animal groups as a way of assessing the effects of neural degeneration on these two physiological measures. The duration of deafness has been shown to correlate with the density of spiral ganglion neurons present in the cochlea and the number of peripheral fibers present (see Figure 4)(Leake et al., 1987; Leake et al., 1988). Thus, examining the responses in these animals in which we have carefully documented ganglion cell survival (See Table 1) provides some insite into how progressive neural degeneration might effect CNS processing of electrical stimulation.

Figure 6 compares the mean response sensitivity for each stimulating condition in the control, neonatally deafened animals (<1.5 yrs) and long deafened animals. Interestingly, despite very significant differences in spiral ganglion cell survival (see Table 1) and peripheral dendrite survival (see Figure 4) the mean ICC response sensitivity (minimum neural threshold) for any selected electrode configuration was not significantly different between the three groups .

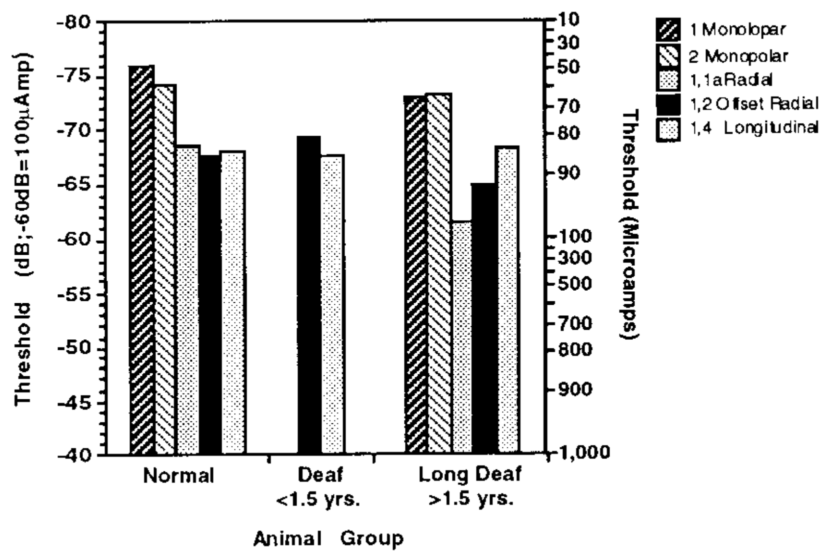


Figure 6. *Effects of Electrode Configuration on Threshold for Three Groups of Animals*

Figure 7 compares the spatial tuning for each electrode configuration measured between the three groups of animals. In each condition the distribution of responses was broader in the long term deafened animals than in the control or neonatally deafened animals less than 1.5 yers of age. As mentioned previously, the monopolar and radial configurations were not tested in the deafened animals less than 1.5 years of age due to technical considerations in these early experiments. It is particularly interesting to note that with each of the electrode configurations tested the STCs from

