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HISTOPATHOLOGY OF COCHLEAR IMPLANTS IN HUMANS

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The insertion of an intrascalar electrode array during cochlear implantation causes immediate damage to the inner ear and may result in delayed onset of additional damage that may interfere with neuronal stimulation. To date, there have been reports on fewer than 50 temporal bone specimens from patients who had undergone implantation during life. The majority of these were single-channel implants, whereas the majority of implants inserted today are multichannel systems. This report presents the histopathologic findings in temporal bones from 8 individuals who in life had undergone multichannel cochlear implantation, with particular attention to the type and location of trauma and to long-term changes within the cochlea. The effect of these changes on spiral ganglion cell counts and the correlation between speech comprehension and spiral ganglion cell counts were calculated. In 4 of the 8 cases, the opposite, unimplanted ear was available for comparison. In 3 of the 4 cases, there was no significant difference between the spiral ganglion cell counts on the implanted and unimplanted sides. In addition, in this series of 8 cases, there was an apparent negative correlation between residual spiral ganglion cell count and hearing performance during life as measured by single-syllable word recognition. This finding suggests that abnormalities in the central auditory pathways are at least as important as spiral ganglion cell loss in limiting the performance of implant users.

KEY WORDS — cochlear implantation, electrode trauma, neo-osteogenesis, spiral ganglion.

INTRODUCTION

The insertion of an intrascalar electrode array during cochlear implantation causes immediate damage to the inner ear and over time may cause additional changes that can interfere with neuronal stimulation. The effects of cochlear implantation have been studied histopathologically on 3 classes of temporal bones: 1) animal bones,[1-10] 2) human bones implanted after death ("cadaveric implants"),[11-14] and 3) human bones from patients who in life had undergone cochlear implantation.[15-24]

Animal models of cochlear implantation offer advantages such as control over individual variability, cause of deafness, and surgical technique, but extrapolation of effects to humans requires assuming similar cross-species responses to trauma, which may not always be valid. Study of normal cadaveric human specimens offers the advantage of differentiating insertional trauma from preexisting damage, but long-term changes, particularly degenerative phenomena among remaining spiral ganglion cells, cannot be studied in this manner. Thus, studies of temporal bones from humans who in life had undergone implantation are essential to better understanding of long-term effects of implantation in humans. To date, however, there have been reports on fewer than 50 temporal bone specimens from patients who had undergone implantation. Furthermore, the majority of these implants were single-channel, whereas the majority of implants inserted today are multichannel systems with longer and possibly more traumatic electrode arrays.

This report presents the histopathologic findings in temporal bones from 8 individuals who in life had undergone multichannel cochlear implantation, with particular attention to 1) the type and location of trauma at the cochleostomy site and to the spiral ligament, osseous spiral lamina, and basilar membrane, 2) delayed changes at the cochleostomy site and along the course of the electrode array, 3) the effect of these

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TABLE 1. PATIENT DATA

Case No.	Sex	Age at Death (y)	Age Deaf (y)	Age Implanted (y)	Years Implanted	Implant Type (Ear)	Cause of Deafness	Preoperative Radiology	Operative Findings
1	F	54	48	52	2	Ineraid (R)	Unknown	CT: diffuse intracochlear opacity, both ears	Bony obliteration of round window and basal turn
2	M	67	65	65	2	Nucleus 22 (R)	Head trauma	Not available	Full insertion without difficulty
3	M	67	47	53	6	House single-channel (L)	Bilateral temporal bone fracture	Polytomography: bilateral temporal bone fractures, no intracochlear bone	Full insertion without difficulty
				59	8	Nucleus 22 (L)			
4	F	70	68	69	1	Ineraid (L)	Streptomycin ototoxicity	MRI: normal	Bony obliteration of round window and basal turn
5	M	84	77	77	7	Nucleus 22 (R)	Unknown	CT: normal	Full insertion without difficulty
6	M	73	65	70	3	Nucleus 22 (L)	Bacterial meningitis	CT: normal	Full insertion without difficulty
				68	5	Single-channel (R)			Fibrosis in basal turn
7	M	70	56	68	2	Ineraid (L)	Pneumococcal meningitis	CT: fibrous occlusion of basal turn	Round window normal; full insertion without difficulty
8	M	72	20	65	5	Ineraid (R)	Bacterial meningitis	CT: normal	Full insertion without difficulty

CT — computed tomography, MRI — magnetic resonance imaging.

changes on spiral ganglion cell counts, and 4) the correlation between performance as measured by speech comprehension and spiral ganglion cell counts and new bone formation within the cochlea.

