2011 년 2 월

박사학위논문

The histopathologic changes of revision cochlear implantation in human

조선대학교 대학원

의학과

이 준 한

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인공와우이식 재수술 후
인간 측두골의 병리조직학적 변화

2011 년 2 월 25 일

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이 논문을 의학박사학위신청 논문으로 제출함.

2010 년 10 월

조선대학교 대학원

의학과

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이준한의 박사학위논문을 인준함

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인공와우 이식 수술은 전세계적으로 증가하고 있으며, 이에 따라 재수술도 증가하고 있다. 그러나 인공와우 이식 재수술 후 달팽이관의 병리 조직학적 변화에대한 연구는 부족한 실정이며, 인간 측두골에 대한 연구는 검체 확보의 어려움으로 인해 매우 미미한 상태이다. 본 연구에서는 인공와우이식 재수술을 시행받은 네명의 환자로부터 사후 기증받은 측두골을 부검시 획득하여 병리조직학적 연구를 위해서 일반적인 표준화된 방법으로 고정, 절개, 염색을 시행한 후, 조직 슬라이드를 광학 현미경으로 관찰 하여, 와우의 구조를 이차원적인 평면에 재구성 시키고, 그 위에 인공와우 이식시에 삽입된 전극을 그린후 그 궤도를 분석하고 , 전극의 궤도 주변의 신생골, 섬유조직, 염증세포, 와우액이 차지 하는 면적을 계산 하였다. 전극의 궤도는 일차 수술 시 만들어진 궤도와 재수술시 만들어진 궤도가 서로 합쳐져서 형성된 'common track', 두가지 전극이 서로 다른 궤도를 가지면서 만들어진 'two track', 일차 수술 시 만들어진 전극 궤도를 넘어서 재수술시의 전극이 더 깊게 삽입되어 생긴 한 개의 궤도인 'one track'의 세가지로 그분 되었다. 전극 궤도 주변의 병리 조직학적 변화를 서로 비교 분석 한 결과 네명의 환자 모두 인공와우 이식 재수술 시 전극의 삽입 깊이는 일차 수술시 전극 삽입 깊이 보다 깊었다. 일차 인공와우 이식 수술 시 만들어진 기존의 전극 궤도는 재수술시 전극 삽입에 저항을 주거나 영향을 끼치지 않았으며, 재수술시의 전극 삽입은 기존의

궤도를 항상 따라 가지는 않았다. Common track 과 Two track 에서 전극궤도 바깥쪽 와우 공간에 비정상 조직(신생골, 섬유조직,염증세포)이 차지하는 평균면적은 43.2% 로서, 와우액이 차지하는 평균면적 (13.4%)보다 유의하게 높았으며 (p=0.003), One track 에서의 전극궤도 바깥쪽 와우 공간의 비정상 조직은 29.9 %, 와우액의 평균면적은 40.0%로 와우액이 차지하는 면적이 많았으나 통계적인 유의성은 없었다 . 따라서, 인공와우 이식 재수술 시 기존 궤도에 의한 저항으로 전극의 삽입이 않되거나, 기존궤도에 밀려 주변의 와우 구조가 더 많이 파괴 되거나 하는 소견은 없었고, 오히려 기존의 궤도를 이용하거나 약간 벗어나면서 더 깊이 삽입 되었고, 수행 능력이 재수술 후 전반적으로 호전되었던 것으로 보아, 인공와우 이식 재수술은 병리학적 안정성과 유용성이 있다고 생각된다.

핵심어: 전극 궤도, 인공와우 이식 재수술, 병리조직학적 연구

Abstract

The histopathologic changes of revision cochlear implantation in human

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The current study evaluates histopathologic changes in the temporal bones of four human subjects who underwent revision cochlear implantation. Specimens were removed at autopsy, fixed and prepared for histological study by standard techniques. Specimens were serially sectioned, reconstructed by two-dimensional methods, and the tracks of the initial and revision cochlear implant electrodes identified. The tracks were of three types: a “common track” (shared by the reimplantation electrode and initial electrode), “two tracks” (where the reimplantation electrode was in a different track than that of initial electrode) and “one track” (where the reimplantation electrode extended beyond the initial electrode forming a single electrode track). Associated histopathologic findings (new bone formation, fibrosis or inflammatory cells, and cochlear fluid) were evaluated for the three types of tracks. In all four subjects, the insertion depth of the revision cochlear implant was deeper than that of the initial cochlear implant. The primary track of the initial implantation did not interfere with insertion of a revision cochlear implant, and the trajectory of the revision electrode did not always follow the primary track. In revision cochlear implantation, the initially using main track was common track rather than new track. The revision electrode was not leaded to wrong course as a resulting more trauma to cochlear structure. The performances after revision cochlear implantation were more improved generally. In cochlear segments with a common-electrode track or a two-electrode track, the mean (across-subject) percent area of the perielectrode cochlear duct filled with

abnormal (new-bone or fibrotic) tissue (43.2%) was significantly greater than the mean percent area occupied by fluid (13.4%; t=3.12, df=19.9, p=0.003). In cochlear segments with a one-electrode track, the mean percent area filled with abnormal tissue (29.9%) is not significantly different than the mean percent area occupied by fluid (40%). We can identify histopathological safety of revision cochlear implant surgery and its usefullness.

Key Words: Electrode track, Histopathology, Revision cochlear implant

Introduction

Cochlear implantation has become a standard medical procedure for the rehabilitation of profoundly deaf postlingual adults, prelingually and postlingally deafened children. Cochlear implant can to replace a nonfunctional inner ear hair cell transducer system by converting mechanical sound energy into electrical signals that can be delivered to the cochlear nerve in profoundly deaf patients. The 3M/House device (3M, US) is an example of the analog transformation schem and provided limited frequency information in the lower frequency range. It was the first cochlear implant to receive U.S. FDA approval for adult. Multichannel , multielectrode cochlear implants use place coding to transfer frequency information in addition to providing time and intensity information accurately. The three multichannel cochlear implants presently are available such as Nucleus 22 (Cochlear Limited , Australia), Clarion (Advanced Bionics, US), MED-EL Combi 40 (MED-EL, Austria). With the use of cochlear implants, people who have severe-to-profound hearing loss may perceive sounds and learn to speak. As the cochlear implants done internationally has increased, there are increasing reports of revision cochlear implantation. The reasons for reimplantation included the following six categories: documented failure of the internal device, decreased performance of unknown cause, technology upgrade, unsatisfactory initial electrode placement, scalp flap complications, and intratemporal pathology. The previous reports about revision cochlear implants show that "high rate" of surgical success with resolution of the patient's presenting signs and symptoms and significant improvement in auditory performance. Perioperative complications were uncommon. (Buchman et al.,2004, Rivas et al., 2008, Cullen et al., 2008, Sorrentino et al., 2009, Zeitler et al., 2009) However, the clinical experience with revision cochlear implantation is not always as positive. Henson et al (1999) reported on 28 adults who required cochlear re-implantation using the same implant design. In this study 37% of patients had significantly higher sentence or word scores with their replacement cochlear implantation, 26% had no significant change and 37% had significantly poorer scores. Similarly Miyamoto et al. (1997) reported a retrospective study of 17 revision cochlear implants. In most cases insertion length and number of channels remained unchanged but based on a few patients in whom this was not the case the mean depth of insertion was statistically lower in revision cases.

There are increasing demand for identify reasons of poor performance after revision cochlear implantation in some cases and change of cochlear structure after revision surgery. There have been three published reports of the effect of cochlear reimplantation on the inner ear studied histologically in experimental animals. Jackler et al. (1989) performed reimplantation using either a single ball electrode or a longer electrode in eight adult cats. They reported that cochlear explantation followed by immediate reimplantation may be accomplished without damage to the cochlea or its neural population. However, proliferation of granulation tissue at the round window and in the scala tympani may cause difficulty in insertion of the replacement device and may increase the likelihood of induced trauma. Greenberg et al. (1992) reported in the guinea pig that there was no significant difference in the pathology of singly implanted or reimplanted cochleae. However, the experimental protocol was limited to a single wire ball tip intracochlear electrode. Shepherd et al. (1995) reported the histopathologic change after cochlear re-implantation using long multichannel intracochlear electrodes in the macaque. Electrode insertion trauma involving the osseous spiral lamina or basilar membrane was more common in the re-implanted cochleae. The damage, however, was usually restricted to the lower basal turn and also resulted in more extensive loss of basal ganglion cells particularly when proliferation of granulation tissue at the cochleostomy was identified. There has been little histopathologic study of reimplanted temporal bone in human especially due to rare human temporal bone specimens that received revision cochlear implantation. Rubinstein et al.(1998) presented the temporal bone histopathology in one patient who underwent a single channel electrode in the left ear and four years later underwent explantation and reimplantation with a conventional multichannel implant (same case as patient #4 in the current series). They identified two separate electrode tracks but just in one case. The previous reports of quantitative evaluation of the volume of new bone or fibrous tissue were for the perielecrode space after primary cochlear implantation not after revision cochlear implantation (Li et al.,2007, Somdas et al., 2007) . The present study characterizes the temporal bone histopathology of four subjects who underwent at least one revision cochlear implant surgery in life. We compare the 3 types of tracks, insertion depth, and performance associated with the primary and revision implantations and evaluate abnormal tissues (new-bone, fibrotic or inflammatory) as an indicator of trauma in the cochlear structure or tissue reaction.