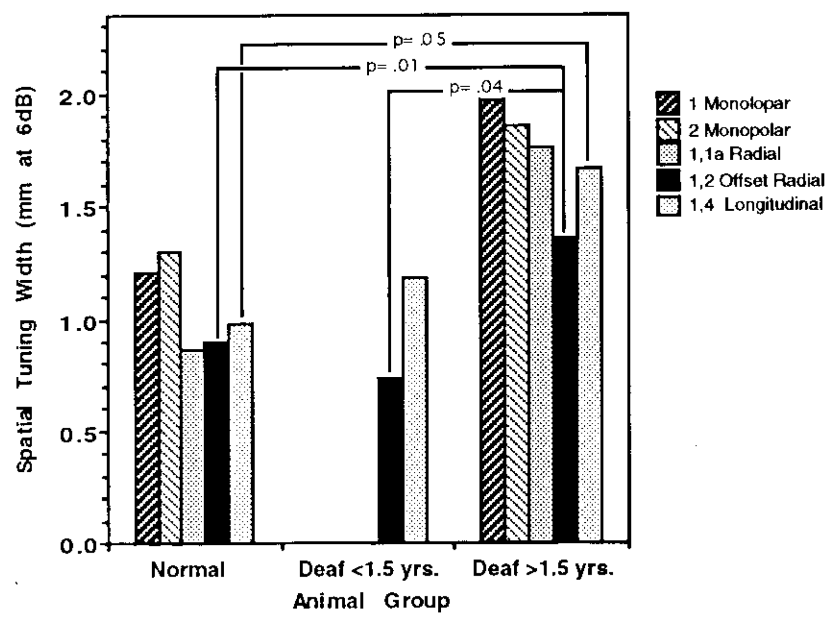
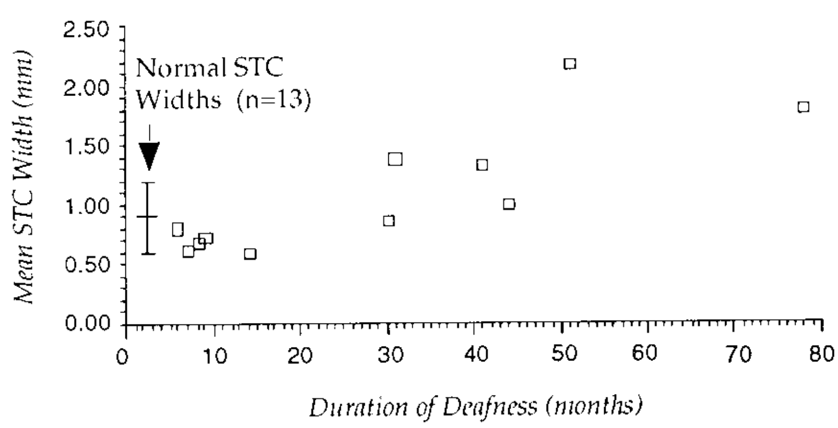


Figure 7. *Effects of Electrode Configuration on Spatial Tuning for Three Groups of Animals*

chronically deafened animals (<1.5 yrs.) were equal in selectivity to those of control animals even though the spiral ganglion cell population of these animals had degenerated significantly, i.e. the spiral ganglion cell density mean was ≈43% in this group of animals.

To examine the progression of the loss of spatial selectivity which occurs between the animals younger than 1.5 years and the long deafened group we plotted the STC widths, for electrode pair 1,2, versus the age of each animal in Figure 8. As shown above the patial tuning in animals up to 1.5 years was unchanged. In fact, these animals all fall at or below the mean STC width for control animals. In contrast, the older animals demonstrate a roughly linear increase (r^2=0.70) in mean STC width as a function of age.

Figure 8. *Spatial Tuning Vs. Duration of Deafness Neonatally Deafened Cats*



Discussion

The animal experiments presented above represent a systematic comparison of several intracochlear electrode configurations with a carrier geometry which is similar to that applied in a large clinical population. In human cochlear implant subjects it is clear that multichannel cochlear implants provide far greater benefits than single channel devices (NIH Consensus Statement, 1995). Previous animal studies, particularly those by van den Honert and Stypulkowski (van den Honert and Stypulkowski, 1987), and the results of computer modeling studies suggest that current spreads rapidly within the scala tympani for most intracochlear electrode designs. This rapid spread of current would theoretically result in broadly distributed neural excitation along the length of the cochlea and the prediction that patients would experience large interactions between electrode sites which might negate or substantially reduce the benefits of multiple information channels. Indeed, interactions between adjacent stimulating sites have been observed with all clinically applied cochlear implant systems. However, the overwhelming success of these devices is a clear indication that at least some level of channel independence is achieved by all multichannel devices tested to date.

In the present study, we used the systematically organized central nucleus of the inferior colliculus to compare the response selectivity and threshold to four different electrode contact configurations in deafened animals with varied neural degeneration. By comparing these response patterns for all electrode configurations during single microelectrode penetrations both the variation between subject responses and between individual penetrations within a given subject were eliminated.

