COCHLEAR PATHOLOGY FOLLOWING REIMPLANTATION OF A MULTICHannel SCALA TYMPANI ELECTRODE ARRAY IN THE MACAQUE

Robert K. Shepherd, Ph.D., Graeme M. Clark, F.R.A.C.S., Shi-Ang Xu, M.D., and Brian C. Pyman, F.R.A.C.S.

ABSTRACT

The histopathologic consequence of removing and reimplanting intracochlear electrode arrays on residual auditory nerve fibers is an important issue when evaluating the safety of cochlear prostheses. The authors have examined this issue by implanting multichannel intracochlear electrodes in macaque monkeys. Macaques were selected because of the similarity of the surgical technique used to insert electrodes into the cochlea compared to that in humans, in particular the ability to insert the arrays into the upper basal turn. Five macaques were bilaterally implanted with the Melbourne/Cochlear banded electrode array. Following a minimum implant period of 5 months, the electrode array on one side of each animal was removed and another immediately implanted. The animals were sacrificed a minimum of 5 months following the reinser­tion procedure, and the cochleas prepared for histopathologic analysis. Long-term implantation of the electrode resulted in a relatively mild tissue response within the cochlea. Results also showed that inner and outer hair cell survival, although signifi­cantly reduced adjacent to the array, was normal in 8 of the 10 cochleas apicalward. Moreover, the electrode reinsertion procedure did not appear to adversely affect this apical hair cell population. Significant new bone formation was frequently observed in both control and reimplanted cochleas close to the electrode fenestration site and was associated with trauma to the endosteum and/or the introduction of bone chips into the cochlea at the time of surgery. Electrode insertion trauma, involving the osseous spiral lamina or basilar membrane, was more commonly observed in reimplanted cochleas. This damage was usually restricted to the lower basal turn and resulted in a more extensive ganglion cell loss. Finally, in a number of cochleas part of the electrode array was located within the scala media or scala vestibuli. These electrodes did not appear to evoke a more extensive tissue response or result in more extensive neural degeneration compared with electrodes located within the scala tympani. In conclusion, the present study has shown that the reimplantation of a multichannel scala tympani electrode array can be achieved with minimal damage to the majority of cochlear structures. Increased insertion trauma, resulting in new bone formation and spiral ganglion cell loss, can occur in the lower basal turn in cases where the electrode entry point is difficult to identify due to proliferation of granulation and fibrous tissue.

Multichannel cochlear implants have become a viable surgical treatment in the clinical management of profound deafness in both adults and, more re­cently, children. The success of these devices rests not only on encouraging clinical performance, but also on their long-term safety. A number of studies have shown that chronic implantation and electrical stimulation of intra-cochlear electrodes does not adversely affect the residual auditory nerve popula­tion provided that the array is manufactured from biocompatible materials; the electrical stimulus con­sists of short duration charge-balanced biphasic cur­rent pulses; and the cochlea remains free of infection following implantation.

A potential source of neural loss can occur as a result of trauma during the insertion of the electrode array. Studies in normal-hearing animals have consistently shown that damage to the osseous spiral lamina...
ina (OSL) or the basilar membrane results in a significant loss of auditory nerve fibers localized to the region of trauma. Moreover, the extent of trauma associated with the insertion of a scala tympani electrode array depends on several factors, including surgical techniques, the dimensions of the array, and mechanical properties of the array.

There have been a number of studies examining the extent of electrode insertion trauma in human cadaver temporal bones using the Melbourne/Cochlear electrode array. These studies have shown that this electrode array can be inserted with minimal trauma for distances of up to 25 mm from the round window, providing the insertion is stopped at the point of first resistance. The most common form of insertion trauma observed was tearing in the spiral ligament produced as the electrode array came into contact with, and passed along, the outer wall of the scala tympani. This damage was generally restricted to a region 7–13 mm from the round window and revealed that the electrode array lay along the outer wall of the scala tympani. Clinical data obtained from the cochleas of deceased implant patients suggest that this trauma would result in a fibrous tissue reaction and possible new bone growth in the region of the tear. Significantly, localized neuronal loss associated with this trauma was not observed in these studies.

Whereas the response of the cochlea to electrode implantation is now relatively well documented, little is known about the histopathologic response following the replacement of a multiple electrode array. This is despite the fact that the removal and reimplantation of cochlear implants has been performed clinically for a number of years. Moreover, the procedure is likely to become more common as the increasing numbers of pediatric implantees seek device upgrades throughout their lifetime. The purpose of the present study was to compare the extent of cochlear histopathology following the surgical replacement of chronically implanted multichannel electrode arrays, with that of cochleas implanted using identical electrodes but without having undergone electrode explantation/reimplantation. Macaque monkeys were used in the present study, because it had previously been demonstrated that multi-electrode arrays could be readily inserted into the upper basilar turn of these animals, therefore producing similar mechanical characteristics to the insertion of multi-electrode arrays in humans.