Material and Methods

1) Materials

The donated temporal bone specimens are permitted from patients or their family for research before cochlear implant surgery or before death. In four subjects, the cause of deafness was a temporal bone fracture in two subjects, mumps and/or chemotherapy in one subject, and measles and chronic otitis media in one subject. In two subjects (subjects 1,4), the first cochlear implant was a single-channel device and was then converted to a multichannel device at revision cochlear implantation. Details of the clinical demographics are shown in Table 1 in outline form and in more detail in the following case reports (Table 1). The temporal bones were fixed in 10% buffered formalin, and decalcified in ethylenediamine-tetraacetic acid. Those specimens in which the electrode array was left in situ were postfixed in 2% osmium tetroxide. All specimens were dehydrated in graded alcohols. The specimens in which the electrode array was left in situ were exchanged with propylene oxide and embedded in araldite, whereas specimens in which the electrode array had been removed before fixation were embedded in celloidin. The embedded specimens were serially sectioned in the horizontal (axial) plane at an average thickness of 20 μm. Specimens embedded in araldite with the electrode array left in situ were sectioned by a technique previously described (Nadol et al., 1994). Every tenth section of specimen embedded in araldite was either left unstained or stained in toluidine blue O. Every tenth section from specimens embedded in celloidin were stained with hematoxylin-eosin.

The serial sections were reconstructed by conventional two-dimensional methods (Guild, 1921; Nadol, 1988; Schuknecht, 1993). The total length of the cochlea and the depth of insertion of the electrode as measured from the round window were determined from two-dimensional reconstructions. The track of a cochlear implant electrode was documented by direct microscopic observation when the electrode was cut in place or, in specimens in which the electrode had been removed prior to histological preparation, using histological evidence such as perielectrode fibrosis.

2) Classification of electrode tracks

The electrode tracks were classified into three types based on their size, shape, and trajectory. Nearest the cochleostomy the initial and revision insertions always shared a "common track." Longitudinal cochlear segments where the primary and revision electrodes took separate tracks were classified as "two tracks." The presence of "one track" implies a single electrode.

3) Histopathology of perielectrode space

To compare the amount of perielectrode space occupied by new bone, fibrosis, or cochlear fluid across the three types of tracks, every tenth section was magnified with a microprojector (x15.6), and, for each cochlear turn with an electrode track, the cross section of the turn , the electrode track, and regions of new bone, fibrosis, inflammatory cells and fluid were traced on graph paper (250 x 180 mm). The perielectrode area of each cochlear turn represented by each histological section was computed by subtracting the area of the electrode track from the turn's cross-sectional area. The areas occupied by new bone, fibrosis, inflammatory cells or cochlear fluid were calculated for each turn and the percentage of the perielectrode area of each computed by dividing the area for each tissue by the perielectrode area and multiplying by 100. The percentages for each histological section were weighted by the longitudinal length represented by each turn of each segment and summed across section by tissue type, track type and subject to compute the weighted mean percentage of the perielectrode space occupied by each tissue for each track type and subject. To compare the differences of percentage area between different tissue groups, paired t tests were performed. The level of significance applied was p=0.05. SPSS version 14 (SPSS, Inc., Chicago, IL,USA) was used.

4) Post operative performance

The performance (NU-6) measures after the initial and revision cochlear implantations were available in some subjects, and in others an NU-6 score was estimated from other speech-reception test results based on a technique described by Rabinowitz et al. (1992) (see Table 1).

Results

Case reports

Subject 1

In this 80 year old woman, hearing loss was first noticed on the right at age four years following an episode of measles and on the left at age 42. There was a progressive loss of hearing in both ears over the years, and she was profoundly deaf at age 50. Otorrhea was first noted on the right side at age 40 and on the left side at age 42. She underwent mastoidectomy of the right ear at age 40 with revision on the right at age 64. Mastoidectomy of the left ear was done at age 67. She underwent a right cochlear implantation using a 3M House single channel device at age 65, but nine years later, that implant began to malfunction. At age 74, the single channel device was explanted, and a Nucleus 22 device was reimplanted.

Subject 2

This 88 year old man had normal hearing until he sustained a skull fracture at age 70. Following recovery from the injury, he had "20 percent" residual hearing. Residual hearing was lost five months later after a second skull fracture. He underwent a right cochlear implantation using an Ineraid device (Smith and Nephew, US) at age 71. One year later the pedestal of the implant was sheared off while getting out of an automobile. He then underwent reimplantation of the right ear with another Ineraid device at age 72. His second pedestal was also damaged, and he therefore underwent a second reimplantation using a Nucleus 22 device at age 75.

Subject 3

This 79 year old woman was profoundly deaf in the left ear from early in life which was attributed to mumps or polio. A progressive hearing loss of the right ear started at age 20 with a significant additional loss in hearing at age 72 while on chemotherapy for metastatic lung carcinoma. She was profoundly deaf at age 75 when she underwent a right cochlear implantation using a Nucleus 22 device. At surgery, resistance to

insertion was encountered in the ascending basal turn. The cochleostomy was enlarged in an attempt to insert the electrode into the scala vestibuli. Resistance was encountered at the same location and only half of the active electrodes were inserted. A postoperative plain X-ray showed the implant to be in the cochlea with a small bend at it's tip where the electrode curled back on itself. Performance was poor with this implant and a CT scan one-year post-implantation showed the electrode array only partially inserted. Therefore at age 76, she underwent a revision right cochlear implantation using a Nucleus 22 device. Her word recognition improved from 2% to 16% (NU6).

Subject 4

This 67 year old man became profoundly deaf bilaterally as a consequence of a bilateral temporal bone fractures at age 47. Audiometry showed no response in both ears at age 50. At age 53, he underwent a left cochlear implant using a House single channel device but, because of intermittent performance with this device, he underwent explantation and reimplantation using a Nucleus 22 device at age 57. The performance after the second implantation was similar to that after the first implantation (Table 1).

Discrimination of 3 types of tracks

While following the tracks from the cochleostomy site to the tip of the electrode, transition from a common track to two single tracks was seen (subject 1, Fig.1, top panel). Transitions from a larger single track ("common track") to a smaller single track were also observed (in subject 2, 13.2 mm from round window in Fig.2, top panel; in subject 3, 12.8 mm from round window in Fig.3, top panel). The track of an Ineraid electrode (subject 2) was oval or bilobed which was easily distinguished from the track of a Nucleus electrode.

In cases with two tracks, the track with an electrode in situ was judged to be the revision track (subjects 1,2,3) whereas the other with no electrode was judged to be the primary track. If both tracks were empty (because of removal of the electrode at the time of histologic preparation, subject 4), the larger track was assumed to contain the multichannel electrode and the smaller track to have contained the single channel electrode. Subject 2 was implanted three times (Ineraid, Ineraid, Nucleus 22). In this case, the size and shape of

the Ineraid and Nucleus 22 tracks were distinguished by referring to other temporal bone specimens implanted with similar multichannel devices. In this subject, the tracks of the first Ineraid and second Ineraid electrodes could not be distinguished. However, the operative record described the insertion depth of both primary and revision Ineraid electrodes as nearly the same. In subject 3, the primary and revision electrodes were both Nucleus 22 and the different insertion depths were supported by information in the operative record. Thus a total of 14 electrode contacts of the primary implant were inserted and resistance was encountered 10 mm within the cochlea. The common track and the more apical single track (occupied by the revision cochlear implant) were distinguishable based on differences in size and shape of the tracks. In subject 4, in which the scala media was dilated by endolymphatic hydrops, the electrode track could be identified by the presence of perielectrode fibrosis.

Insertion depths and tracks (Fig. 1,2,3,4)

The insertion depth of each revision cochlear implant was greater than that of the initial cochlear implant in all four patients. The mean insertional depth of the revision electrodes (19.4 mm) was significantly greater ($t=-3.8$, $df=3.3$, $p=0.014$) than the mean insertional depth of the initial electrodes (14.0 mm). The trajectory of the revision electrode did not always follow the primary track. In all cases the revision electrode started within the common track and then diverged to create another track.

In subject 1, the revision electrode (Nucleus22) shared a common track with the 3M House single channel device to a depth of 10.3 mm and then diverged to another trajectory causing two tracks. The track of the 3M House single channel electrode was no longer visible after 12.3 mm and the track of the Nucleus 22 electrode could be followed to 19 mm (Fig.1,5,6,7). In subject 2, the last revision electrode (Nucleus 22) followed the track created by the two Ineraid electrodes to 13.2 mm in depth, except for a short segment (0.3 mm) with two tracks present between 8.4 mm and 8.7 mm from the round window (Fig.2,8) and then diverged into another track and terminated at 20.3 mm. In subject 3, the revision electrode (Nucleus 22) entered the previous track created by the initial Nucleus 22 device to 12.8 mm in depth and then diverged to a create a single new track to 19.5 mm in depth. A 3mm segment of buckled electrode was found within the common track beginning about

5.5 mm. The common track split into two tracks for a short segment (0.1mm) at 8.8 mm (Fig.3,9). In subject 4, the revision electrode (Nucleus 22) followed the track created by the House single channel device to 16.7 mm in depth and then diverged to create a short segment (1.5mm) with two tracks and finally continued as a short segment (0.7mm) of one track (Fig.4,10).

In the four subjects, the point of divergence from the common track to two tracks (subjects 1,4) or one track (subjects 2,3) were at 10.3 mm (mid. point of ascending basal turn) in subject 1, at 13.2 mm (end point of ascending basal turn) in subject 2, at 12.8 mm (end point of ascending basal turn) in subject 3, and at 16.7 mm (mid. point of descending basal turn) in subject 4, as measured from the round window. In all four subjects, the last single track was presumed to have been occupied by the revision electrode. The differences between insertion depths of the revision and primary electrode tracks were + 6.7 mm (subject 1), + 7.1 mm (subject 2), + 6.7 mm (subject 3) and + 0.7 mm (subject 4).