Evaluation of Neural Survival

It has long been assumed that the loss of neurons and other changes in the biophysical environment of the cochlea following deafness significantly effects the performance of individual cochlear implant patients. Thus, from a device development perspective studies designed to model the function of these devices either mathematically or in animals should include a measure of this variable. In this study we examined animals which were grouped into three categories based on their duration of deafness and associated neural survival. As shown in Table 1 and in the micrographs in Figure 4 the control, neonatally deafened (<1.5 yrs.) and neonatally "long term" deafened animals (>1.5 yrs.) represent three distinct groups based on their anatomical features. Leake (Leake et al., 1987) demonstrated that prior normal adult cats deafened with kanamycin and aminooxyacetic acid showed no loss of peripheral fibers or spiral ganglion cells for up to four weeks following deafening. Because eight of the ten control animals in this study were deafened either immediately prior to the physiology experiment or within this four week period the adult animals were considered to have normal neural populations.

The neonatally deafened adult animals which were examined at less than 1.5 years of age were characterized by a mean spiral ganglion survival of 42.7% of normal. This value agrees with measurements of aminoglycoside neonatally deafened animals studied at similar ages in previous reports (Leake, Hradek et al., 1991; Leake et al., 1992; Leake et al., 1995). Histologic examination of cross sections through the scala tympani and osseous spiral lamina of these subjects also revealed a moderate number of surviving peripheral fibers extending from the spiral ganglion to the habenula perforata with a few of these fibers passing into the degenerating tunnel of corti. In contrast, the mean spiral ganglion survival in the long term neonatally deafened animals (>1.5 yrs.) measured only 9.9% of normal and no peripheral fibers were seen in these cases. This dramatic loss of both spiral ganglion neurons and peripheral fibers at durations of deafness exceeding 1.5 years has also been previously documented (Leake and Hradek, 1988). To add context to these neural population measures and how our animal models might relate to human cochlear implant design we examined the reported histopathology of deaf human subjects with mixed etiology.

Table 9. Summary of Human Pathological Data

Group	Number of Subjects	Hearing Loss (dBSPL)	Dendrite Survival (% Normal)	Basal (to 20mm) Dendrite Surv. (% Normal)	Ganglion Survival (% Normal)	Basal (to 20mm) Ganglion Surv. (% Normal)	Number of Ganglion Cells (Total)
Disease/Genetic[1]	n=14	Profound	21.8	13.0	47.3	48.6	16,084
Disease/Genetic[2]	n=3	Profound	46.8	30.0	70.9	58.7	23,839
Disease/Genetic[3]	n=6	Profound	3.3	1.1	54.1	51.3	18,196
Ototoxicity[1]	n=1	≈90dB	10.0	0.0	57.8	54.0	19,608
Ototoxicity/Trauma[2]	n=10	≈90dB	71.8	64.5	77.0	73.5	25,900
Cochlear Implant[4]	n=13	na	21.4	na	40.6	na	12,175
Varied Pathology[5]	n=66	na	na	na	49.5	47.9	14,061

[1]Hinojosa and Marion, 1983
[2]Suzuka and Schuknecht, 1988
[3]Hinjosa, et al, 1991
[4]Lithicum, et al, 1991
[5]Nadol, et al, 1989

Table 9 summarizes the data presented in studies of 113 human cadaver temporal bones from patients which would be considered appropriate for cochlear implantation. The survival of spiral ganglion cells and peripheral dendrites was highly variable for the etiologies examined. Mean values for spiral ganglion cells, expressed as percentage of normal, ranged from 41% to 77% (48% to 74% over the basal region adjacent to most clinically applied implant electrodes) with and average value of 52.9% for the cochlea overall and the range of survival of peripheral fibers was 3% to 72% (0% to 65% in the cochlear base). It should be noted that in approximately one half of the donors (11 of 23) in the broadly mixed classification of disease and genetic deafness no peripheral fibers were found. The three groups of animals which are compared in this study were chosen to represent stages in the degenerative processes which are seen across the population of human subjects as shown in Table 9.