Only three previous experimental studies have addressed this issue. Using both single platinum/iridium (Pt/Ir) ball electrodes and Melbourne/Cochlear multi-electrode arrays, Miller et al reported a significant reduction in both hair cells and spiral ganglion cells in reimplanted monkey cochleas compared with implanted control cochleas following an implant period of 16 months. Jackler et al observed similar results following an electrode implantation/reimplantation study in cats, using both Pt/Ir ball electrodes and 7-mm long silicon electrodes designed to model a multichannel array. Although no evidence of ganglion cell loss in three of eight reimplanted cochleas was reported, the incidence of at least moderate ganglion cell loss, as a result of electrode insertion trauma, was twice that observed in the implanted control group. This increased incidence of insertion trauma was attributed to surgical complications associated with reimplantation due to the proliferation of granulation tissue both at the round window and within the scala tympani. Using similar electrodes, Greenberg et al performed a reimplantation study in guinea pigs and concluded that reimplantation can be performed with little additional risk to spiral ganglion cells following implantation periods of 4 months. However, the lack of extensive damage observed in this study may be owing to the short insertion depth used (2 mm into the scala tympani).

In addition to these experimental studies, a recent clinical report described the extent of cochlear histopathology following cochlear reimplantation in three patients. In all cases one or more platinum ball electrodes were replaced with a similar electrode inserted to a depth less than the original insertion distance. Although the authors concluded that there was no reported difficulty during reimplantation, and the three cochleas did not exhibit histopathologic changes that could be directly attributed to the second insertion procedure, all three cochleas were noted to have relatively large amounts of new bone and fibrous tissue. Moreover, they had among the lowest ganglion cell counts in a clinical study of 16 implanted cochleas.

Although there are a number of variables associated with any electrode exploration/reimplantation study (e.g., type of initial and replacement electrodes, depth of insertion, period between exploration and reimplantation), in the present study, the authors chose to investigate the response of the cochlea to exploration/reimplantation of a Melbourne/Cochlear multi-electrode array. There was no delay between exploration and reimplantation, and the electrode arrays were inserted to the point of first resistance, using a surgical approach similar to that used clinically.

**MATERIAL AND METHODS**

**Animal Model**

The primate *Macaca fascicularis* (macaque) was used in the present study. Its mastoid is of a reasonable size and, when drilled, offers a similar surgical approach to the round window as in humans. Four of the five animals used in this study had been partially deafened via systemic administration of kanamycin and ethacrynic acid 2 years prior to the initial implant surgery. The co-administration of these drugs is known to produce a highly symmetrical and stable high frequency hearing loss. The fifth animal in this study had normal hearing as indicated by click
evoked auditory brainstem response thresholds of less than 32 dB peak equivalent sound pressure level (p.e. re 20 \mu Pa).

**Implant Electrodes**

Melbourne/Cochlear electrode arrays were used in the present study. Details of these electrode arrays have been presented previously.\(^5\) Briefly, the array consists of 22 platinum electrodes on a Silastic carrier. Each Pt electrode was 0.3 mm wide and was welded to a 25 \mu m Pt/ Ir (90%/10%) leadwire. This smooth, free-fitting electrode array tapers from a diameter of 0.4 mm at its tip, to 0.6 mm at a point 15 mm from the tip. The 22 Pt electrodes are spaced evenly along the first 17 mm of the electrode array with an inter-electrode spacing of 0.45 mm. An additional 10 Pt rings located in the 17-25 mm region were added to optimize the array’s mechanical properties.\(^6\) The electrode arrays used in the present study were manufactured and sterilized according to clinical standards by Cochlear Pty Ltd, Sydney, Australia.

**Surgical Procedures**

The surgical technique essentially followed clinical procedure.\(^5\) All surgery was performed under aseptic conditions by an otologic surgeon with experience in cochlear implant surgery. The animals were anesthetized with ketamine hydrochloride (10 mg/kg) and xylazine hydrochloride (2 mg/kg) and maintained with halothane and nitrous oxide. Body temperature was maintained at 37°C. A postauricular skin flap was made and the muscle was dissected from the underlying mastoid. After a mastoidectomy and posterior tympanotomy were performed, a fenestration was created by drilling the otic capsule anteroinferior to the round window, using a 0.6 mm diameter diamond paste burr. A small amount of perilymph was gently aspirated to facilitate visualization and to remove bone fragments from the field. The electrode array was inserted to the point of first resistance, and the electrode entry point was sealed with fascia. The leadwire within the middle ear was fixed at the fossa incudis, using a multistranded Pt wire tie. Both cochleas of each animal were implanted during this procedure. The wounds were closed using two to three layers of sutures, and the animal was given both short-term (cloxacillin) and long-term (procaine penicillin) antibiotics. All animals made uneventful recoveries from the procedure.