MATERIALS AND METHODS

The temporal bones were removed, fixed in 10% buffered formalin, and decalcified in ethylenediaminetetraacetic acid. Those specimens in which the electrode array was left in situ were postfixed in 2% osmium tetroxide. All specimens were then dehydrated in graded alcohols. The specimens in which the electrode array was left in situ were exchanged with propylene oxide and embedded in araldite. In

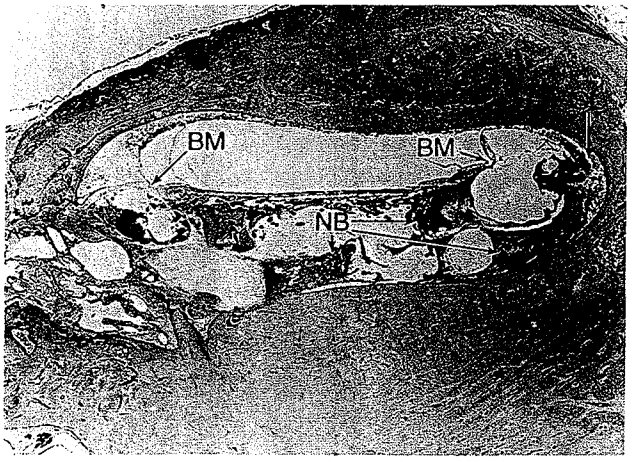

Fig 1. Basal turn near cochleostomy site of case 7, in which there was no radiographic or clinical evidence of new bone formation before operation (original ×18.5). Scala tympani contains new bone (NB). There is trauma to basilar membrane (BM) and to spiral ligament (SL), caused by electrode array.

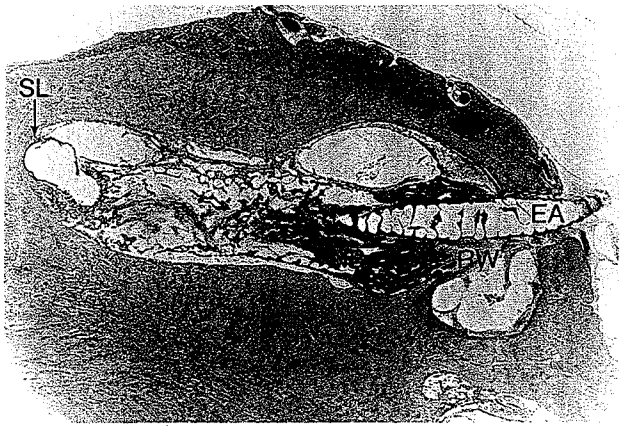

Fig 2. Basal turn near cochleostomy site of case 8, in which there was no radiographic or clinical evidence of new bone formation before operation (original ×15). Electrode array (EA) can be seen entering cochlea near round window (RW). There is new bone (NB) in scala tympani. Basilar membrane of basal turn is displaced, and trauma to spiral ligament (SL) is apparent.

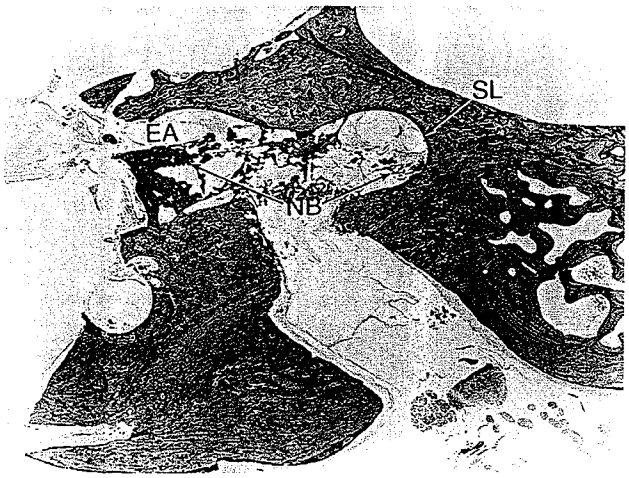

Fig 3. Basal turn near cochleostomy site of case 3, in which there was no clinical or radiographic evidence of new bone formation before operation (original ×9). Electrode array (EA) can be seen entering scala vestibuli, and there is new bone formation (NB) in scala tympani and scala vestibuli. In addition, there is trauma to spiral ligament (SL).

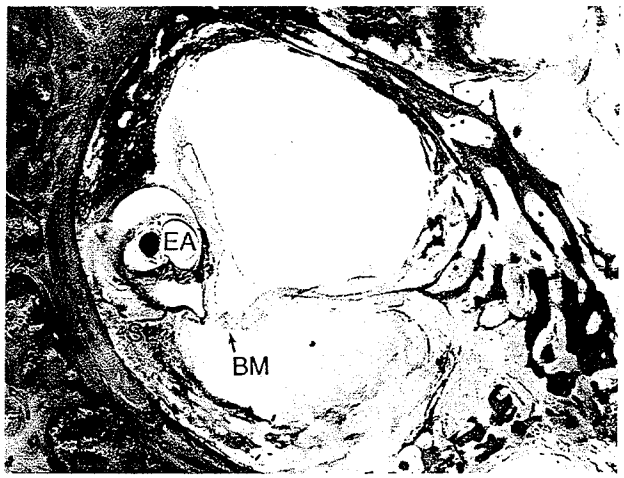

Fig 5. Basal turn of case 7, in which there was no evidence of new bone formation before operation (original ×52). Electrode array (EA) has caused displacement of basilar membrane (BM) and has dissected stria vascularis and spiral ligament (SL).

those specimens in which the electrode array was removed before fixation, the temporal bones were embedded in celloidin.