Response Thresholds to Intracochlear Electrical Stimulation

After taking into account the different phase durations of stimuli used in other studies the EABR and ICC response thresholds observed in these experiments were similar to, but in most cases lower than, those in previous reports. It seems clear that the presence or absence of a relatively large insulating carrier is a major physical factor affecting threshold for various electrode configurations. In this study a silicone rubber carrier held the stimulating contacts. In the apical electrode set the carrier occupied most of the volume of the scala tympani and in most cases positioned the contacts close to either the upper or modiolar surface of the cavity. The carrier holding the basal electrodes occupied approximately 50% of the scala tympani volume and was located nearer the center of the fluid volume in most cases.

As observed in previous animal studies, and in human studies, the threshold to monopolar stimulation within the cochlea was consistently lower than that for bipolar stimulation. In this study the averge IC minimum threshold difference between monopolar and bipolar stimulation with 100Hz sinusoids was 7.2 dB in control animals and 6.3 dB in the neomycin deafened group.

In contrast, the results of threshold measurements for different bipolar electrode combinations were somewhat surprising. We found that varying the longitudinal separation of bipolar stimulating contacts from radial (no separation) to 1.0 mm separation to 6.00 mm separation had no significant effect on the IC response threshold in control animals. van den Honert and Stypulkowski (1987) also observed that radial bipolar thresholds were equal to, or lower than, the threshold to a longitudinal bipolar pair (2mm separation) in two of the three control animals studied. However, Shepard, et al (1993) and Merzenich, et al, (1979) found that threshold decreased systematically with increasing electrode separation. The difference in these observations may be attributable in part to the physical properties of the electrodes used. Shepard et al used an electrode consisting of a series of conductive bands (.3mm in width, .47mm2 area, separated by .45mm) around a silicone carrier. In this electrode, stimulating contacts have comparatively large surface areas and are relatively closely spaced. Such a configuration is much more sensitive to direct shunting between contacts than an electrode with smaller contacts having greater separation (.225mm diameter, 0.04mm2 area, separated by .5mm, 1mm, or more in this study). Modeling predicted that this effect would lead to higher overall thresholds for the banded electrode and that these thresholds would increase as the distance from the electrode to target neurons increases (Finley, Wilson et al., 1990). The Shepard study confirmed that indeed the location of these electrodes within the scala tympani volume had a significant effect on threshold, i.e. the mean EABR threshold (200μSec stimuli) was 320μA near the osseous spiral lamina and increased to 1.1mA near the spiral ligament. Comparison of these results with those from this study confirm that thresholds were generally lower for an electrode with relatively small, closely spaced contacts than for an electrode with larger contacts having less separation. Based on comparable stimuli (200μSec pulses), animal histories and electrode separation (comparing the +1 configuration in Shepard (1993) with a contact separation of 1.2mm to the offset radial configuration in this study with a separation of 1.0 mm) we can compare the EABR threshold for these two electrode designs. Mean thresholds for the banded electrode ranged from 260μA to 590μA depending on scala tympani location while the mean value for the UCSF style electrodes was 108μA (combining data from both the control group and animals deafened less than 1.5 years of age to match the animal histories in the Shepard study).

For the long term deafened animals the significant threshold difference between radial bipolar, offset radial and longitudinal configurations (Table 7) presumably reflects differences in anatomy and/or physiology specific to this group of animals and may be relevant to the application of human devices in subject populations with severe neural degeneration. Anatomically, these animals are distinguished by absence of most, or all, peripheral fibers, greatly reduced spiral ganglion cell density (9.9% of normal) and by higher electrical conductivity both through the habenula perforata and within Rosenthal's canal. Although the number of patients expected with this level of degeneration in the peripheral auditory system is relatively small it would be advantageous to design cochlear implant systems with the ability to vary the longitudinal separation of stimulating sites to ensure that these patients would achieve comfortable perception levels on as many information channels as possible.