Histopathology of perielectrode space

The histopathology of all 4 specimens showed evidence of trauma to the inner ear structures by electrodes. In subject 1, the initial electrode track passed through the basilar membrane from one scala to another scala at 2 locations (8.8 mm, 10.3 mm) and the revision electrode track at 1 location (12mm). In addition, dissection of the spiral ligament to the bony cochlear wall was also found (Fig.6,7). In subjects 2 and 4, the electrode track penetrated the basilar membrane at 2 separate locations, and dissection of the spiral ligament was found (Fig.8,10). In subject 2, the first and second Ineraid electrodes did not penetrate the basilar membrane but the revision Nucleus 22 electrode did so at 2 separate locations (16.5 mm, 19.3 mm). In subject 4, the initial electrode penetrated the basilar membrane at 8.2 mm and the revision electrode penetrated the basilar membrane at 16.5 mm. In subject 3, dissection of the spiral ligament by both the initial and revision electrode tracks was identified. The bottom panel of Figs. 1, 2, 3 and 4 each plot the percentage of extraelectrode space in the cochlear duct occupied by new bone (red), fibrous or inflammatory tissue (yellow) and fluid (blue) as a function of distance from the round window. In an effort to differentiate the amount of new bone, fibrous or inflammatory tissue caused by the cochlear implantation process from that caused by the creation of the

cochleostomy, only the cochlear segments 5mm apical to the apical margin of the cochleostomy (apical to the vertical dashed line in the bottom panel of Fig. 1,2,3,4) were included in the following analyses. Table 2 lists the weighted mean percentage (see methods) of extracochlear space occupied by new bone, fibrous or inflammatory tissue and fluid by type of electrode track and subject. There is not a significant difference between the mean (across-subject) percentages of new bone in common-track segments (51.7%) vs. one-track segments (30.5%) or between two-track segments (56.3%) vs. one-track segments (30.5%). Also, there is not a significant difference between the mean (across-subject) percentages of new fibrotic tissue in common-track segments (33.3%) vs. one-track segments (29.3%) or between two-track segments (31.8%) vs. one-track segments (29.3%). There is not a significant difference between the mean (across-subject) percentages of fluid in common-track segments (15.0%) vs. one-track segments (40.0%; $p=0.08$) or between two-track segments (11.8%) vs. one-track segments (40.0%; $p=0.0598$). The cochlear segments can be divided into two groups by the number of electrode insertions they experienced: one insertion (one-track segments) and multiple insertions (common-track and two-track segments). The mean (across-subject) percent area of the perielectrode cochlear duct filled with abnormal (new-bone or fibrotic/inflammatory) tissue (43.2%) was significantly greater than the mean percent area occupied by fluid (13.4%; $t=3.12$, $df=19.9$, $p=0.003$) in cochlear segments with a common-electrode track or two-electrode tracks. The difference in mean percent area between abnormal tissues (29.9%) and fluid (40.0%) was not significantly different in the one-insertion group of segments. There was not a significant difference between the mean percent area of abnormal tissue in segments with common-electrode or two-electrode tracks (43.3%) and segments with a one-electrode track (29.9%).

Performance after revision cochlear implantation

Word recognition scores after primary and revision implantation are displayed in Table 1. Word recognition scores after reimplantation in these 4 cases was not obviously different from that after the first implantation. Incomplete data for two subjects and the small number of patients did not allow statistical analysis.

Discussion

There has been little histopathologic study of the reimplanted temporal bone. In previous reports of cochlear histopathology in animals, the re-implanted cochlea showed evidence of increased trauma, more new bone and fibrous tissue (Shepherd et al., 1995). Furthermore, there has been a paucity of cochlear histopathology reported in humans who had undergone revision implantation. Linthicum et al. (1991) reported on three such patients. In all cases the first electrode was a platinum ball and was replaced by similar electrode to a depth less than that of the original insertion distance. All three cochleae were noted to have large amounts of new bone and fibrous tissue and among the lowest ganglion cell counts compared to 16 singly implanted cochleae. Fayad et al. (2006) report an adult implant user who had undergone bilateral revision implantation, replacing a single channel electrode (20 mm in length) on one side with a Nucleus 22 multichannel device and a 3M/House single channel short electrode (6 mm) on the opposite side with a Nucleus 24 multichannel device. They found new bone formation around the electrode path in the scala tympani of the basal turn of the cochlea. The spiral ganglion cell counts were extremely low in both ears, representing less than 10% of the normal spiral ganglion cell population. Despite the low spiral ganglion cell counts, the patient derived benefit from the implants with scores of 30% open set word recognition and 66% on open-set sentences in both ears.

Somdas et al. (2007) developed a methodology to quantitatively evaluate new bone and fibrous tissue using 3-D reconstruction (Amira). They evaluated seven temporal bones and demonstrated the greatest volume of new bone formation at the cochleostomy site and at sites of trauma to the lateral cochlear wall in the ascending limb of the basal turn. They suggested that trauma to the endosteum or lateral cochlear wall may be a factor in induction of this tissue reaction. By using a scoring system for damage to the lateral cochlear wall and a 3-D reconstruction method, Li et al. (2007) evaluated new bone and new fibrous tissue formation in the inner ear following cochlear implantation in twelve temporal bones. They evaluated spearman correlation coefficients (RHO) between histopahologic and clinical variables and demonstrated the volume of new bone (0.15~18.43 μm^3), new fibrous tissue (0.80 ~ 32.30 μm^3), total new tissue (2.97 ~ 42.19 μm^3), depth of electrode insertion (7 ~ 23 mm) , damage to lateral cochlear wall (total damage score) (8 ~ 60), They reported a

significant correlation between total damage to the lateral cochlear wall and total volume of new bone (Spearman rho = 0.783, p=0.0026), new fibrous tissue (Spearman rho = 0.762, p=0.0040), and total new tissue (Spearman rho = 0.853, p=0.0004). They suggested that insertional trauma to the lateral cochlear wall may play a role in subsequent fibrosis and neo-ossification following cochlear implantation. High levels of osteoprotegerin within the spiral ligament may serve to inhibit bone remodeling, and exposure of the underlying endosteum may provide a nidus of inflammation to promote ossification. Inflammatory mediators may contribute to a general increase in new bone formation. In previous two studies (Li et al., 2007; Somdas et al., 2007), the volumes of new bone and new fibrous tissue were computed from 3-dimensional reconstructions. But. the limitation of that method was difficult to accurate margination between different pathology groups because of technical problem when using computer mouse or digital pencil of soft ware. In present study, manual counting of the pixels in ossified and fibrous areas was done for every tenth section (200 μm interval), this manual counting is more precise than Amira's interactive alignment tool.

In present study, the mean (across subjects) percent area of abnormal (new-bone, fibrous and inflammatory) tissue was: 29.9% for one-track segments, 44.0% for two-track segments and 42.5% for common-track segments. The difference between the means of each of the possible pairs (two vs. one; two vs. common; and common vs. one) were not significant (all $p>0.050$). The difference between the means of each of these possible pairs were also not significant when the new bone, fibrous/inflammatory tissues and fluid were analyzed separately.

When the segment within 5 mm of the cochleostomy where included in the statistical analyses, there was not a significant difference between the mean (across-subject) percentages of new bone in common-track segments (65.0%) vs. one-track segments (30.5%) or between two-track segments (56.3%) vs. one-track segments (30.5%). Also, there was not a significant difference between the mean (across-subject) percentages of new fibrotic tissue in common-track segments (25.0%) vs. one-track segments (29.3%) or between two-track segments (31.8%) vs. one-track segments (29.3%). But, there was a significant difference between the mean (across-subject) percentages of fluid in common-track segments (10.0%) vs. one-track segments (40.0%; t=-1.9; df=9; p=0.04); but not between two-track segments (11.8%) vs. one-track segments (40.0%; p=0.053).

These differences are may be explained as that one track segments have relatively less trauma rather than common track or two track segments and it may be possible that one track segments can preserve more large fluid spaces. The trauma to the bony lateral cochlear wall by cochleostomy and electrode insertion trauma are mainly developed in cochlear basal turn. The type of track in cochlear basal turn was usually common track.

Many authors have reported superior performance after revision cochlear implant surgery using multichannel electrodes and a low percentage of perioperative complications. (Buchman et al., 2004; Cullen et al., 2008; Rivas et al., 2008). Buchman et al. (2004) reported on 33 revision cochlear implant operations in 30 patients, and resolution of the patient's presenting signs and symptoms occurred in nearly 90% of cases with significant improvement in auditory performance. Perioperative complications were uncommon. Sorrentino et al. (2009) reported on their experience with 20 revision implantations. They reported audiologic performance as stable or improved in 90% of cases. Rivas et al. (2008) reported on 48 revision cochlear implant procedures. Resolution of the preoperative symptoms was achieved in 83% of cases, and speech perception was lower in only one of the 48 cases. Notably, all cases of "hard failure" regained or surpassed previous peak performance whereas in "soft failures" 75% of patients did so, and these tended to be patients of age greater than 70 years. Cullen et al. (2008) reported on 93 revision cochlear implants in pediatric patients. Auditory performance of the revision implant equaled or surpassed the best preoperative performance in "most patients". Zeitler et al. (2009) also reported a "high rate" of surgical success in revision cochlear implantation with preservation or improvement of preoperative performance in the majority of patients and alleviation of preoperative symptoms.