At a minimum of 5 months after implantation, one electrode array from each animal was surgically removed and immediately replaced with a new Melbourne/Cochlear multi-electrode array. The ear chosen for reimplantation was selected randomly. Both anesthetic and surgical techniques were similar to the original procedure. All animals made uneventful recoveries from the revision surgery.

**Procedures for Euthanasia**

Five to seven months following the reimplantation surgery (Table 1) each animal was sacrificed by an overdose of anesthetic (pentobarbital sodium) and systemically perfused intra-arterially with a solution containing heparinized normal saline, buffered to a pH of 7.35 with 0.1 M phosphate buffer followed by a 0.1 M phosphate buffered (pH 7.35) 1% paraformaldehyde/1% glutaraldehyde fixation solution. The temporal bones were dissected and the cochleas processed for light microscopic histology.

**Histologic Techniques**

The temporal bones were placed in 0.1 M phosphate buffered (pH 7.35) 2.5% glutaraldehyde solution at 4°C for at least 48 hours and then rinsed in distilled water. During the fixation schedule, each temporal bone was trimmed and the otic capsule thinned to within 1 mm of the membranous labyrinth using diamond paste drills. The cochleas were then decalcified in 4% EDTA in phosphate buffered 2.5% glutaraldehyde, dehydrated, and finally embedded in Spurr's resin. The blocked cochleas were sectioned at 2 \mu m in the horizontal plane, and sections every 126 \mu m were collected and stained with hematoxylin and eosin.

The histopathologic assessment of each cochlea was made by examining all sections serially. This included the status of the basilar and Reissner's membranes, the stria vascularis and spiral ligament; the presence, extent, and nature of an inflammatory cell response; evidence of electrode insertion trauma; a

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<th>Table 1. Summary of Electrode Implantation/Reimplantation Strategy</th>
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<td><strong>Monkey Implanted</strong></td>
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\(^{1}\) Monkey identification follows the nomenclature previously used.\(^5\)

\(^{2}\) Initial implant surgery involved bilateral implantation, whereas reimplantation was unilateral.
percentage estimate of new bone growth in each scala; an evaluation of hair cells; the presence of supporting cells of the organ of Corti; and an estimate of the survival of the spiral ganglion cells within Rosenthal's canal and their peripheral processes within the OSL. The inflammatory responses were categorized as acute, chronic, or resolved inflammation. The inflammation grade for each cochlea was assessed on the basis of the number and distribution of polymorphonuclear and mononuclear leukocytes, the degree of fibrous tissue, and the extent of this reaction within the cochlea.

Graphic reconstruction of each cochlea was carried out using the technique of Guild. This enabled the microcochlear electrode to be located accurately within the scala tympani and cochleograms of the resultant pathology to be constructed and plotted as a function of basilar membrane length. The histologic evaluation was performed blind in that the experimenter did not know whether the cochlea was from an implanted or a reimplanted side.

### Spiral Ganglion Cell Densities

Spiral ganglion cell densities were calculated for all ganglion cell populations within each cochlea. All cells containing a nucleus were counted; however, any cells exhibiting cytoplasmic vacuoles or other degenerative changes were not included in the analysis. The area of Rosenthal's canal was calculated using image analysis techniques. Any blood vessels or isolated bony structures within Rosenthal's canal that had an area greater than 100 μm² were not included in the area calculation.

### Statistical Analysis

For each cochlea, ganglion cell density was expressed as a function of basilar membrane length. To evaluate the effects of electrode reimplantation, both adjacent and apical to the electrode array, ganglion cell densities for each pair of cochleas were divided into three specific sectors: (1) the most basal 50% of each cochlea in the region of the fenestration; (2) from 50% to the tip of the shortest implant of each pair; (3) from the tip of the longest implant of each pair to the cochlear apex. By dividing each cochlea into these sectors, ganglion cell densities in specific regions common to both the reimplanted cochlea and its control could be evaluated. This was necessary because ganglion cell density varies along the cochlea in normal hearing macaques (Shepherd, unpublished data). The ganglion cell density of these specific cochlear regions for the two cochleas of each animal were compared statistically using the non-parametric Mann-Whitney U test.

The care and use of the animals described in this study were approved by the Animal Experimentation Ethics Committee, Melbourne University (“Studies on Pediatric Auditory Prosthesis Implants” NIH Contract NOI-DG-7-2342).

### RESULTS

#### Monkey M1

In the first specimen (M1), both cochleas were initially implanted with Melbourne/Cochlear electrode arrays via fenestrations created anteroinferior to the round window. An electrode array was inserted to a depth of 12 mm (16 electrodes) in the left cochlea and 15.75 mm (21 electrodes) in the right cochlea. In both cases the electrodes were inserted with ease and insertion was stopped at the point of first resistance. After an implantation period of 5 months, the electrode array in the right cochlea was removed and a second array inserted, with relative ease, to a depth of 15.75 mm (21 electrodes)—the same insertion depth as that achieved during the initial insertion. Following a further 5-month implantation period the animal was sacrificed, and the cochleas examined histologically.

