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Long-term hearing preservation in cochlear implant patients

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PUBLICATIONS RELATED TO THE THESIS

I. **Dimak Balazs**; Nagy Roland; Perenyi Adam; Jarabin Janos Andras; Schulcz Rebeka; Csanady Miklos; Jori Jozsef; Rovo Laszlo; Kiss Jozsef Geza: Review of Electrode Placement with the Slim Modiolar Electrode: Identification and Management
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II. Perenyi Ádám; Toth Ferenc; **Dimak Balazs**; Nagy Roland; Schoerg P; Jori Jozsef.; Kiss Jozsef Geza; Sprinzl Georg; Csanady Miklos; Rovo Laszlo: Electrophysiological measurements with electrode types of different perimodiolar properties and the same cochlear implant electronics – a retrospective comparison study
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III. Nagy Roland; Jarabin Janos Andras; Perenyi Adam; **Dimak Balazs**; Toth Ferenc; Jori Jozsef; Kiss Jozsef Geza, Rovo Laszlo: Long-term Hearing Preservation with Slim Perimodiolar CI532® Cochlear Implant Array
AMERICAN JOURNAL OF OTOLARYNGOLOGY 1:4 Paper: 1019 (2018)

IV. Nagy Roland; Jarabin Janos Andras; **Dimak Balazs**; Perenyi Adam; Toth Ferenc; Szuts Viktória; Jori Jozsef; Kiss Jozsef Geza, Rovo Laszlo: A maradványhallás megőrzésének lehetőségei cochlearis implantáció során Nucleus CI532 Slim Modiolar elektródasorral
ORVOSI HETILAP 159:41 pp. 1680-1688. 9 p. (2018)
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V. Perenyi Adam; Nagy Roland; **Dimak Balazs**; Csanady Miklós; Jori Jozsef; Kiss Jozsef Geza, Rovo Laszlo: Cochlearis implantátumok különböző, előre görbített elektródasorainak elhelyezkedése a cochlea tengelyéhez viszonyítva. Radiológiai vizsgálat a perimodiolaritás mértékének megállapítására
ORVOSI HETILAP 160:31 pp. 1216-1222. 7 p. (2019)
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INTRODUCTION

Hearing loss

Hearing loss affects about 1.33 billion people (Global Burden of Disease) with around 466 million people (World Health Organization) worldwide with disabling hearing loss, and 124 million of these have moderate to severe disability. Hungarian Central Statistical Office results (2020) show that 716,00 people in Hungary live with severe hearing loss, 2000 are under the age of 14. Hearing loss is assessed at different frequencies (from 0.5kHz to 4kHz) and decibels (dB(HL)) using pure tone audiometry.

Severe hearing loss before the age of 3 can delay or even impede speech development and language acquisition. This may also lead to issues in learning, have a severe effect on classroom learning and socialization. Meanwhile, in adults disabled hearing can also have an impact on employment, confidence and it can also be linked to an increased risk of dementia. It is also a potential cause for cognitive impairment and decline in socially isolated elderly patients.

Hearing loss rehabilitation using implantable hearing devices

The most common form of treatment for hearing loss is to provide the ear with a hearing aid. Hearing aids can be used in cases from minor hearing loss to the utilization of hearing loss. A special variant of hearing aids is the group of implantable hearing aids, in which the functional unit is implanted by a surgical procedure. The three groups of these implantable hearing aids are middle ear implants (for moderate SNHL), bone conduction implants (for conductive hearing loss), and cochlear implants (CI) (for severe SNHL).

A cochlear implant is an electronic medical device that replaces the function of the damaged inner ear.

Unlike hearing aids, which make sounds louder, cochlear implants replace the function of damaged structures in the inner ear (cochlea) to provide sound signals to the brain. The cochlea is the part of the inner ear that converts sound waves into nerve signals, which the brain processes as hearing. The apical region of the cochlea is responsible for detecting low-pitched sounds, while the basal region is responsible for detecting high-pitched sounds. The cochlea is lined with thousands of sensory cells, known as hair cells, which detect sound waves and send sound information as nerve signals through the auditory nerve to the brain. CI provides rehabilitation for individuals with severe to profound hearing loss in a uni, – or bilateral way. For people with this level of disability, most of their hair cells do not function normally and are not able to send the nerve signals properly. The CI system bypasses these non-functioning hair cells by using electrical pulses to send sound signals directly to the auditory nerve.