The embedded specimens were serially sectioned in the horizontal (axial) plane at an average thickness of 25 μm. Those specimens embedded in araldite with the electrode array left in situ were sectioned by a technique previously described.[23] For specimens embedded in celloidin, every 10th section was stained with hematoxylin and eosin and mounted on a glass slide. Every 10th section of those specimens embedded in araldite was either left unstained or stained in toluidine blue O before mounting on a glass slide. The serial sections were reconstructed by conventional 2-dimensional methods, including counting of neurons of the 4 segments of the spiral ganglion.[25,26]

Correlations were then performed between various histologic findings and the premortem clinical data, including performance with the implant as measured by speech comprehension tests. For uniformity, the NU-6 score without lipreading was used. For the patients for whom a measured NU-6 score was not available (cases 1 and 8), an estimate of the NU-6 score was calculated from available speech reception test scores and their relationship to single-syllable word recognition as described by Rabinowitz et al.[27]

RESULTS

The clinical data on the 8 patients are presented in Table 1. The patients ranged in age from 54 to 84 years and had been implanted from 1 to 8 years before death. In 1 case (case 3), the left cochlea had undergone implantation with a single-channel (House)

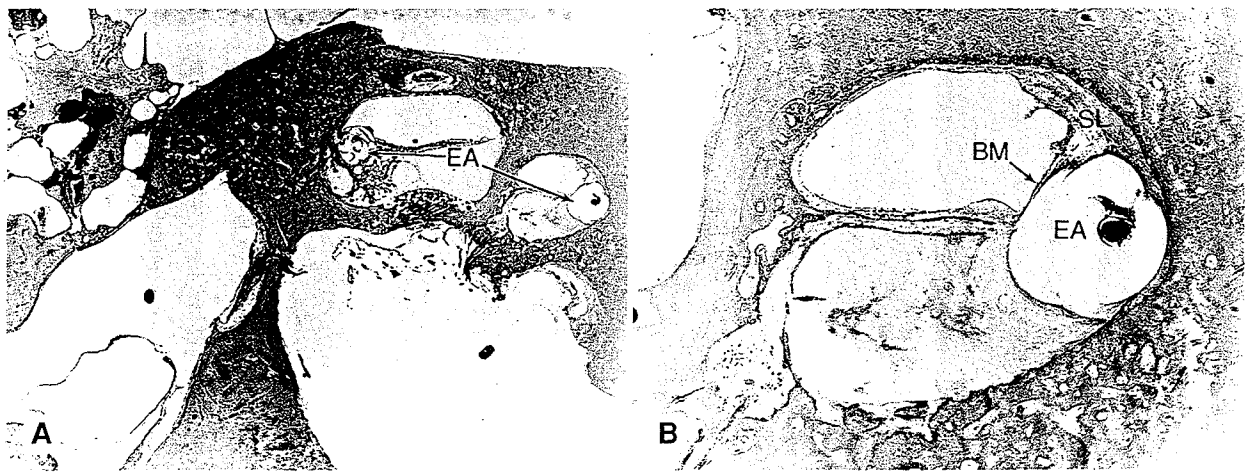

Fig 4. Basal turn of case 4, in which there was evidence of preoperative new bone formation. Electrode array (EA) has displaced basilar membrane (BM) and dissected spiral ligament (SL). **A)** Original ×13.5. **B)** Original ×53.

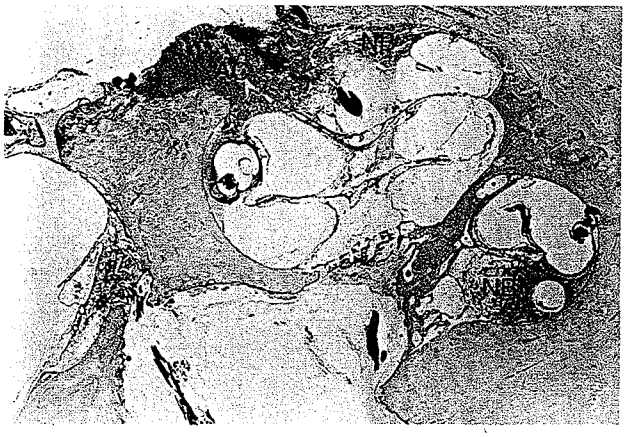

Fig 6. Midmodiolar section of cochlea of case 7, in which apical cochleostomy (AC) had been done (original ×17). There was no evidence of new bone formation before operation. However, there is new bone formation (NB) both in basal turn and at apical cochleostomy.