Cochleograms of both cochleas are illustrated in Figure 1. In both cases the electrode array was located, for much of its length, in the region of the scala media, resulting in displacement of the spiral ligament, stria vascularis, and the basilar membrane (Figs. 2 and 3). Hair cell survival was evident only apical to the electrode array, with the reimplanted cochlea exhibiting more extensive hair cell loss than the control cochlea. The reimplanted cochlea showed evidence of trauma to the basilar membrane and multiple fractures of the OSL that extended from the region of the fenestration (see Fig. 1, asterisk) into the upper basal turn (see Figs. 1, downward arrows, and 2). Although it was not possible to establish whether this damage occurred during the initial or the reinsertion procedure, greater neutral loss and more extensive new bone growth was nevertheless observed. The control cochlea evoked a relatively mild soft tissue reaction in response to the electrode array. Surprisingly, the ganglion cell and peripheral process populations appeared only slightly less than normal, despite displacement of the basilar membrane and spiral ligament and loss of the organ of Corti (see Fig. 3). Apical to the electrode arrays both cochleas exhibited near-normal ganglion cell and peripheral process survival. Finally, statistical analysis of the ganglion cell density confirmed that the reimplanted cochlea exhibited a highly significant (p < .01) reduction in ganglion cell density adjacent to the electrode array compared with the control cochlea (Tables 2 and 3, Figs. 1 and 5). In contrast the ganglion cell density apical to each electrode array showed no statistically significant difference (Table 4, Fig. 6).

#### Monkey M2

In the second specimen (M2), both cochleas were initially implanted with Melbourne/Cochlear electrode arrays via fenestrations. The electrodes were inserted with ease to the point of first resistance.
The two electrode arrays depicted in the cochleogram of M1-R indicate that this cochlea was reimplanted. Note that in both cochleas the fenestration site (*) is associated with new bone growth and reduced neural survival. Damage to the OSL and basilar membrane (↓) was more commonly observed in the lower basal turn of the reimplanted cochlea. The arrow head above the electrode arrays indicates the approximate site at which the electrode entered the scala media.

11.25 mm (15 electrodes) in the left cochlea and 13.5 mm (18 electrodes) in the right cochlea. Following a 5-month implantation period, the electrode array in the right cochlea was removed with ease after an initial resistance, and a second array was inserted through the original fenestration to a depth of 14.25 mm (19 electrodes). After an additional 5-month implantation period the animal was sacrificed, and the cochleas were prepared for histologic examination. During dissection of the right temporal bone the electrode array was found to be in the middle ear rather than the cochlea. Therefore, it is not known how long the reimplanted electrode array remained within the right cochlea.

Both cochleograms are illustrated in Figure 7. Hair cells were observed only in the right cochlea (M2-R), and then only apical to the electrode array. As with M1, the reimplanted cochlea showed evidence of damage to the OSL and basilar membrane that extended into the upper basal turn, resulting in considerably less neural survival in this region of the cochlea compared with the control side. Again, in

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<tr>
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NS < not significant (p > .05)
Figure 2. Photomicrograph of the upper basal and upper middle turns of cochlea M1-R. This cochlea was implanted for a total period of 10 months and was reimplanted half way through this period. The electrode array was located for much of its length in the scala media, causing damage to both the basilar membrane and the spiral ligament. This trauma evoked localized new bone growth adjacent to the electrode (b) and a reduction in the spiral ganglion cell population within Rosenthal's canal. Only partial hair cell survival was observed apical to the electrode array, although ganglion cell survival appeared normal. e = electrode track.

Both cochleas the electrode array was located within the scala media for much of its length. This caused considerable displacement of the basilar membrane, spiral ligament, and the stria vascularis and was associated with a loss of hair cells and spiral ganglion cells and new bone growth (see Fig. 7; Fig. 8). It is possible that this extensive mechanical displacement of the membranous labyrinth also resulted in the loss of hair cells apical to the electrode array in the left cochlea (M2-L). Although there was considerable displacement of the basilar membrane close to the tip of the electrode, which presumably contributed to the loss of hair cells, the adjacent spiral ganglion cell population appeared almost normal (see Fig. 8). Apical to the electrode array both cochleas exhibited near-normal ganglion cell and peripheral process survival. Statistical analysis of the ganglion cell density showed no significant difference between the control and reimplanted cochleas for any of the three regions sampled (see Tables 2-4 and Figs. 4-6). Finally, a small amount of new bone growth was observed adjacent to the fenestration site in both cochleas.