A CI implant system has two parts: the sound processor and an implanted part. The external sound processor (SP) is worn behind the ear, the implant is surgically placed under the skin and attached to a flexible electrode array that is inserted into the cochlea. The sound processor detects environmental sounds and digitally converts them into coded electrical signals. A transmitter coil transfers these signals through the skin to the implant. The implant translates these coded signals into electrical pulses, which are transmitted along the electrode array to stimulate specific locations of the cochlea responsible for specific pitches. This targeted stimulation across the whole cochlea provides a more accurate pitch perception for better sound quality. By mimicking the natural function of hair cells, these pulses can deliver sound signals directly to the auditory nerve. Then these signals are transmitted by the auditory nerve to the brain, where they are interpreted as sound.

Types of electrodes

CI512 (CA)

The apical electrode diameter of current stylet-based perimodiolar electrodes is 0.5 mm (Contour Advance from Cochlear Ltd), which is a technical constraint created by the requirement of an internal stylet. Although a 0.5 mm apical electrode dimension is not dissimilar to the dimensions of contemporary lateral wall electrodes, space within the narrowing scala tympani is not the concern, but rather the ability to insert via the round window. So, a separate cochleostomy has typically been required, which then exposes the risk of incorrect cochleostomy placement and in many cases an anterior cochleostomy directly into scala vestibuli or contributing to early translocation from scala tympani to scala vestibuli.

CI532

The Slim Modiolar Electrode (CI532 implant) from Cochlear Ltd. introduced a new concept of a “sheath-based” perimodiolar electrode, as opposed to “stylet-based”. This difference in approach to straighten and insert a pre-curved electrode is a significant advancement that addresses the two main challenges identified as contributing to the higher rates of trauma with stylet-based perimodiolar electrodes, being 1) variability or compliance with the AOS insertion technique, and 2) the ability to insert via the round window. The sheath-based design also allows for ease of reloading the electrode if required.

Hearing preservation following CI

Hearing preservation following CI particularly at the low frequencies can significantly improve hearing, speech reception, speech comprehension, accuracy in melody recognition, frequency discrimination, and the localization of tone in patients in particularly challenging environments (e.g. prominent background noise). Therefore, preservation of endocochlear microstructure during CI is one of the most significant goals for both low-frequency hearing preservation and optimized electrical stimulation.

The physical parameters (curved vs. straight; short vs. long; with rounded vs. smoothened tip; with or without stylet, etc.), and the intrascalar position of the electrode configuration (perimodiolar, mid-scala, lateral wall) are well-known to have an impact on post-implant performance. For example, imaging techniques (CT, X-ray) demonstrate an increased susceptibility of suboptimal intracochlear CI electrode array placement (i.e. the dislocations from scala tympani to the scala vestibuli) with the Contour than with the Contour Advance array. The dislocation was significantly associated with a lower speech recognition score for those individuals with the Contour array. The applied surgical approach (Round Window (RW), Extended Round Window (ERW), Cochleostomy (CS)) and the implanted electrode profile mainly lead to immediate or short-term damage, while delayed alteration in cochlear function usually derives from the fibrous or bony remodelling of the endocochlear compartments. Iatrogenic intracochlear trauma during CI surgery is highly dependent on the type of fenestration (RW, ERW, CS) and the method of electrode insertion (standard vs. “soft”). Further support could be provided through the administration of lubricants or drugs (e.g. intravenous or intrascalar corticosteroids). The beneficial effects of glucocorticoids are thought to be mediated through several different pathways: the anti-inflammatory effects; the down-regulation of production of inducible nitric oxide synthase; and direct inhibition of the MAP/JNK cell death signal cascade.

Furthermore, the possible disproportion between the physical dimensions of the electrode profile and the endocochlear compartments (diameter, shape, length of scala tympani) play a significant role in preserving inner ear structures and functions.

However, by the broader application of perimodiolar electrodes various challenges have been brought to light. One infrequent issue is that these thin and flexible electrode arrays are potentially more susceptible to tip fold-over, where the tip of the electrode is folding on itself as a ‘hairpin curve’. Various surgical complications (gusher, oozing, etc.), or anamnesis of previous diseases (meningitis, sclerosis of the cochlea) increase the risk of tip fold-over. We have detected three tip fold-over phenomena of the 143 cases (approx. 3%). This incidence corresponds to the published international data.