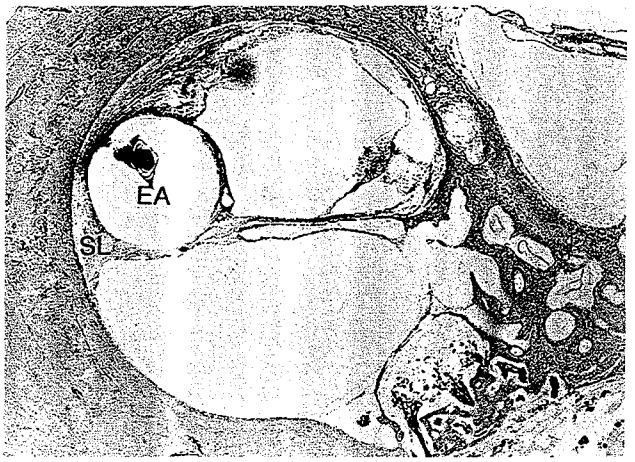

Fig 7. Basal turn of case 8 (original ×45). Electrode array (EA) is in scala vestibuli and has damaged spiral ligament (SL) and is ensheathed in fibrous capsule.

device 14 years before death, followed by explantation and reimplantation of the same cochlea with a Nucleus 22-channel system 8 years before death. In 1 case (case 6), a bilateral cochlear implantation had been done with the Nucleus 22-channel system on the left and a single-channel system on the right. Of the 8 temporal bones from patients who had undergone multichannel implantation before death, 4 had been implanted with the Symbion (Ineraid) device and 4 with the Nucleus 22 device. In 2 cases (cases 1 and 7), an apical cochleostomy[28] was done in addition to the cochleostomy done near the round window. The deafness was attributed to streptomycin ototoxicity in 1, head trauma in 2, and bacterial meningitis in 3, and the cause of deafness was unknown in 2 individuals. Radiographic and clinical intraoperative observations were available for all patients. Clinical and/or radiographic evidence of preoperative fibrosis or new bone formation within the inner ear was present in 3 patients, while in the remaining 5, there was no evidence, either radiographically or clinically, of significant preoperative intracochlear fibrosis or bone formation.

Immediate Trauma Secondary to Implantation. In addition to the trauma induced at the cochleostomy site (Figs 1-3), evidence for immediate trauma to the spiral ligament and stria vascularis was universal, particularly in the ascending limb of the basal turn (Figs 1-5). In all cases, the electrode array appeared to have penetrated the spiral ligament and then to have been deflected by the lateral cochlear wall. This penetration resulted in variable trauma to the spiral ligament and stria vascularis. Distortion or fracture of the osseous spiral lamina occurred in some cases. In 3 cases of implantation of multichannel electrodes,[6-8] the electrode array traversed the scalae, in 1 case from the scala vestibuli to the scala tympani, in another case from the scala tympani to the scala vestibuli, and in the third case from the scala tympani to the scala vestibuli and then back again to the scala

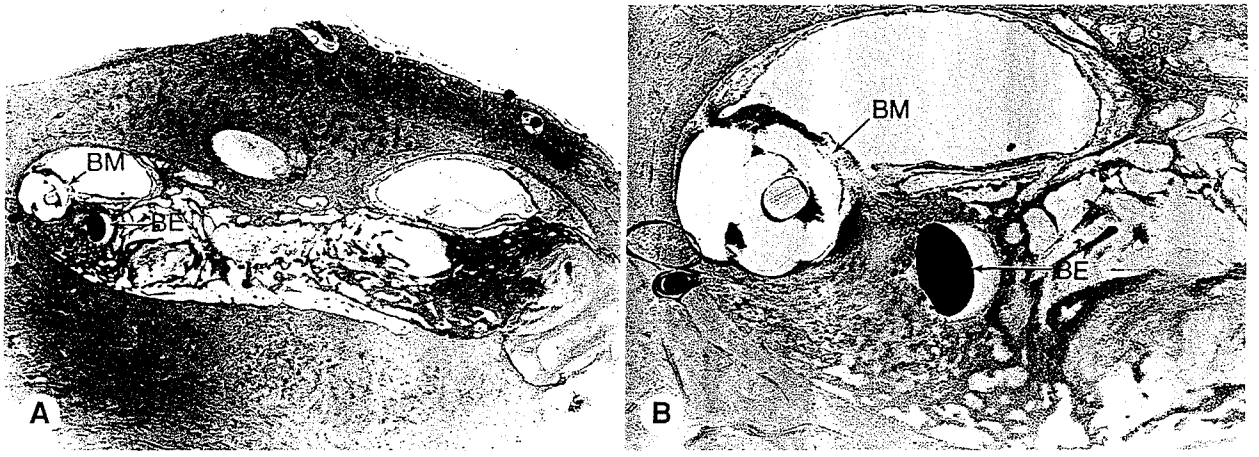

Fig 8. Basal turn of case 8, in which there was no evidence of new bone formation before operation. **A)** Electrode array can be seen elevating basilar membrane (BM; original ×16). Ball electrode (BE) of this Ineraid device is totally embedded in new bone, which is shown in higher magnification in **B** (original ×52).