Monkey M3

In the third specimen (M3), during the initial implant surgery the electrode array could be inserted a distance of only 9 mm into the left cochlea. In an attempt to improve the insertion distance the ele-
trode array was removed and reinserted to a point where there was slight buckling of the array. However, this procedure could not improve the insertion distance of 9 mm (12 electrodes). A fenestration created in the right cochlea allowed more bone dust than usual to enter the scala tympani. In this side, the electrode was inserted with ease to the point of first resistance (9 mm, 12 electrodes). Five months following the initial surgery the right mastoid was surgically exposed for reimplantation. At this time the original electrode was not found within the cochlea. It is likely that the array had been dislodged during the surgical exposure. However, it is also possible that the electrode had been displaced from the cochlea some time following the initial surgery. As the initial fenestration could not be readily identified, a second fenestration was created close to the round window. Two attempts at insertion failed. Only four or five electrodes entered the cochlea, and this was associated with insertion resistance. The array was removed, the fenestration site covered with soft tissue, and a third fenestration created into the scala vestibuli just anterior to the oval window. The electrode array was inserted with some difficulty to include 16 intracochlear electrodes (12 mm), and insertion was stopped when the electrode array buckled. Five months following this revision surgery the animal was sacrificed, and the cochleas were processed for histology. Both electrode arrays were removed from the cochleas only after considerable tension was applied to the leadwire.

Cochleograms of both cochleas are illustrated in Figure 9. No hair cells were observed adjacent to either electrode array, whereas apical to the array near-normal hair cell populations were found. Both cochleas exhibited extensive electrode insertion trauma in the lower basal turn, reflecting the difficult insertion procedures experienced in this animal. The resultant damage caused a significant loss of neural elements in the lower basal turn and was also associated with a large amount of new bone formation. The electrode array in M3-R was located within the scala media and was associated with damage to both the OSL and basilar membrane. This damage evoked moderate to extensive new bone growth and moderate ganglion cell loss in the basal turn (see Fig. 9). The electrode array in M3-L remained located within the scala tympani for its entire length, and, although associated with significant insertion trauma close to the fenestration site, the array caused little pathologic change in the upper basal turn. There was no significant difference in ganglion cell density within the lower basal turn due to the extensive ganglion cell loss observed in both cochleas (see Table 2 and Fig. 4). However, neural loss in the reimplanted cochlea extended through the upper basal and middle turns, resulting in statistically significant differences in ganglion cell densities in the region of, and apical to, the electrode tip (see Tables 3 and 4 and Figs. 5 and 6).

**Monkey M4**

Slight difficulty was associated with the initial implantation of the right cochlea. After an initial insertion attempt of 2-3 mm it was found that the fenestration site required enlarging. The electrode array was removed and the fenestration increased in diameter. The electrode was then readily inserted with ease to the point of first resistance (15 mm; 20 electrodes). The left cochlea was readily inserted 14.25 mm (19 electrodes). Five months following the initial surgery the electrode array in the left cochlea was removed with ease and a second electrode inserted, via the original fenestration, a distance of 12.75 mm (17 electrodes). As a kink in the leadwire prevented further insertion, the array was withdrawn,

![Figure 5](image-url)  
**Figure 5.** Mean ganglion cell density over the range 30% from base to the shortest electrode tip of each set of cochleas. Open = control; solid = reimplanted cochlea. (**p < .01; ***p < .001).

![Figure 6](image-url)  
**Figure 6.** Mean ganglion cell density apical to the longest electrode in each set of cochleas. Open = control; solid = reimplanted cochlea. (\*p < .05; ***p < .001).
Figure 7. Cochleograms illustrating the degree of pathologic changes observed in the left (A) and right (B) cochleas of monkey M2. As in the case for M1, the fenestration site was associated with new bone growth, although in both cochleas new bone was also associated with the electrode array in the upper basal and middle turns. Note that there was also a greater incidence of electrode insertion trauma associated with the reinserted cochlea, resulting in an increased loss of ganglion cells in the upper basal turn compared with the control cochlea.

Figure 8. Photomicrograph of the lower middle and lower apical turns of cochlea M2-1. This cochlea was implanted for a period of 10 months. During the insertion, the electrode array passed from the scala tympani in the basal turn to the scala media in the middle turn by tearing the spiral ligament. A small amount of new bone (arrows) illustrates part of the healed spiral ligament. Significant distortion of the spiral ligament is evident in the lower apical turn, and is associated with a total loss of hair cells. Despite this damage there was a relatively high incidence of spiral ganglion cell survival. e = electrode track.

straightened, and reinserted a distance of 11.25 mm (15 electrodes). Five months following the revision surgery the animal was sacrificed, and the cochleas were processed for histology. Both cochleas contained electrodes at sacrifice, and both arrays were withdrawn with ease after slight initial resistance.