Lassig et al (2005) reported on 58 cochlear reimplantations. Electrode insertion depth was equal or deeper in 53 of 58 cases. Of the 35 patients for whom comparison data are available, speech recognition scores after reimplantation were improved in 25 (71.4%), little or no change in 7 (20.0%), and decreased in 3 (8.5%). Cote et al. (2007) reported on 45 cochlear implant revisions. Electrode reinsertion depth was comparable with the initial surgery, with full reinsertion with the same type of electrode array as in the primary implantation in 33(76.7%) cases. But, in three cases (7.0%) only partial insertion was achieved at revision surgery despite complete insertion during the initial implantation. Speech perception was maintained after reimplantation. Of the 19 children with available data, five had higher scores after the revision surgery, 12 had a similar scores,

and only two had lower scores. Gosepath et al. (2009) reported on 56 surgical revisions of cochlear implantation. In all revisions the electrode insertion depth at the time of reimplantation was similar to that at the initial implantation. In 20 cases in which speech audiometry data was available, 19 showed similar or better scores than before reimplantation. In present study, insertion depths of revision electrodes were greater than at initial implantation in all 4 subjects. Subject 2 and 3 showed increased speech recognition after revision cochlear implantation.

Conclusions

1. The depth of insertion of a cochlear implant electrode array at reimplantation was not limited by the depth of insertion of the initial implant. In all four cases the depth of insertion of the final implant was greater than that of the initial implant. The revision electrode did not always share the previously formed track but, in each of the four bones studied, diverged from the common track for at leas a short distance to create a new track.
2. There is not a significant difference between the mean percent area of abnormal tissue in segments with common-electrode or two-electrode tracks (43.3%) and segments with a single-electrode track (29.9%).
3. In cochlear segments with a common-electrode track or a two-electrode track, the mean (across-subject) percent area of the perielectrode cochlear duct filled with abnormal (new bone, fibrotic or inflammatory) tissue (43.2%) is significantly greater than the mean percent area occupied by fluid (13.4%; t=3.12, df=19.9, p=0.003).
4. In cochlear segments with a one-electrode track, the mean percent area filled with abnormal tissue (29.9%) is not significantly different than the mean percent area occupied by fluid (40%).
5. In revision cochlear implantation, the initially using main track was common track rather than new track. And revision electrode was not disturbed by already established tracks and did not leaded to wrong course as resulting more trauma to cochlear structure. The performances after revision cochlear implantation were improved generally. This study identifies histopathological safety of revision cochlear implantation and its usefulness.

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Table 1. Clinical demographics of revision cochlear implantation. In all 4 subjects, the depth of revision electrodes were deeper than that of the initial electrode.

Name	Sex/ Age at death (years)	Cause of Deafness or Indication for reimplantation	Device (Age at CI)	Duration of electrode insertion (months)	Depth of insertion (mm)	Performance after Cochlear implant (NU6 score)
Subject 1 (Rt)	F/ 80	Measles and Chronic otitis media	3M House single channel device (65)	120	12.3	No record
1st revision of subject1		Malfunction of device	Nucleus 22 (74)	70	19	4%
Subject 2 (Rt)	M / 88	Temporal bone fracture	Ineraid (71)	17	13.2	11 % *
1st revision of subject 2		Sheared off the pedestal of the Implant	Ineraid (72)	30	13.2	10%
2nd revision of subject 2		Subsequently broke pedestal for second time	Nucleus 22 (75)	153	20.3	26%
Subject 3 (Rt)	F / 79	Mumps, Chemotherapy	Nucleus 22 (75)	13	12.8	2%
1st revision of subject 3		Poor word recognition	Nucleus 22 (76)	31	19.5	16%
Subject 4 (Lt)	M / 67	Temporal bone fracture	House single channel device (53)	54	18.2	12 close-set word testing 50 % environmental noises 80%
1st revision of subject 4		Intermittent performance	Nucleus 22 (57)	117	18.9	CID sentence 4% NU6 0%*

* = word score estimated by the method of Rabinowitz et al. 1993.

NU 6 word score = Northwestern University Auditory test # 6 (50 monosyllabic word test)

CID = Central Institute of Deafness (sentence test)

Table 2. Percentage of area occupied by new bone, fibrosis, inflammatory cells and cochlear fluid in the perielectrode space according to type of tracks.

	New bone formation (%)			Fibrosis or inflammatory cells* (%)			Cochlear fluid (%)		
	Common Track	2 Tracks	1 Track	Common Tack	2 Tracks	1 Track	Common Track	2 Tracks	1 Track
Subject 1	60.0	56.2	24.4	40.0	43.8	54.9	0	0	20.7
Subject 2	44.1	68.3	11.9	37.9	30.3	21.4	17.9	1.3	66.7
Subject 3	84.8	100.0	86.4	9.8*	0*	3.5*	5.4	0	10.1
Subject 4	18.0	1.3	0	45.4	52.9	37.7	36.6	45.8	62.3

* = Percentage of space occupied by inflammatory cells.

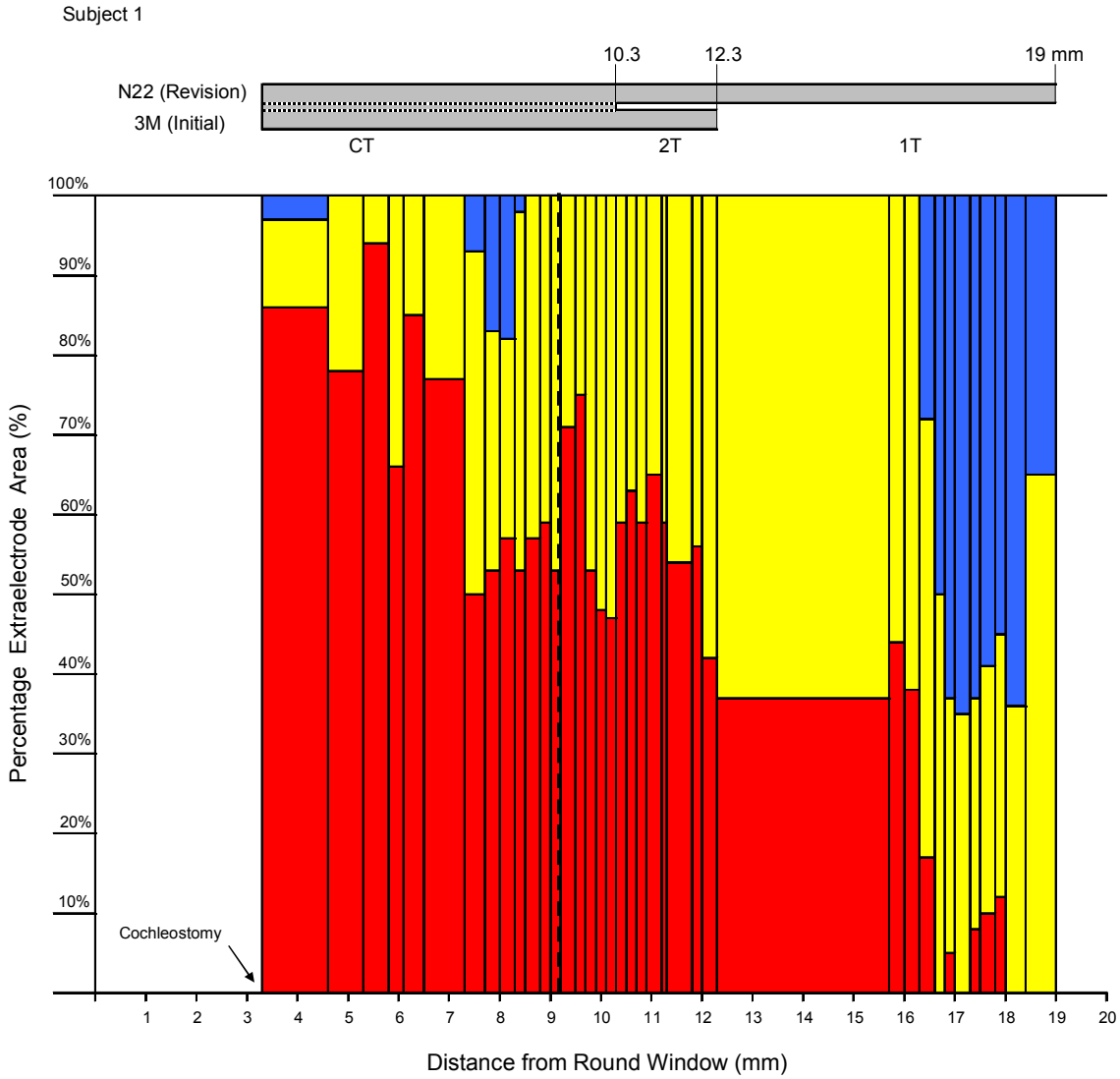

Fig.1. Subject 1. (Top Panel) Schematic representation of the type of electrode track as a function of distance from the round window. From the cochleostomy to 10.3 mm the 3M House single electrode and the Nucleus 22 (N22) revision electrodes occupied a common electrode track (CT). From 10.3 mm to 12.3 mm, two separate electrode tracks were identified (2T). A single electrode track (1T) extended from 12.3 mm to 19 mm.

(Bottom Panel) Plot of the percentage extraelectrode area occupied by new bone (red), fibrous/inflammatory tissue (yellow) and fluid (blue) as a function of distance from the round window. The solid vertical lines mark the boundaries between cochlear segments represented by the histological sections of the cochlear duct used to estimate the percentages. The weighted (see

methods) mean data of Table 2 and the statistical analyses were computed from the cochlear segments apical to the dashed vertical line marking the location 5 mm apical from the apical margin of the cochleostomy. In this case, the cochleostomy extended from 3.3 mm to 4.2 mm from the round window.