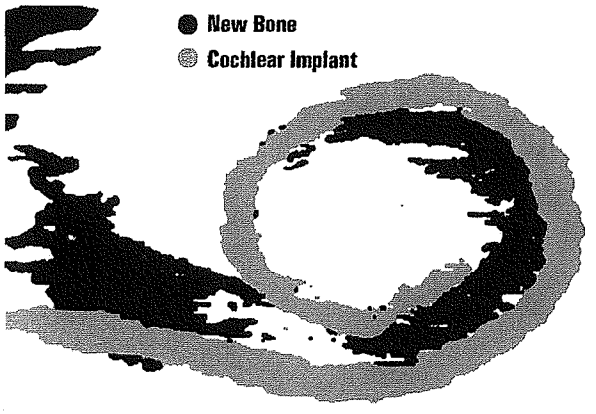

Fig 9. Computer reconstruction of electrode array and new bone formation in case 3, in which there was no evidence of new bone formation within cochlea before operation. There was new bone formation at cochleostomy site and at ascending limb of basal turn.

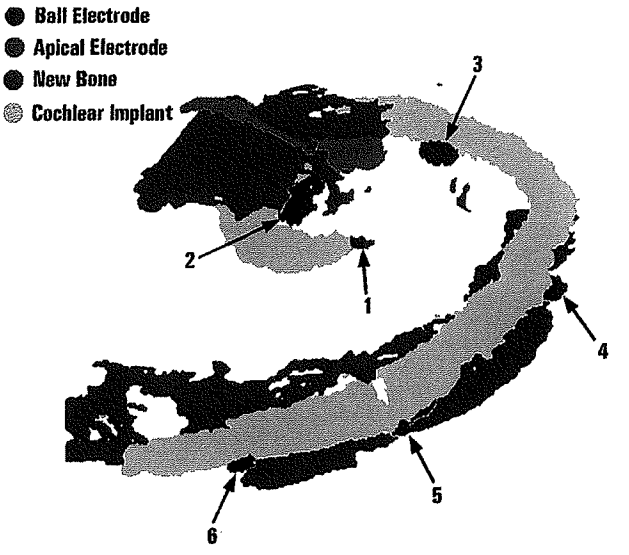

Fig 10. Computer reconstruction of cochlea in case 7, in which there was no evidence of new bone formation before operation. New bone could be seen at cochleostomy site near round window, at apical cochleostomy site, and in ascending limb of basal turn. Numbers 1 through 6 refer to 6 ball electrodes.

tympani. In the other 5 cases, the electrode array stayed within the same perilymphatic scala in which it was originally inserted in the basal turn.

Long-term Changes Induced by Implantation. In all 8 cases, new bone formation occurred at the cochleostomy site in the basal turn (Figs 1-3). In 2 cases (cases 1 and 7), a more apical cochleostomy was performed in addition to that at the round window. New bone formation also occurred at both of these apical cochleostomies (Fig 6). Along the electrode tract, a fibrous sheath surrounding the electrode array was common (Fig 7).

Postimplantation Neo-osteogenesis. In 6 of the cochleas that had been implanted with a multichannel system, there was no radiographic clinical evidence of new bone formation before implantation (Table 1). However, in all 6 patients, some degree of labyrinthitis ossificans was observed histologically. In at least some cases, there was convincing histologic evidence that this new bone formation occurred after implantation. For example, in Fig 8, the electrode array, including a protruding ball electrode, is seen to be totally ensheathed in new bone (ie, ensheathed after implantation was performed). The most common site of postoperative new bone formation, other than the cochleostomy site, was the ascending limb of the basal turn, coinciding with the universal location of trauma to the lateral cochlear wall (Figs 6 and 8-10). The second most common location of new bone formation was the descending limb of the basal turn. In 2 of the 6 cases (cases 2 and 7) with multichannel implants, new bone formation extended into the apical turn, and in only 1 of these (case 7) was an apical cochleostomy performed.