Cochleograms of both cochleas are illustrated in Figure 10. In both cases the electrode arrays lay in the region of the scala media for much of their length. Surprisingly, the control cochlea (M4-R) exhibited more widespread insertion trauma within the basal turn despite the reported ease of insertion. The pathology included extensive new bone formation in the region of the fenestration, complete loss of hair cells throughout all cochlear turns, and a reduction in ganglion cells and peripheral processes that extended through to the cochlear apex. It would appear that the extended hair cell loss observed in this cochlea was a result of electrode insertion trauma, as there was no evidence of prior infection (e.g., widespread acute or chronic inflammatory cells or cosinophilic exudate). Although the reimplanted cochlea also exhibited insertion trauma at several sites within the basal turn, the extent of the damage was not as
Figure 9. Cochleograms of the left (A) and right (B) cochleas of monkey M3. In both cochleas the fenestration site and the lower basal turn were associated with new bone growth and electrode insertion trauma, reflecting the difficulty experienced in inserting electrode arrays in this animal. The insertion damage produced quite extensive neural loss in the lower basal turn, and in the reimplanted animal some evidence of neural loss was observed extending through the middle turn apical to the electrode array.

Figure 10. Cochleograms of the left (A) and right (B) cochleas of monkey M5. Both cochleas were implanted via the round window rather than through fenestrations created in the otic capsule. The arrays were inserted with ease to the point of first resistance, in both cases an insertion distance of 9 mm (12 electrodes). Reimplantation surgery on the left side took place 24 months following the initial procedure. There was extensive non-pneumatized new bone in the mastoid and fibrous tissue in the middle ear. During dissection the electrode array was inadvertently removed from the cochlea, and there was considerable difficulty in identifying the round window. However, an electrode array was inserted with ease to 22.5 mm (30 electrodes). Because of concern over the depth of insertion, the animal was x-rayed a week following the revision surgery. It was found that the electrode had not been inserted into the cochlea. At sacrifice, 7 months following this surgical procedure, the electrode was found to be lying entirely within the middle ear.

The cochleograms are illustrated in Figure 11. Unlike the majority of cochleas implanted via a fenestration, both cochleas from this animal had an electrode array that lay completely within the scala tympani. The control cochlea (M5-R) exhibited a restricted ganglion cell and hair cell loss in the upper basal turn that was associated with the electrode slightly deflecting the basilar membrane toward the scala media (Fig. 12) and causing a microfracture to the adjacent OSL. The extent of neural loss was somewhat surprising considering the relatively mild form of the insertion trauma. Patchy hair cell survival was observed basalward, and normal hair cell and
neural survival was observed apicalward to this localized damage. Finally, only a small amount of new bone was observed in the cochlea; this was restricted to the region of the round window.

The left cochlea exhibited more extensive neural degeneration in the lower basal turn in association with several localized fractures of the OSL. This damage was also associated with a loss of hair cells adjacent to the electrode array and moderate new bone growth in the region of the fractures. Hair cell and spiral ganglion cell populations appeared normal apical to the electrode array (Fig. 13). Despite the fact that the electrode array in this cochlea had been removed 7 months prior to the animal's death, the electrode tissue capsule had remained patent throughout its length. The pattern of pathologic change was also observed in the statistical analysis of spiral ganglion cell densities. There was a statistically significant reduction in ganglion cell density in M5-1 compared with M5-R in the basalmost 30% of the cochlea (see Fig. 4). Whereas no statistically significant difference in ganglion density was observed in the region just basalward to the electrode tips (see Fig. 5), a significant difference was noted between the two cochleas in the region apical to the electrode array (see Fig. 6).

**DISCUSSION**

Despite the relatively small number of cochleas involved, the results of the present study indicate that there is a slightly greater incidence of electrode insertion trauma associated with the replacement of a multichannel scala tympani electrode array when compared with implanted controls. Of the four animals that had undergone reimplantation in one cochlea, two animals (M1 and M3) showed a highly significant reduction in ganglion cell density adjacent to the electrode array compared with their controls. A third animal (M2) showed no statistically significant difference between the control and reimplanted cochlea, whereas the fourth animal (M4) exhibited a highly significant reduction in the ganglion density of the control cochlea when compared with the reimplanted side.

The present results highlight the additional surgical complications potentially associated with cochlear reimplantation. In particular, a granulation or fibrous tissue reaction in the middle ear and scala tympani in response to the original implant procedure can complicate the identification of important surgical landmarks, including the electrode entry point, which may lead to increased electrode inser-
Figure 11. Cochleograms of the left (A) and right (B) cochleas of monkey MS. Note that this monkey was not treated with ototoxic drugs prior to cochlear implantation. Both cochleas exhibited normal hair cell and ganglion cell survival apical to the electrode arrays and at restricted sites adjacent to the arrays. Cochlea MS-R showed a restricted region of severe neural loss localized to a region where the electrode array had deflected the basilar membrane and produced a microfracture of the OSL. The minimal new bone in this cochlea may be associated with the electrode array being inserted via the round window. Cochlea MS-L exhibited more extensive damage in the lower basal turn, resulting in a slightly more widespread ganglion cell loss and new bone formation. It was not possible to establish whether these changes occurred as a result of the initial insertion or the removal of the electrode array 7 months before sacrifice. Note that this cochlea was not reimplanted.