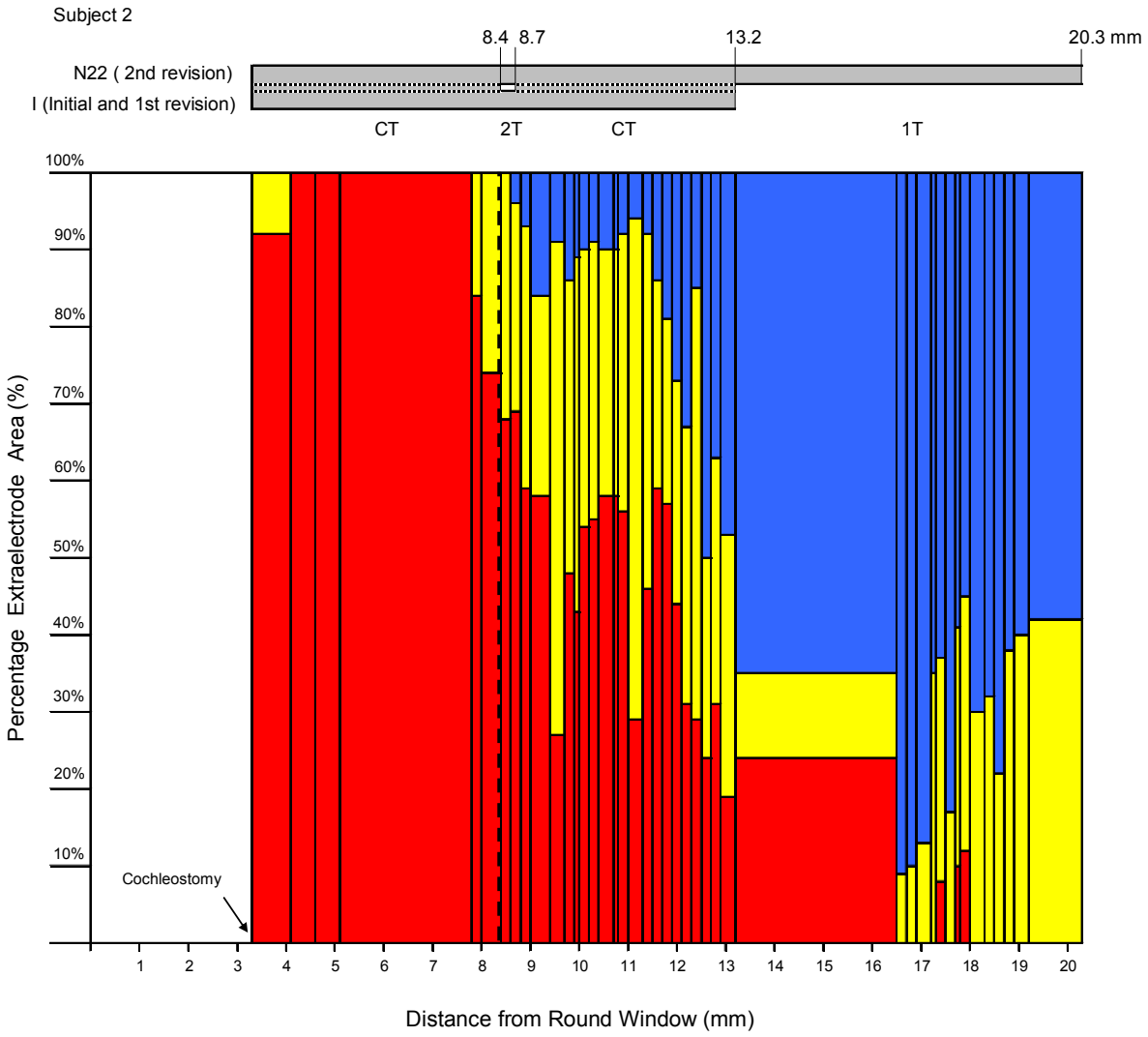

Fig.2. Subject 2. (Top Panel) Schematic representation of the type of electrode track as a function of distance from the round window. From the cochleostomy to 8.4 mm the Ineraid (I) initial and first revision electrode and the Nucleus 22 (N22) second revision electrodes occupied a common electrode track (CT). From 8.4 mm to 8.7 mm, two separate electrode tracks were identified (2T). From 8.7 mm to 13.2 mm the Ineraid (I) initial and first revision electrodes and the Nucleus 22 (N22) second revision electrode again occupied a common electrode track (CT). A single electrode track (1T) extended from 13.2 mm to 20.3 mm.

(Bottom Panel) Plot of the percentage extraelectrode area occupied by new bone (red), fibrous/inflammatory tissue (yellow) and fluid (blue) as a function of distance from the round window. The solid vertical lines mark the boundaries between cochlear segments represented by

the histological sections of the cochlear duct used to estimate the percentages. The weighted (see methods) mean data of Table 2 and the statistical analyses were computed from the cochlear segments apical to the dashed vertical line marking the location 5 mm apical from the apical margin of the cochleostomy. In this case, the cochleostomy extended from 3.3 mm to 3.4 mm from the round window.

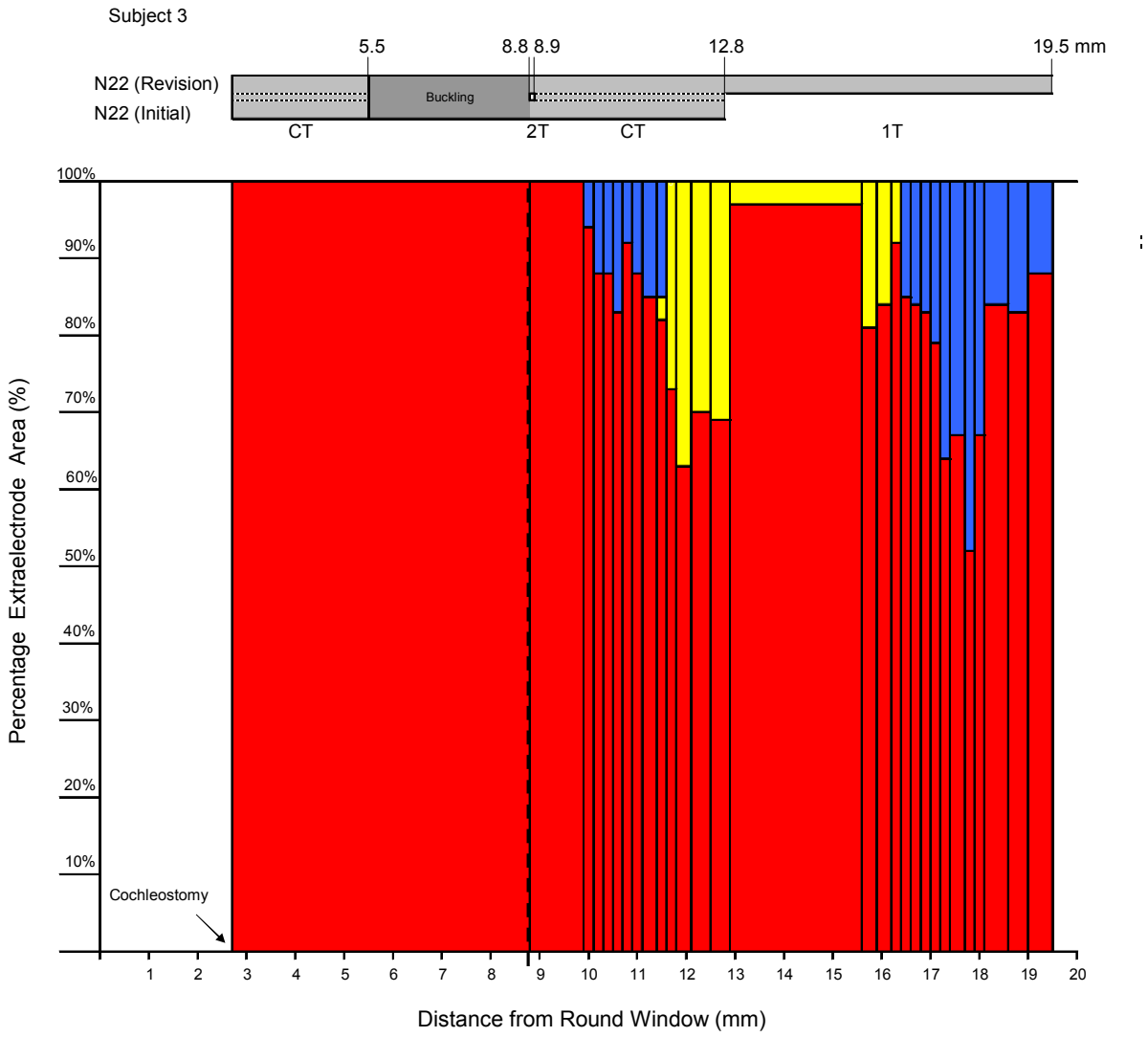

Fig.3. Subject 3. (Top Panel) Schematic representation of the type of electrode track as a function of distance from the round window. From the cochleostomy to 5.5 mm the Nucleus 22 (N22) primary electrode and the Nucleus 22 (N22) revision electrode occupied a common electrode track (CT). From 5.5 mm to 8.8 mm buckling of electrode occurred, and from 8.8 mm to 8.9 mm two separate electrode tracks were identified (2T). From 8.9 mm to 12.8 mm the Nucleus 22 (N22) primary electrode and the Nucleus 22 (N22) revision electrode again occupied a common electrode track (CT). A single electrode track (1T) extended from 12.8 mm to 19.5 mm. (Bottom Panel) Plot of the percentage extraelectrode area occupied by new bone (red), fibrous/inflammatory tissue (yellow) and fluid (blue) as a function of distance from the round window. The solid vertical lines mark the boundaries between cochlear segments represented by

the histological sections of the cochlear duct used to estimate the percentages. The weighted (see methods) mean data of Table 2 and the statistical analyses were computed from the cochlear segments apical to the dashed vertical line marking the location 5 mm apical from the apical margin of the cochleostomy. In this case, the cochleostomy extended from 2.7 mm to 3.8 mm from the round window.