Effects of Implantation and Trauma of Insertion on Spiral Ganglion Cell Counts. In 4 of the 8 cases (cases 2, 3, 5, and 8), the temporal bone of the opposite, unimplanted ear was available for comparison. As shown in Table 2, in 3 of these 4 cases the spiral ganglion cell count in the most basal 2 of 4 segments and the total spiral ganglion cell counts were similar on both sides, and in 2 cases (cases 2 and 8) the spiral ganglion cell counts were greater on the implanted side than on the nonimplanted side. In 3 cases (cases 2, 3, and 8), preoperative audiometry demonstrated a symmetric bilateral profound sensorineural loss. In the third case (case 5), the postimplantation spiral ganglion cell counts were similar on the implanted

TABLE 2. SPIRAL GANGLION CELL COUNTS IN IMPLANTED AND UNIMPLANTED EARS

		Implanted Ear					*Unimplanted Ear*				
Case No.	*Preoperative Hearing*	*Segment 1*	*Segment 2*	*Segment 3*	*Segment 4*	*Total*	*Segment 1*	*Segment 2*	*Segment 3*	*Segment 4*	*Total*
2	Profound loss both ears	524	1,537	1,306	1,578	4,945	354	1,088	1,591	1,945	4,978
3	Profound loss both ears	1,283	6,507	4,605	5,023	17,418	3,076	7,144	4,059	5,041	19,320
5	Residual hearing both ears; worse on right (implanted side)	418	354	245	428	1,075	129	517	340	347	1,333
8	Profound loss both ears	921	4,250	2,939	2,781	10,891	744	3,460	3,395	2,158	9,757

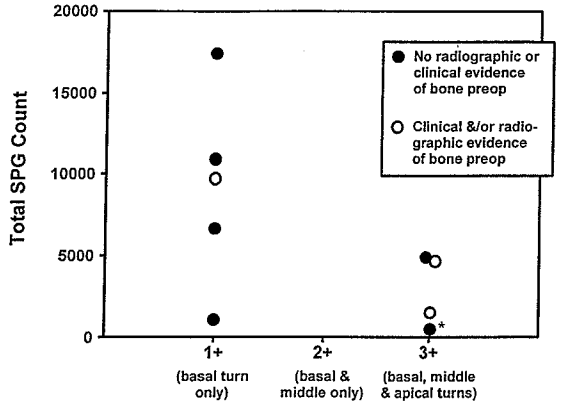

Fig 11. Scatter plot demonstrates correlation of labyrinthitis ossificans and total spiral ganglion (SPG) cell count. One case (asterisk) was from single-channel implant (case 6, right ear).

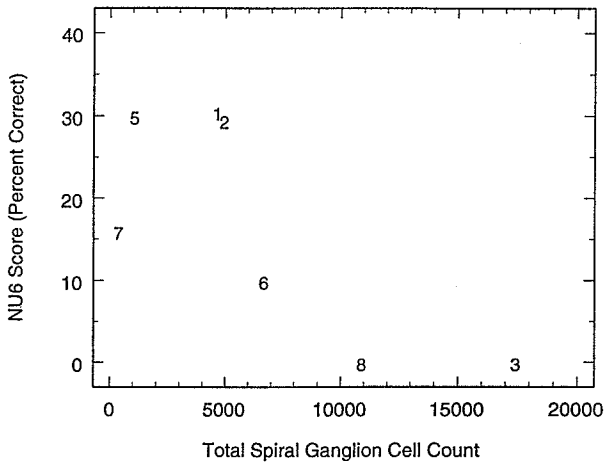

Fig 12. Implantee speech comprehension (NU-6 word score) plotted as function of total spiral ganglion cell count for each subject (see Table 3 for numerical data). Plotted numbers identify case number used to identify temporal bones.

and unimplanted sides, despite the fact that the implanted ear had worse hearing on preoperative testing.

In the fourth case (case 3), significantly fewer spiral ganglion cells were found in the 2 basal segments, and on the implanted side as compared to the nonimplanted side. This patient had a bilaterally symmetric profound hearing loss before implantation. However, in this patient, a single-channel implant placed 14 years before death was explanted 8 years before death, and then a multichannel system was implanted immediately.

As shown in Fig 11, in those temporal bones with labyrinthitis ossificans, no matter whether attributed to the preoperative period or to the postoperative period, there were fewer spiral ganglion cells in those bones with the greatest new bone formation.

Correlation of Histopathology and Speech Comprehension. Figure 12 plots NU-6 word scores as a function of the total spiral ganglion cell count for 7 subjects (see also Table 3). It is notable that the 2 individuals with the lowest number of total spiral ganglion cells (391 for case 7 and 1,075 for case 5) posted respectable NU-6 scores for the implant systems they used (16% for the Ineraid and 30% for the Nucleus 22). The best-performing subjects of this group (cases 1, 2, and 5) each had less than 15% of the average spiral ganglion cells found in temporal bones from normal-hearing individuals. The 2 individuals with the largest number of surviving spiral ganglion cells (case 3 with 17,418 and case 8 with 10,891) posted NU-6 scores under 15% (Fig 13). The apparent negative correlation between NU-6 score and total spiral ganglion cell count is unchanged when the NU-6 scores are compared with the sum of the spiral ganglion counts in segments 1 and 2 only (millimeters 0 to 15).