The present results are in general agreement with two previous reimplantation studies that also showed an increased incidence of insertion trauma associated with reduced surgical visibility during electrode reimplantation. It should be noted that although moderate-to-severe damage to cochlear structures was observed in this study, particularly in the lower basal turn, as a result of electrode insertion trauma, these results should be regarded as worst case, as the macaque cochlea is considerably smaller than the human. Two previous studies have shown that the larger the electrode array relative to the cochlea, the greater the incidence of electrode insertion trauma. In addition, it was evident from the present data that electrode arrays inserted via a fenestration into the macaque cochlea tended to be located, for at least part of their length, within the scala media or scala vestibuli. This high incidence is attributable to: (1) variations in the orientation of the surgical exposure of the cochlea between the macaque and humans, and (2) variations in the size of the cochleas. The restricted size of the posterior tympanotomy and the more vertical orientation of this exposure in the macaque significantly increased the chance of an electrode array being inserted into the scala media or vestibuli. In contrast, the two electrode arrays inserted via the round window lay completely within the scala tympani (MS-L and R). In general, these cochleas exhibited less incidence of insertion trauma compared with cochleas implanted with an electrode in the scala media or vestibuli.

However, the present findings do indicate for the first time in experimental animals that it is possible to insert an electrode array into the scala media or scala vestibuli while evoking a minimal tissue reaction and spiral ganglion cell loss (e.g., M1-L) (see Figs. 1 and 3). Therefore, this implantation site could be considered in cases of extensive ossification of the scala tympani.

It would also appear that the insertion of an electrode array via a fenestration is more likely to lead to increased new bone growth and insertion trauma in the lower basal turn than an array inserted via the
warded as a primary site of osteoneogenesis when

The buckling of the basilar membrane was restricted to a localized sector of the upper basal turn, upper middle turns of cochlea MS-R. This cochlea was shown to form a focus for new bone growth within surmably associated with two factors: (1) the introduction of bone dust into the scala tympani. This electrode array lay completely within the scala tympani, illustrating the biocompatible nature of this electrode array. The buckling of the basilar membrane (arrow head), which was restricted to a localized sector of the upper basal turn, resulted in a moderate hair cell and spiral ganglion cell loss. Hair cell and spiral ganglion cell populations both basal and apical to this site appeared normal.

round window. Increased new bone growth is presumably associated with two factors: (1) the introduction of bone dust into the scala tympani during drilling to create the fenestration, as bone dust has been shown to form a focus for new bone growth within the scala tympani, and (2) trauma to the endosteal lining of the cochlea, a structure long regarded as a primary site of osteoneogenesis when damaged.

Whereas 8 of the 10 cochleas in the present study showed normal hair cell survival apicalward to the electrode array, evidence of hair cell survival was observed adjacent to the electrode in only two cochleas; in both cases the electrode array was located in the scala tympani (M5-L and R; see Fig. 11). There was little doubt that electrodes located in the scala media or scala vestibuli resulted in more extensive displacement of both the spiral ligament and the basilar membrane (compare Figs. 2, 3, and 8 with Figs. 12 and 13), although even slight displacement of the basilar membrane appeared to be associated with a complete and relatively widespread loss of the organ of Corti (e.g., Fig. 13). Although it would appear that the loss of hair cells and the organ of Corti were usually a direct result of mechanical trauma (e.g., Figs. 2 and 3), it is possible that in some cases this loss was secondary to other forms of damage, such as the tearing of Reissner's membrane.

It should be noted that quite variable neural survival was observed in cochlear regions completely devoid of the organ of Corti. For example, whereas the electrode array caused extensive displacement of the spiral ligament and basilar membrane of cochlea M1-L (see Figs. 1 and 3), presumably resulting in the widespread loss of the organ of Corti, near-normal populations of spiral ganglion cells and their peripheral processes were evident adjacent to this trauma (see Fig. 3). More typically, however, large numbers of spiral ganglion cells survived this form of trauma in the absence of peripheral processes (see Figs. 8 and 13). Studies of human temporal bones have also shown that large numbers of spiral ganglion cells survive for long periods of time despite degeneration of their peripheral processes, whereas studies using subprimate mammals generally exhibit a more rapid and extensive spiral ganglion cell loss. It is possible that the time-course of retrograde degeneration of the auditory nerve in both humans and primates is somewhat longer than the time-course observed in lower mammals. Finally, electrode insertion trauma, leading to fractures of the OSL and direct trauma to peripheral processes resulted in an extensive ganglion cell loss localized to the site of trauma (e.g., Fig. 11). The extent of this degeneration was similar to that observed in other mammalian species.