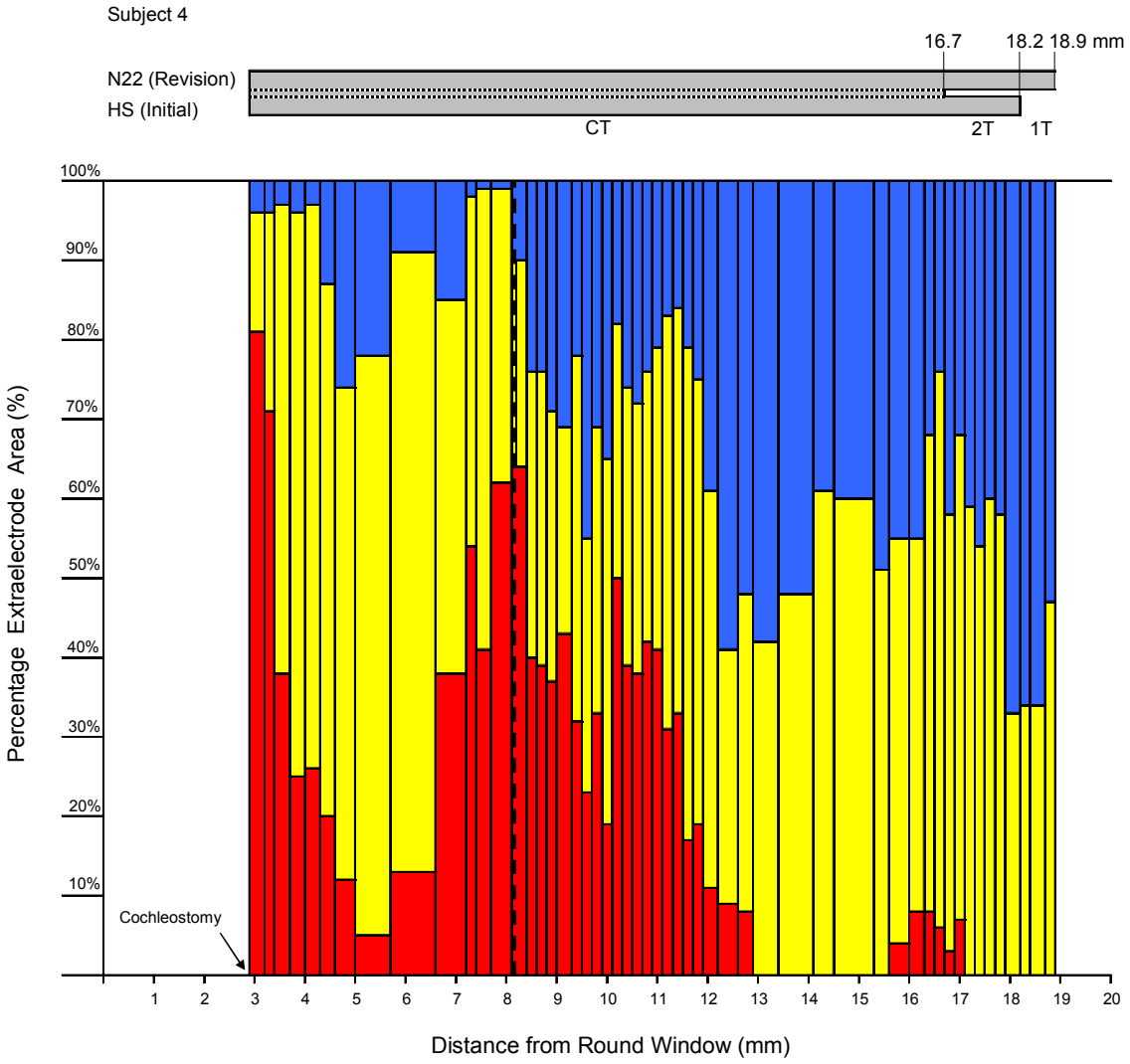

Fig.4. Subject 4. (Top Panel) Schematic representation of the type of electrode track as a function of distance from the round window. From the cochleostomy to 16.7 mm the House single channel (HS) primary electrode and the Nucleus 22 (N22) revision electrode occupied a common electrode track (CT). From 16.7 mm to 18.2 mm, two separate electrode tracks were identified (2T). A single electrode track (1T) extended from 18.2 mm to 18.9 mm.
(Bottom Panel) Plot of the percentage extraelectrode area occupied by new bone (red), fibrous/inflammatory tissue (yellow) and fluid (blue) as a function of distance from the round window. The solid vertical lines mark the boundaries between cochlear segments represented by the histological sections of the cochlear duct used to estimate the percentages. The weighted (see methods) mean data of Table 2 and the statistical analyses were computed from the cochlear

segments apical to the dashed vertical line marking the location 5 mm apical from the apical margin of the cochleostomy. In this case, the cochleostomy extended from 2.9 mm to 3.2 mm from the round window.

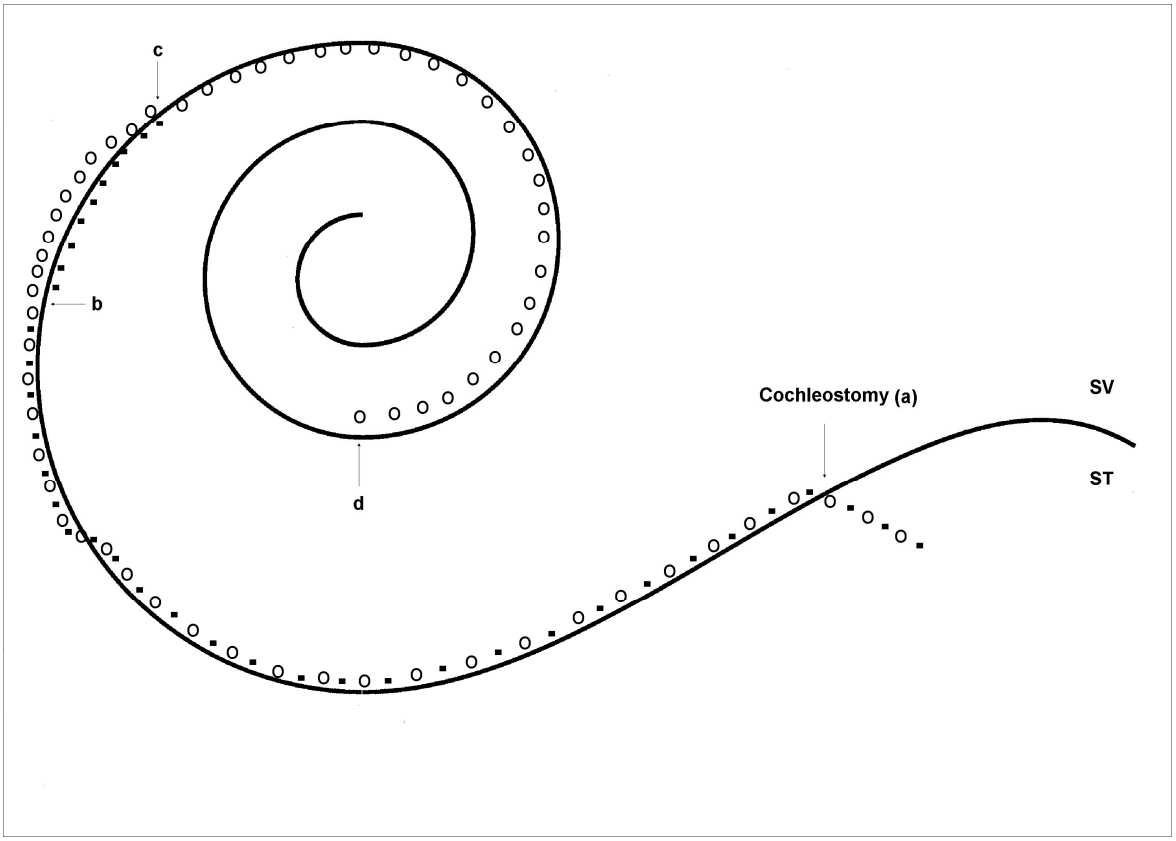

Fig.5. Example of 2-dimensional reconstruction of the cochlea and electrode tracks (Subject 1). The primary electrode track (3M House single channel device) is shown by the filled black squares and the revision electrode track (Nucleus 22) is shown by open circles. There was a common track between a and b, two tracks between b and c, and 1 track between c and d. The distances along the cochlear duct of each point were: a: 3.3 mm, b:10.3 mm, c: 12.3 mm, d: 19 mm, as measured from the round window.
SV = Scala vestibuli; ST = Scala tympani.