AIMS OF STUDY

Studies in implanted recipient groups using multiple implant types make it difficult to compare the influence of the implant electrode characteristics on outcomes in the presence of additional variables such as implant electronics, sound processors, and speech coding paradigms. Hence, to reduce the number of variables, a comparison of the influence of electrode designs on outcomes could be interpreted more effectively if a consistent receiver-stimulator design and a common sound processor are used. Recent publications represent imaging and electrophysiological results with CI532.

Our centre’s postoperative radiological comparative study demonstrated that the Slim Modiolar electrode array took a closer position to the modiolus than the Contour Advance electrode array.

We aimed to study long-term hearing preservation in a non-randomized, prospective clinical cohort with cochlear implant systems, limited to ones produced by Australian and Austrian leader companies, provided and fully financed by the Hungarian National Health Insurance.

Thus, here we report our subsequent results with a 3-year-long follow-up to investigate possible changes in residual hearing over time with Slim Modiolar electrode profile.

SUBJECTS AND METHODS

Study cohort

Out of the total number of cochlear implantees with slim perimodiolar implant system (n=143) – at the University of Szeged – our study population was recruited based on the following criteria: (1) patient with good compliance; (2) measurable preoperative hearing threshold; (3) slim perimodiolar electrode array implant system; (4) minimum one-year follow-up period. Thirty consecutive subjects were enrolled in this prospective, non-randomized clinical study. Twenty females and ten males with a mean age at implantation of 43.32 years, ranged between 10 years to 77 years. All subjects were implanted at the University of Szeged from 2015 until 2020. The postoperative follow-up duration lasted 1.72 years on average (ranged between 1.1 and 2.55 years). All subjects met the official indication criteria of CI. Anatomical/structural malformation was not revealed by the preoperative radiological examinations.

Firstly 30 consecutive subjects were enrolled into a prospective, non-randomized clinical study, based on similar inclusion criteria detailed below. From that results cohort 9 patients (9/30=30%) showed up with a total loss of residual hearing at every measured frequency following surgery. From patients who had preserved hearing (21/30=70%), we recruited those with 3-years long follow-up period into this present study. Finally, 11 patients with 13 implanted ears were subjects to this analysis.

Inclusion criteria were as follows: (1) Nucleus CI 532 (Slim Perimodiolar®); (2) postlingual uni-, or bilateral SNHL; (3) normal middle ear function; (4) normal anatomy of the inner ear; (5) full-length electrode insertion.

All implantations were performed by two skilled surgeons (Professors Laszlo Rovo and Jozsef Jori). The approach of “soft surgery” was applied. Round window insertions were performed in all cases.

Implant configuration

The studied cochlear implant system provides full-length cochlear coverage with a slim, perimodiolarly positioned electrode array (Nucleus CI532 Slim Modiolar electrode (Cochlear Ltd., Sydney, Australia)). The thin implant body has no pedestal and is designed to minimize bone excavation and skin protrusion. The side-by-side symmetrical shape makes the implantation easier for the surgeon. The titanium casing has been used for high impact resistance, and the smooth external geometry to minimize biofilm formation, which reduces the risk of infection. The total length of the electrode array is 98 mm, while the diameter is 0.35 × 0.4 mm at the tip and 0.45 × 0.5 mm at the base. At the last edge of the electrode array, there are three white marker rings for controlling the insertion depth that is followed by 22 half-banded platinum electrode contacts. The insertion assistant reloadable sheath platform and the physical attributes of the electrode array facilitate to proximate the modiolus and thus prevent the electrode from dislocation into the scalae media or vestibuli. These properties make this implant configuration easier to use with short incision and surgery time.

Soft surgery

Preserving the residual hearing requires minimally invasive techniques of (1) cochlear fenestration, (2) management of endocochlear fluid compartments, and (3) atraumatic electrode insertion, known as soft surgery. Thinner and atraumatic electrode arrays are also designed to accomplish these aims, as postoperative hearing performance can be maximized by minimizing the insertion trauma.

Several important factors contribute to intracochlear damage during implantation: (1) direct physical trauma, (2) pressure wave propagation in the perilymphatic fluid, (3) vibration and/ or heat trauma from drilling, (4) loss of perilymph, (5) changes in homeostasis/hydrodynamics of the endocochlear fluid compartments, (6) delayed fibrotic alteration and new bone formation within the cochlear lumen.