There was no obvious correlation between the amount of new bone within the cochlea and the results of the speech comprehension test (Fig 14). Table 4 displays the correlation of performance in speech comprehension with the scalar position of the electrode and with the total spiral ganglion cell count. In 3 cases, the electrode array traversed the plane of the basilar membrane. Although this penetration intuitively would suggest increased trauma to the or-

TABLE 3. MULTICHANNEL COCHLEAR IMPLANT NU-6 PERFORMANCE AND SPIRAL GANGLION CELL COUNTS

Case No.	*Depth of Insertion (mm)*	*Segment 1*	*Segment 2*	*Segment 3*	*Segment 4*	*Total*	*NU-6 Score (%)*
1	22	394	1,680	959	1,605	4,638	30*
2	19	524	1,537	1,306	1,578	4,945	30
3	23	1,283	6,507	4,605	5,023	17,418	0
4	22	843	4,250	2,400	2,237	9,730	N/A
5	20	418	354	245	428	1,075	30
6	22	0	3,087	1,607	1,997	6,691	10
7	21	56	102	205	28	391	16
8	24	921	4,250	2,939	2,781	10,891	13*

N/A — not available.

*Estimated (see Rabinowitz et al[27]).

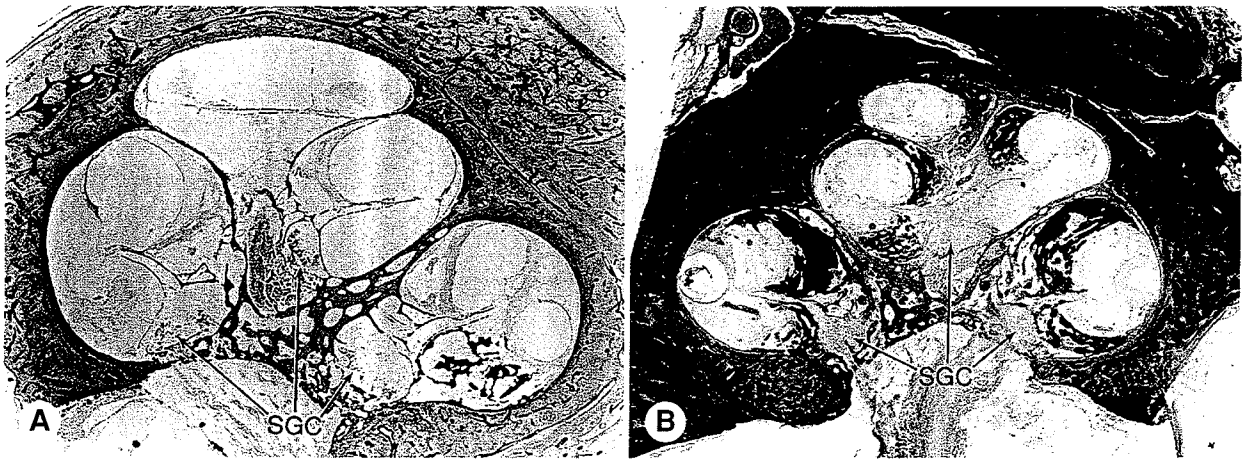

Fig 13. Midmodiolar sections. **A)** (Case 3) Residual spiral ganglion cells (SGC) can be seen in Rosenthal's canal (original ×24). Despite residual SGC count of 17,418, NU-6 word score was 0%. **B)** (Case 2) Very few SGCs can be seen in Rosenthal's canal (original ×20). Despite total SGC count of 4,945, NU-6 word score was 30%.

gan of Corti, there was no obvious impact on performance or total spiral ganglion cell count.

DISCUSSION

Immediate Trauma to Organ of Corti. In these 8 cases in which a multichannel electrode had been placed from 1 to 8 years before death, dissection of the soft tissue of the lateral cochlear wall (particularly in the ascending segment of the basal turn) was universal and consistent with data from experimental animals, human cadaveric specimens, and prior reports of in vivo implantations. In monkeys, common electrode insertion trauma has included damage to the osseous spiral lamina, basilar membrane, and spiral ligament, particularly in the basal turn.[9] Similarly, in cadaveric human specimens, tears in the spiral ligament and breaks in the basilar membrane, particularly in the basal turn, have been reported.[11-14] In specimens from patients who underwent cochlear implantation during life, dissection of the spiral ligament, fracture or dislocation of the osseous spiral lamina, and displacement or perforation of the basilar membrane have been described.[17-23] Likewise, postoperative computed tomography scans have demonstrated trans-scalar passage of electrodes.[29]

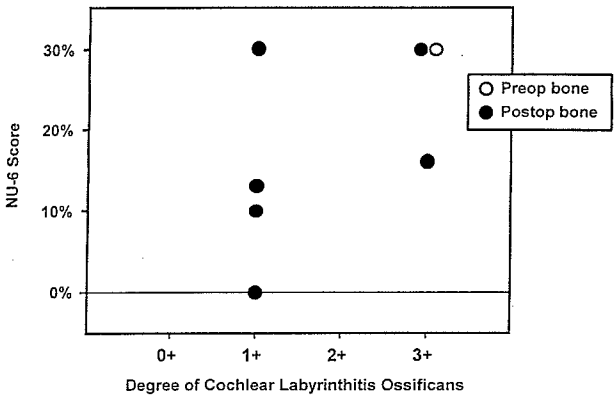

Fig 14. There was no obvious correlation between extent of labyrinthitis ossificans and speech comprehension as measured by NU-6 word score.