It is clear from histologic examination, that the electrode array used in the present study lay along the outer wall of the cochlea. This finding is consistent with previous insertion trauma studies using cadaver temporal bones and clinical data from the temporal bones of implant patients. A recent electrophysiologic study demonstrated the advantage of re-positioning the electrode to a site closer to the modiolus. The benefits of this site included significantly reduced thresholds, increased dynamic

Figure 12. Photomicrograph of the upper basal and upper middle turns of cochlea M5-R. This cochlea was implanted for a period of 31 months, and the electrode array lay completely within the scala tympani. The minimal tissue response evident in the basal turn (arrows) illustrates the biocompatible nature of this electrode array. The buckling of the basilar membrane (arrow head), which was restricted to a localized sector of the upper basal turn, resulted in a moderate hair cell and spiral ganglion cell loss. Hair cell and spiral ganglion cell populations both basal and apical to this site appeared normal.

Figure 13. Photomicrograph of the upper basal and upper middle turns of cochlea M5-L. This cochlea was implanted for a period of 24 months after which the electrode array was withdrawn. A second array was not inserted during this procedure. As in the right cochlea, the electrode array lay completely within the scala tympani and evoked a minimal tissue response (arrows) indicating the biocompatible nature of this type of electrode array. Moreover, there was no evidence of tissue obliteration of the scala tympani following the removal of the array. Although hair cells were absent adjacent to the array, presumably associated with a slight displacement of the basilar membrane (arrow head), apicalward normal hair cell populations were observed.
ranges, and the potential to provide patients with an increased number of discriminable electrodes. A prototype electrode array designed to lay closer to the modiolus is currently under investigation.\(^\text{49}\)

The present study also highlighted a number of observations made in previous studies. First, the generally minimal tissue reaction associated with these chronically implanted electrodes highlights their biocompatibility and is consistent with findings following implant periods of more than 3 years in macaques.\(^\text{50}\) Second, as noted, near-normal hair cell survival generally was observed apicalward to the electrode array. This is consistent with a number of previous experimental and clinical studies reporting hair cell survival apical to chronically implanted and electrically stimulated electrode arrays.\(^\text{3, 5, 6, 14, 18}\)

The long-term survival of hair cells apical to the electrode array may mean that electrophoretic activation of residual hair cells could be used to provide cochlear implant patients with additional pitch and temporal cues useful for speech comprehension.\(^\text{50}\) Only in cases where the electrode array caused significant displacement of the basilar membrane (M2-L, see Fig. 8), or following widespread damage to the OSL (M4-R, see Fig. 10), was extensive hair cell loss apical to the electrode array observed. Third, there was no evidence of infection associated with the 10 implanted cochleas examined in the present study. This lack of infection contrasts with the 10% rate of spontaneous infection observed in implanted cats,\(^\text{8, 12}\) and may be a result of the increased new bone formation associated with the fenestration site, resulting in a more efficient barrier to the spread of infection from the middle ear.

Although the majority of experimental studies have shown a general increase in ganglion cell loss in the basal turn following the reinsertion of an electrode array, evidence from clinical observations suggest that there are no untoward effects associated with this revision procedure. Hochmair-Desoyer and Burian reported no evidence of a change in the psychophysical and speech perception abilities of two patients who had their scala tympani arrays removed and replaced with identical arrays.\(^\text{51}\) Similar findings have been reported by other investigators using both single and multichannel electrode arrays.\(^\text{5, 14}\)

Recently, a detailed clinical survey of revision implant surgery within the United States reported that the replacement of short single-channel scala tympani electrodes with large multichannel arrays was performed successfully in all 23 cases sampled.\(^\text{50}\) Replacement of a longer multichannel electrode with one of similar dimensions also appeared to be a relatively effective procedure, although arrays with protruding electrodes tended to have a higher incidence of explantation difficulties. This clinical experience emphasizes the importance of using smooth profiled multichannel electrode arrays without protruding electrodes that may be dislodged or tear tissue during their removal. Moreover, the increased incidence of new bone associated with a fenestration is likely to increase the difficulty of removing an array containing protruding electrodes.\(^\text{53}\)

In conclusion, although the present study has shown that the explantation and reimplantation of a multichannel scala tympani electrode array can be achieved with minimal damage to the majority of cochlear structures, increased new bone formation and spiral ganglion cell loss may occur in the base of the cochlea as a result of additional electrode insertion trauma in cases where the electrode entry point is difficult to identify due to proliferation of granulation and fibrous tissue.

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