The physical attributes (length and diameter) of the electrode array may each limit the postoperatively achieved residual hearing.

We routinely applied minimally invasive surgical technique involved electrode insertion *via* the Round Window (RW). To reduce bleeding and to prevent blood from accessing the cochlea, we filled the tympanic cavity with adrenaline solution after having the posterior tympanotomy been completed. To prevent bone fragments from entering the cochlea, the tympanic and mastoid cavities were flushed with an abundant amount of saline. To remove the bony overhang of the round window, we used a 1 mm diamond burr at low speed (max. 350 rpm) to avoid noise and heat injury. We opened the RW membrane with a microscopic needle or hook. After opening the inner ear, suction was applied with care to avoid reducing the amount of perilymph. Furthermore, the scala tympani was left open for the shortest possible period, to prevent bone fragments, blood, or other substances from entering the inner ear, which might have been sources of primary and/or secondary injuries that finally would lead to loss of residual hearing. As a sort of prevention, after having opened the RW, we placed a piece of gel-foam soaked in corticosteroid solution into the RW niche.

The slim modiolar electrode of the CI532 implant was soaked into methylprednisolone solution (40 mg powder dissolved in 10 ml saline) and it was retracted into the insertion sheath. The insertion sheath together with the electrode array was inserted into the scala tympani with the lowest possible force. Any minute resistance felt by the surgeon would have indicated physical contact of the electrode array to the basilar membrane or the lateral wall of the scala tympani or stria vascularis and possible injury of these structures. After the electrode had been inserted in full length, indicated by the 1st marker ring, the RW was immediately sealed with an autologous tissue (e.g. fascia or muscle) to prevent loss of perilymph.

Audiometric testing

Unaided pure-tone air-conduction thresholds were evaluated at frequencies ranging from 125 to 8000Hz preoperatively and at 1-year, 2-years, and 3-years follow-up visits, by skilled audiologists using the Hughson-Westlake method. The audiometer (GSI 61 Clinical Audiometer; GrasonStadler, MN USA) was calibrated according to the standards of the International Organization for Standardization (ISO 389-1:2017). THD-50P (Telephonics Corporation/Griffon Company, NY USA) headphone was used for air conduction hearing measurements.

Electrophysiological testing

Impedance

The evaluation of CI functioning is facilitated by various analysis tools, one of the most important is the electric impedance measurement. While it is impossible to directly assess impedance, its values can be obtained by measuring voltage, as provided by Ohm's law. In CIs, this measurement is performed by using a protocol known as "voltage telemetry".

Electrical stapedius reflex threshold (ESRT)

ESRTs are measured using the pod and Nucleus Custom Sound programming software. Stapedius muscle contractions are observed through the operating microscope after adequate exposure has been achieved. The ESRT measurements are performed using the 22nd, 18th, 14th, 12th, 8th, and 4th electrodes of the Cochlear device. The charges on these electrodes are increased in 15% increments until a reflex is elicited. Thresholds are established by decreasing and increasing the charge levels in 3% increments around this level. The burst duration of the stimulus is set at 300 ms, with 1000-ms gaps between bursts.

Neural response telemetry (NRT)

The threshold levels in cochlear implant patients are well correlated to electrically evoked brainstem responses (E-BERA). The electrically evoked compound action potentials (ECAP) which are closely related to the E-BERA, would also show a similar correlation with the behavioral threshold. In modern cochlear implant systems, bidirectional information flow is available. This creates the right conditions for not only stimulating the cochlea but detecting different signals there. Using this telemetry system, we can perform impedance telemetry, compliance telemetry, and neural response telemetry (NRT). The NRT system measures compound action potential inside of the cochlea. The ECAP from the auditory nerve is characterised by a large negative peak (N1) with a very short latency (within a fraction of a millisecond), followed by a positive peak (P1). The peak-to-peak amplitude value (P1-N1) is usually measured.

The SP sets the appropriate electrode pair into action and stimulates the close spiral ganglion cells and generates action potentials in them. Then the summation action potential can be measured with another electrode pair. The signal returns to the SP and it can be averaged and analysed. With the adequate selection of electrodes, the condition of neurons nearby each electrode can be mapped. The parameters of registered potentials can help in specifying the right programming modes in device fitting.

Impedance was measured for each electrode, the ESRT with 25 μs pulse width for every second electrode contact (No. 2, 4, 6, etc.) and neural response telemetry threshold (T-NRT) for 6 (No. 2, 6, 10, 14, 18 and 22) electrode contacts. A common sound processor (Nucleus CP910) was used.