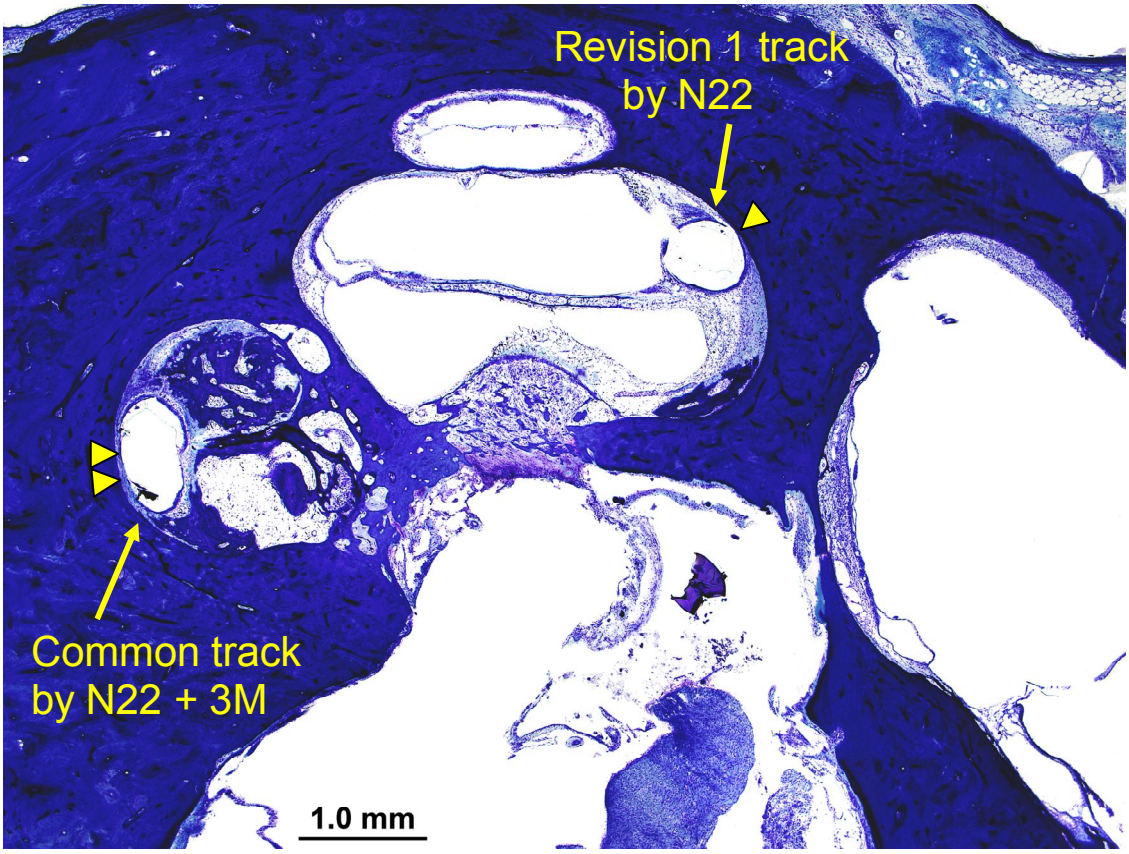

Fig.6. Subject 1. Horizontal section of right temporal bone. The common track in the ascending basal turn presumably had accommodated sequentially the 3M House single channel device and then the Nucleus 22 device. The smaller track in the middle turn was caused only by the Nucleus 22 revision cochlear implant. The circumference of the common track was larger than that of the single track. Dissection of the spiral ligament (single and double arrow heads) and penetration of the basilar membrane by the electrode track (double arrow heads) were identified. N22 = Nucleus 22; 3M = 3M House single channel device. (Toluidine blue O stain)

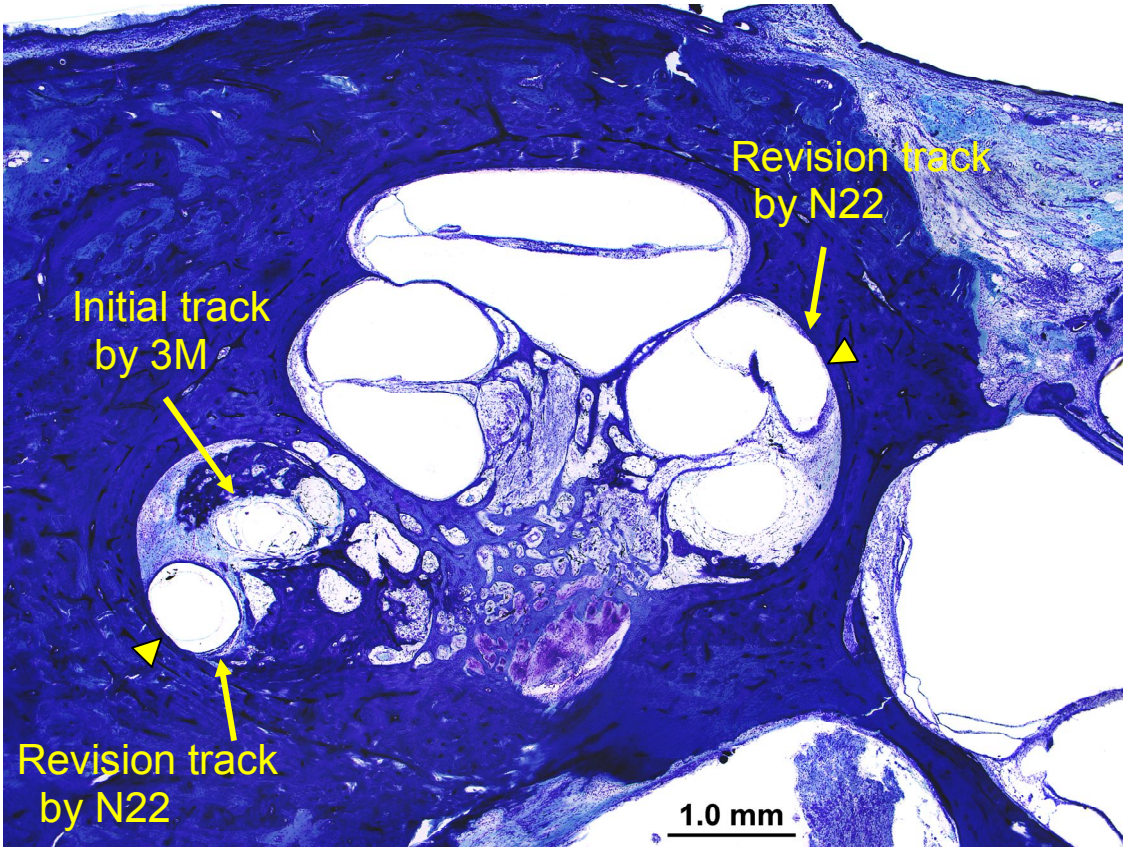

Fig.7. Subject 1. Horizontal section of right temporal bone. Two tracks were visible in the ascending basal turn and one track in the middle turn. The two tracks consisted of the initial track (3M House single channel device) and the revision track (Nucleus 22).The latter is larger than the former. Dissection of the spiral ligament to the lateral bony cochlear wall (arrow head) was seen in both revision tracks. 3M = 3M House single channel device; N22 = Nucleus 22. (Toluidine blue O stain)

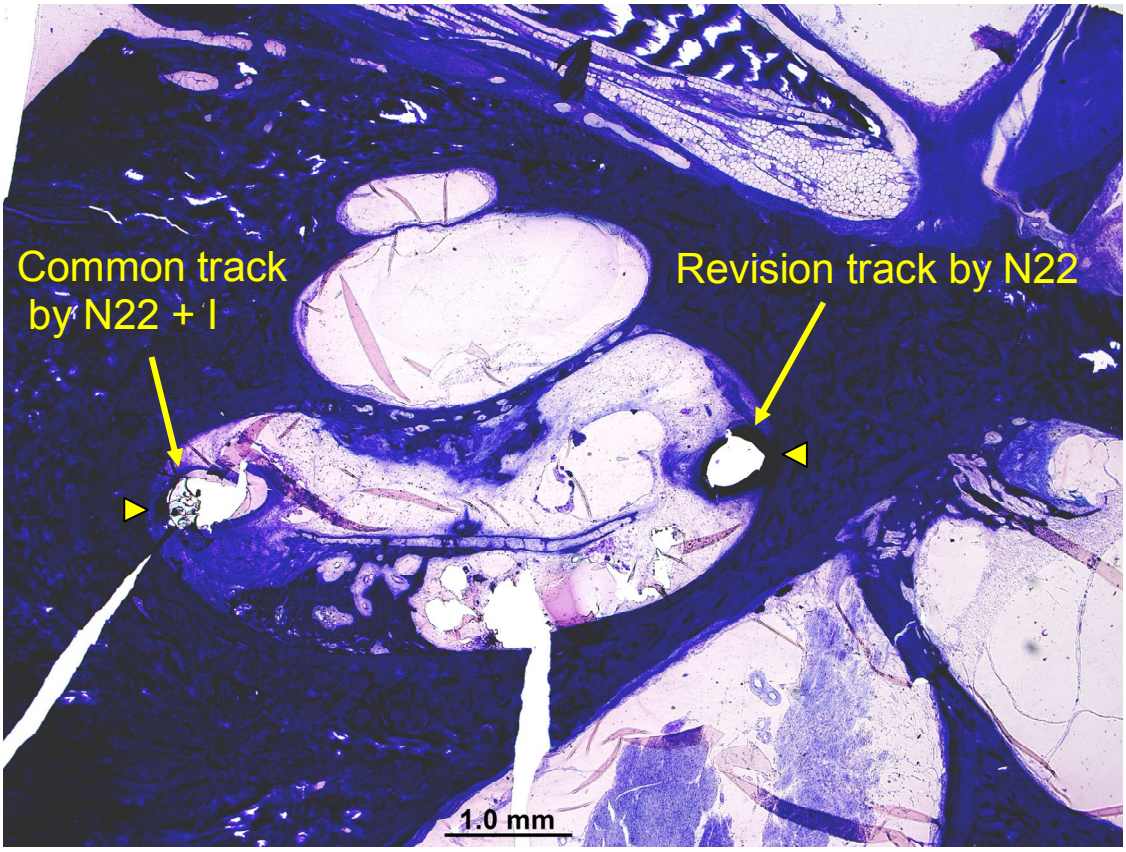

Fig.8. Subject 2. Horizontal section of right temporal bone. The "common track" in the ascending basal turn was presumed to have be occupied sequentially by the Ineraid and the Nucleus electrodes, and the one track in the descending basal turn by the Nucleus 22 at the second revision cochlear implantation. The common track was larger than the revision single track. Dissection of the spiral ligament (arrow heads) occurred in both tracks.