The Effect of Electrode Configuration on Spatial Selectivity

The ability to generate spatially restricted patterns of neural excitation is essential to the development of improved cochlear implants capable of implementing a broad range of speech processing strategies with increased performance. Prior studies have mapped neural response patterns to varied electrode configurations using microelectrode recording techniques in the auditory nerve (van den Honert and Stypulkowski, 1987) and in the inferior colliculus (Merzenich and White, 1977; Snyder, Rebscher et al., 1990) and 2-deoxyglucose (2-DG) autoradiography in the cochlear nucleus and IC (Ryan et al., 1990). Both normal hearing (van den Honert, Ryan) and acutely deafened animals (Merzenich, Snyder) were used in these studies. In each set of experiments the response patterns observed were restricted with at least some electrode configurations and these regions of activation appropriately reflected the cochlear location of stimulation.

In all three animal groups in this study the STC width for monopolar tuning curves was significantly broader than for bipolar stimulation, even when the contact separation of the bipolar pair was as much as 6.0 mm, the greatest separation tested. Although the response patterns were more broadly distributed throughout the ICC the general shape of the tuning curves and location of the threshold minima were very similar to bipolar curves generated in the same penetrations (see Figure 5A). This is contrary to some reports (notably van den Honert, 1987 and Ryan, 1990) which found either no selective tuning for monopolar stimulation or a region of activation which grew to encompass the entire nucleus only a few dB above threshold. Again, the physical design of the stimulating electrode may have played a major role in these differences. The van den Honert study used wires without an insulating carrier which were placed on the wall of the scala tympani. In contast, the electrodes in this study were held in a space filling silicone carrier. In the Ryan study used the anatomical differences between the cat and gerbil may have significantly affected the spread of current within the cochlea.

The effect of electrode separation on spatial tuning is somewhat complex. The spatial tuning of the longitudinal bipolar pair (1,4) was significantly wider than that of the offset radial configuration in only the neontally deafened animals less than 1.5 years of age. However, the variance in the data for the longitudinal configuration in the other groups (see Tables 4 and 8) is much higher than that for the offset radial configuration. This large variance represents not only a decrease in the selectivity of responses to widely separated stimulation sites but also several unique patterns of representation which we have not seen with more narrowly spaced bipolar electrodes. These patterns are illustrated in Figure 9. These effects might be percieved as a distortion or source of confusion between stimulation sites.

In this study we used the offset bipolar configuration (pair 1,2) as the baseline for comparison with other stimulating combinations. We chose this configuration, held in a cylindrical Silastic carrier, because it approximates the overall geometry of the clinical intracochlear electrodes developed at UCSF which are now available commercially. By making these measurements across three groups of animals with diverse patterns of neural survival we hoped to reproduce some of the variation seen throughout the wide range of human cochlear implant users.

In comparison to the offset radial configuration monopolar stimulation resulted in activation at lower current levels but this activation occurred over a broader region of the ICC. Thus, reduced operating power is a trade-off against reduced selectivity with this type of stimulation. The radial bipolar configuration had a significantly higher threshold in the chronically deaf animals, but no improvement in spatial tuning in either group. Third, the widely separated bipolar configuration (1,4) produced significantly broader tuning in the neonatally deafened animals less than 1.5 years of age, with a significant decrease in threshold seen in only the long deafened animals. In addition, several forms of distortion were observed with widely spaced bipolar stimulation which were not seen with other stimulation modes. Thus, in terms of optimum spatial resolution and greatest overall efficiency across these three models of neural degeneration the offset radial configuration produced the best overall results.