The first fitting was performed 4 weeks after surgery in each case. To determine the electric threshold (T-levels), and comfort threshold (C-levels), the subjective fitting method was used in adults and the semi-objective NRT based fitting (based on the intraoperative T-NRT results) was applied in children. Default MAP parameters (25 μs pulse width, 900 Hz stimulation rate, and 8 maxima) were used.

Statistical analysis

Statistical analysis with the Student's t-test ($P < 0.05$) and one-way repeated measures ANOVA test was performed with a 95% confidence interval ($p < 0.05$). Before the calculation, tests for normality of data distribution were performed. Bonferroni correction was used as needed to consider multiple variables (e.g. comparison of all three implant groups). The comparison was made on each electrode and all of the electrodes (Grand average). The tests were performed with Microsoft Excel 2016 and SPSS for Windows.

RESULTS

Hearing preservation

Pre- and postoperative pure tone hearing threshold measurements were completed for all the 30 recruited subjects.

The average preoperative thresholds of the hearing within the lower frequency range were 61.75 dB(HL) at 125 Hz (no response from 10 patients); 78.52 dB(HL) at 250 Hz (no response from 3 patients). At the middle frequency range, mean values were 88.67 dB(HL) at 500 Hz (response from all patients); 97.07 dB(HL) at 1 kHz (no response from 1 patient) and 100.50 dB(HL) at 2 kHz (no response from 10 patients). At the higher frequencies, the average values were 91.36 dB(HL) at 4 kHz (no response from 19 patients) and 84.00 dB(HL) at 8 kHz (no response from 25 patients).

One year postoperatively the average values of the hearing thresholds at the lower frequency range were: 93.89 dB(HL) at 125 Hz (no response from 17 patients); 87.86 dB(HL) at 250 Hz (no response from 10 patients). At the middle frequencies mean values were 102.86 dB(HL) at 500 Hz (no response from 10 patients); 111.61 dB(HL) at 1 kHz (no response from 14 patients) and 113.75 dB(HL) at 2 kHz (no response from 21 patients). At the higher frequencies, average values were 115.18 dB(HL) at 4 kHz (no response from 24 patients) and 99.29 dB(HL) at 8 kHz (no response from 29 patients).

Nine implantees (9/30=30%) showed up with the total loss of residual hearing at every measured frequency following surgery. The measured average hearing threshold – of this subgroup – has been already poorer before surgery compared to those with preserved hearing. Genetic screening of the 30 recruited subjects revealed mutations in three cases in the background of hearing loss. All of these subjects suffered complete hearing loss postoperatively (3/3=100%), that genetic alteration may serve as a predictor when opting for an electro-acoustic/hybrid device, should be taken into consideration when indicating these systems.

Initial sound processor programming and activation were performed approximately one month after surgery.

Preoperative and 1-year, 2-year, and 3-year postoperative pure tone hearing threshold measurements were completed for all patients (Figure 1).