N22 = Nucleus 22; I = Ineraid. (Toluidine blue O stain)

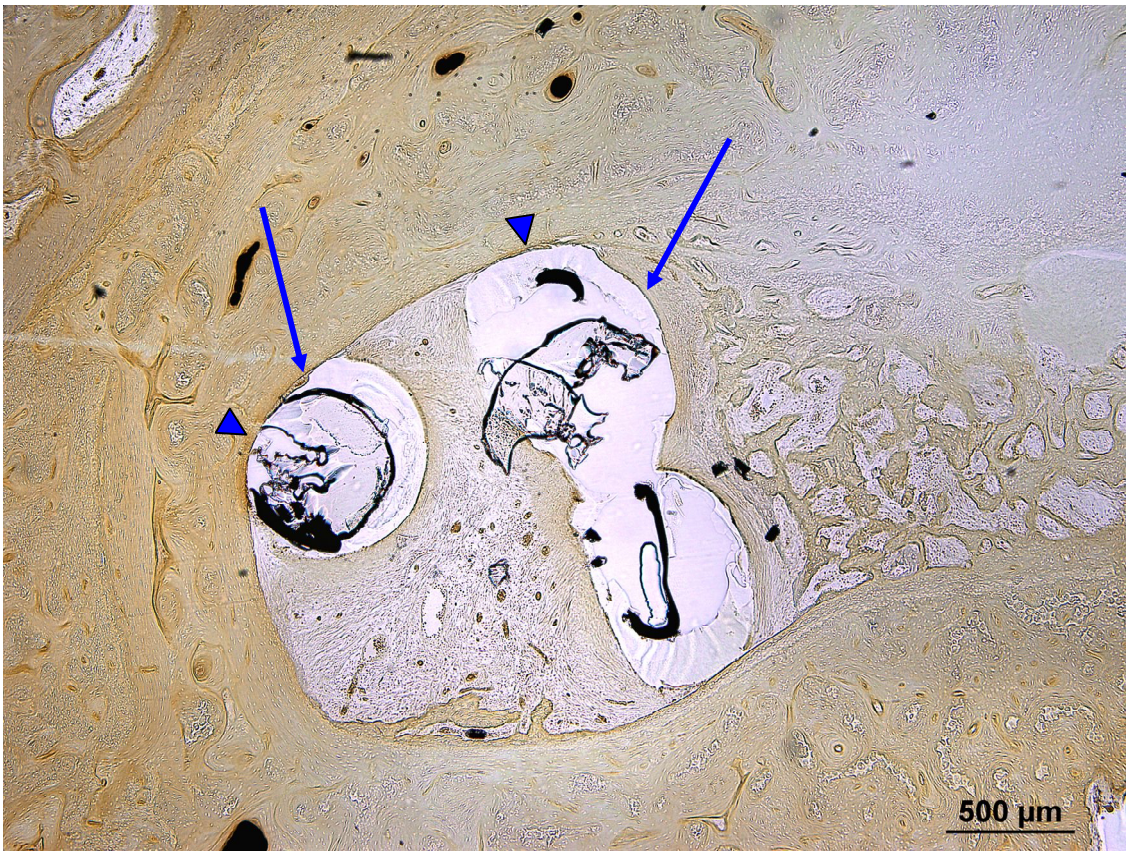

Fig.9. Subject 3. Horizontal section of right temporal bone. In this patient, initial and revision electrodes were both Nucleus 22. The buckling of the revision electrode was visible in basal turn (arrow). Dissection of the spiral ligament to the lateral bony cochlear wall (arrow head) was found. The histopathologic change in the extraelectrode space in the segment containing the buckling electrode was severe ossification and no visible fibrosis or cochlear fluid space. (Unstained)

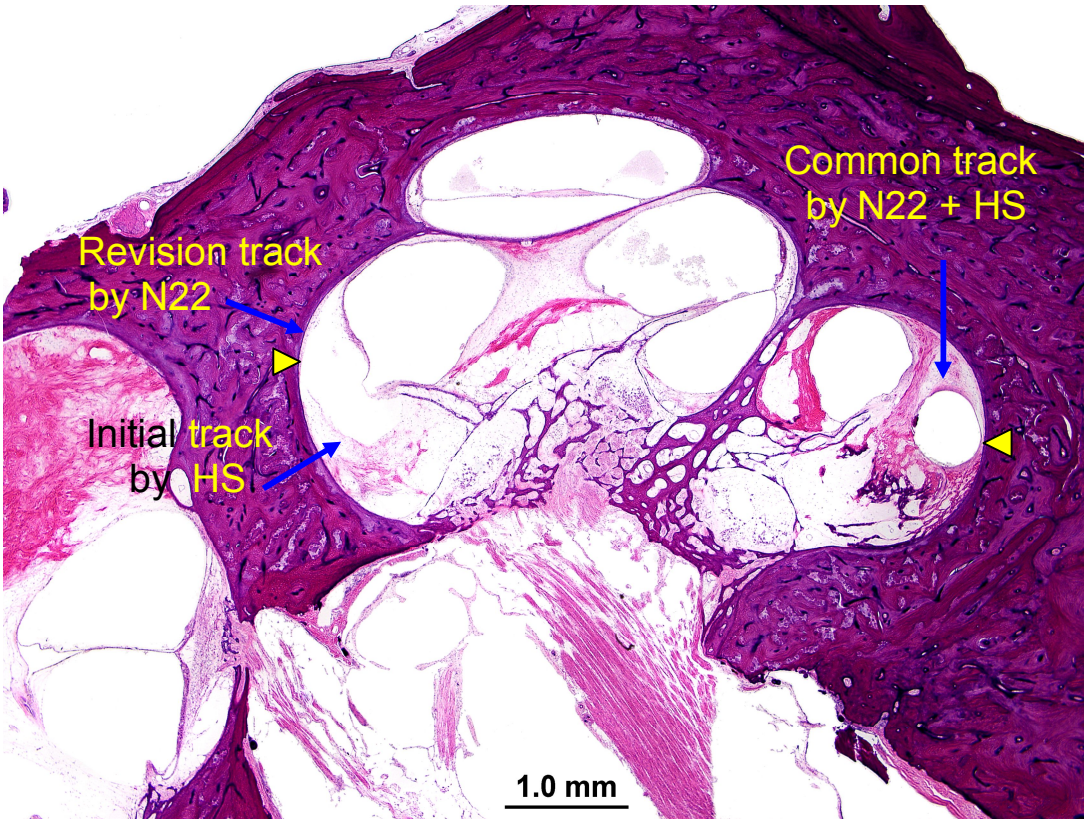

Fig.10. Subject 4. Horizontal section of left temporal bone. The common track was visible in the ascending basal turn, and two tracks were visible in the middle turn. The two tracks consisted of the initial track (House single channel device) and the revision track (Nucleus 22). The common track was larger in diameter than both single tracks. Dissection of the spiral ligament (arrow head) occurred in the common track and in the revision single track. HS = House single channel device; N22 = Nucleus 22 (Hematoxylin-eosin stain)

저작물 이용 허락서

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논문제목	한글 : 인공와우이식 재수술 후 인간 측두골의 병리조직학적 변화 영어 : The histopathologic changes of revision cochlear implantation in human				

본인이 저작한 위의 저작물에 대하여 다음과 같은 조건아래 -조선대학교가 저작물을 이용할 수 있도록 허락하고 동의합니다.

- 다 음 -

1. 저작물의 DB 구축 및 인터넷을 포함한 정보통신망에의 공개를 위한 저작물의 복제, 기억장치에의 저장, 전송 등을 허락함
2. 위의 목적을 위하여 필요한 범위 내에서의 편집・형식상의 변경을 허락함. 다만, 저작물의 내용변경은 금지함.
3. 배포・전송된 저작물의 영리적 목적을 위한 복제, 저장, 전송 등은 금지함.
4. 저작물에 대한 이용기간은 5 년으로 하고, 기간종료 3 개월 이내에 별도의 의사 표시가 없을 경우에는 저작물의 이용기간을 계속 연장함.
5. 해당 저작물의 저작권을 타인에게 양도하거나 또는 출판을 허락을 하였을 경우에는 1 개월 이내에 대학에 이를 통보함.
6. 조선대학교는 저작물의 이용허락 이후 해당 저작물로 인하여 발생하는 타인에 의한 권리 침해에 대하여 일체의 법적 책임을 지지 않음
7. 소속대학의 협정기관에 저작물의 제공 및 인터넷 등 정보통신망을 이용한 저작물의 전송・출력을 허락함.

동의여부 : 동의 (0) 반대( )

2011 년 2 월 일

저작자: 이 준한 (서명 또는 인)

조선대학교 총장 귀하