It should be repeated, however, that a high level of individual variation was observed in the performance of different animals within each group. In some individuals monopolar stimulation produced extremely narrow tuning, even narrower than that seen with bipolar stimuli. In some other cases, the longitudinal pairing produced very low thresholds. These outlying individuals illustrate the advantage of an electrode design which can be customized to meet the needs of each patient. It is important to note that this capability to customize the device must not only be designed into the system but must also be incorporated into the clinical fitting protocols for each patient because even a versatile, complex device design which is only applied in a single strategy will not provide maximum benefit for these unique patients.

The implications of several additional conclusions from this study are significant in terms of future modeling of electrical stimulation in the cochlea.

1. Of particular interest was the maintenance of spatial tuning in neonatally deafened animals studied at less than 1.5 years of age. All of these animals demonstrated tuning that was not statistically different from the average tuning for the control group of animals (see Figure 7). Subsequent histologic examination of these animals demonstrated a range of spiral ganglion survival of 23.5% to 64.4% of normal. This observation indicates that relatively few spiral ganglion cells are needed to accurately convey the spatial distribution of electrical signals from the cochlea to the inferior colliculus. Long term deafened animals, with even fewer surviving peripheral neurons, appear to have significantly degraded spatial selectivity. Also, it seems likely that the later loss of spiral ganglion cells is not the sole cause of broadened tuning in these animals. Additional mechanisms such as degradation of connectional selectivity in the direct pathways leading to the IC and/or changes in inhibitory activity must also be considered.

2. This degradation of tuning in the IC is <u>not</u> accompanied by a significant increase in IC threshold. However, the EABR threshold for the long-deafened animals (> 1.5 yr.) was significantly higher than that of either the control or shorter term animals (< 1.5 yr.). The increase in EABR threshold, for which the synchronized activity of many neurons is needed to generate a detectable response, may be a function of degraded temporal synchrony among the peripheral neurons in these animals. Due to the severe neural pathology individual cells may respond at normal threshold, but at more varied latencies, resulting in responses which are not adequately synchronized to allow detection at low levels.

3. The absence of change in IC threshold between the three animal groups studied has important implications for the theoretical modeling of intracochlear electrical stimulation and the design of future devices. Current modeling techniques predict that optimum electrode placement would be different for cochleae with and without surviving peripheral dendrites. These two conditions are modeled in the animal populations in this study. We would expect the four animals deafened acutely with intracochlear neomycin and the acutely kanamycin deafened adults to have normal, or nearly normal, numbers of peripheral processes extending through the habenula

perforata to the organ of corti. In contrast, the long term deafened animals, with approximately 10% spiral ganglion cell survival have very few or no peripheral neurons. The lack of difference in response threshold between these groups suggests that the spiral ganglion cell body is the probable site of activation for intracochlear electrical stimulation even in the presence of viable dendrites.

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Work Planned for the Next Quarter

1) We will complete the chronic stimulation of two adult deafened, prior normal cats. Acute electrophysiology experiments will be conducted during the next quarter in these animals to obtain additional data to evaluate the effects of chronic stimulation in adult animals and to compare these effects with those seen in neonatally deafened cats.

2) We will continue cochlear histopathology studies examining the effects of GM1 ganglioside administered immediately following neonatal deafening in cats and continued until implantation of a model cochlear implant.

3) We will continue the chronic stimulation of five GM1 ganglioside treated cats throughout the next quarter. This series of animals is receiving a varied matrix of high frequency amplitude modulated (AM) and high rate unmodulated pulse trains in a two channel paradigm. The purpose of this varied higher rate stimulation protocol is to investigate the limits of increased temporal resolution which has been demonstrated in neonatally deafened animals which were chronically stimulated with high rate stimuli.

4) Four members of the laboratory will attend the annual Association for Research in Otolaryngology Midwinter Meeting. Dr. Leake, Dr. Snyder, Dr. Vollmer and Ms. Moore will present results of this Contract research. The abstracts for these presentations are appended to this Report.