New Bone Formation. New bone formation after implantation, presumably secondary to the implantation itself, has been described both in animal specimens[1-3,9] and in human temporal bones that were implanted during life.[15,17,20,21] The formation of bone in humans after implantation does not prove that the bone formation was caused by implantation. However, the location of new bone formation in an area of universal trauma, as shown in this report, coupled with the formation of new bone in experimental animals deafened by administration of ototoxic drugs,[3] in which labyrinthitis ossificans would not be expected, or in animals whose inner ears were completely normal before implantation,[9] argues strongly that at least some new bone formation seen after implantation is caused by insertional trauma.

Effects of Insertional Trauma and New Bone Formation on Spiral Ganglion Cell Count. In the 4 pa-

TABLE 4. CORRELATION OF NU-6 PERFORMANCE WITH SCALAR POSITION OF ELECTRODE (MULTICHANNEL ONLY)

Case No.	*Electrode Position*	*NU-6 Score (%)*		*Total Spiral Ganglion Cell Count*
1	SV only	30		4,638
2	SV only	30	Mean, 20	4,945
3	SV only	0		17,418
4	ST only	N/A		9,740
5	ST only	30		1,075
6	Crosses	10		6,691
7	Crosses	16	Mean, 13	391
8	Crosses	13		10,891

SV — scala vestibuli; ST — scala tympani; Crosses — crosses from ST to SV or SV to ST.

tients with multichannel implantation for whom the opposite nonimplanted temporal bone was available for comparison, there was little evidence to suggest that implantation trauma induced significant degeneration of spiral ganglion cells. Although some studies[20,22] have demonstrated an apparent decrease in the number of spiral ganglion cells on the implanted side, other studies, both in humans[17,21,23] and in experimental animals,[1-3] show no obvious decrease in spiral ganglion cell population. Furthermore, in animal studies, not only was there little evidence of degeneration of the spiral ganglion induced by implantation, but in some studies, implantation coupled with electrical stimulation resulted in preservation of spiral ganglion cells over time.[6,7]

In 1 of the 4 cases presented in this report (case 3), the spiral ganglion cell population was lower on the implanted side than on the nonimplanted side. However, this patient had had a single-channel implant explanted and a multichannel system then implanted. Thus, the decrease in spiral ganglion cell population may have been the result of increased trauma caused by the explantation and reimplantation sequence, as has been demonstrated in an experimental animal model.[9]

The negative correlation between spiral ganglion cell count and the extent of labyrinthitis ossificans as shown in this study is consistent with previous studies in humans[30] and animals.[9]

Correlation of Spiral Ganglion Cell Count With Cochlear Implant Performance During Life. Although counterintuitive, the ganglion cell data show a negative correlation between residual spiral ganglion cell counts, either basal-segment counts or total counts, and performance during life with an implant as measured by scores of single-syllable word recognition. Although animal psychophysical testing has suggested a positive correlation between low thresholds and large dynamic ranges with preservation of sensorineural structures within the inner ear,[31] in human specimens there has been little evidence to suggest correlation of implant performance as measured by speech recognition with the remaining spiral ganglion cell count.[18] However, the majority of the previously reported human cases were single-channel implantations.

Furthermore, it is also clear that factors other than auditory neural integrity are important in performance with multichannel cochlear implants. A study of 48 postlingually deafened adults[32] identified 6 preoperative measures that accounted for 61% of the intersubject variability on NU-6 word understanding. Only 2 of the 6 measures could be attributed to remaining spiral ganglion cell counts.

Although the number of temporal bones in this study is small, the negative correlation between the total spiral ganglion cell counts and single-syllable word recognition is intriguing. One interpretation of this observation is that the central nervous system is more important than peripheral neural integrity in the performance of implant users. Recent functional magnetic resonance imaging of electrically evoked brain activation patterns measured in implantees showed an abnormally small ratio of contralateral to ipsilateral excitation.[33] To the extent that these and other brain abnormalities limit implantee performance and contribute to the negative correlation between spiral ganglion cell counts and performance, the results of this study suggest that a characterization of such abnormalities and their possible effect on performance may provide insight into the design of better speech processors and electrode arrays for cochlear implants. In addition, correlation of intracochlear damage and density of spiral ganglion cells with psychophysical percepts recorded during life, as has been reported on by Kawano et al,[24] may provide valuable additional data and is planned.

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