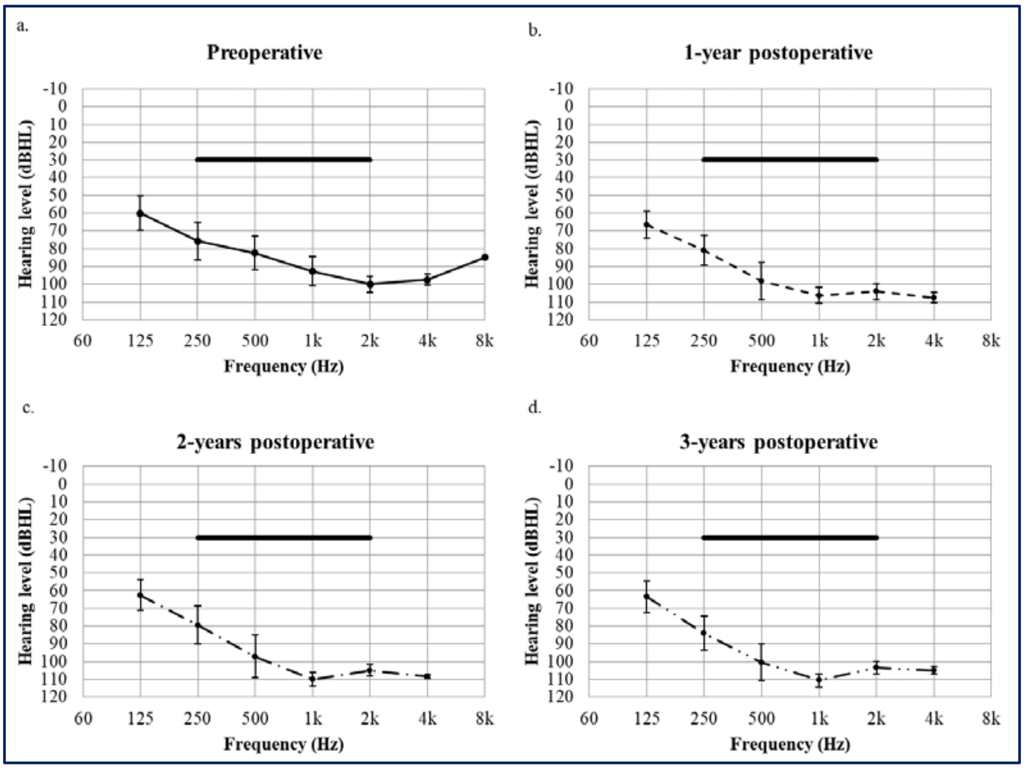

Figure 1. ***a.*** *Preoperative,* ***b.*** *1-year postoperative,* ***c.*** *2-year postoperative and* ***d.*** *3-year postoperative pure tone hearing thresholds in dB(HL) at the measured frequencies.*

Average preoperative pure tone hearing thresholds for the 13 ears were 60–74.6–81.5–92.1–99.5–97.5–85.0 dB(HL) at the seven measured audiometric frequencies between 125 and 8000 Hz respectively.

The overall average change of 9.73 dB(HL) was recorded during pre and first-year postoperative audiological examinations. The greatest change was observed in the mid-frequency range with 16.64 dB(HL) at 500 Hz whilst 14.17 dB(HL) was recorded at 1 kHz. In the low (e.g. 125Hz – 250Hz) frequency range an average decrease of 6.5 dB(HL), while in the high (e.g. 2kHz – 4kHz) frequency range an average progression of 7.3 dB(HL) occurred. At the highest recorded frequency measured in this study (8 kHz) we only recorded in a single patient 85dB(HL) which was not observed at the measurement range in postoperative examinations. The second and third year postoperative data (9.5 and 10.2 dB(HL) respectively) showed was not statistically significant difference from the first-year data.

Complications

Ninety-four (94) CI recipients with pre- and postoperative CT scans and detailed operative reports were available for review for the period from November 2015 to July 2018. Out of these 94 cases, the active electrode was inserted into the cochlea via the extended round window approach in 91 ears. Three electrodes were inserted via cochleostomy because the round window could not be identified. Fifty-seven percent of the cases – 54 out of 94 – were right-sided CI. Tip fold-over was noted in three cases (3.19%) on radiography.

Subject#1

A 60-year-old female subject with severe bilateral SNHL was referred for cochlear implantation of the right ear. The preoperative high-resolution CT scan and MRI revealed normal anatomy and no evidence of cochlear ossification or fibrosis. She had no history of meningitis. The round window niche was widened by drilling the bony rim over the round window to ensure good exposure of the membrane. There was no physical evidence during surgery to suggest the potential for intra-cochlear malposition of the electrode array and the intraoperative tests (impedance, ESRT, and NRT examinations) did not show any abnormality. On the day after the implantation, a postoperative X-ray scan was performed. With the help of the X-ray image, a tip fold-over of the 18th electrode was detected. Unlike our standard protocol, the sound processor was programmed for the patient that day. The four apical electrodes that curved back was switched off so that the patient reported hearing sensations and the frequency discrimination was appropriate. The processor was programmed four weeks after the surgery again. At that time, the subject only reported whistling and beeping, but was unable to discriminate various frequencies. During the next two months, we were unable to produce a hearing experience for the patient. Hence, we decided to reimplant the patient with a contour advanced (CI512) electrode from the same implant family.

Subject#2

A 21-month-old girl with severe hair cell impairment - detected by distortion product brainstem evoked response audiometry (BERA), Auditory Steady State Response (ASSR), and otoacoustic emissions (DPOAEs), - was referred for bilateral cochlear implantation in June 2017. Genetic testing revealed mutation of the connexin 26 gene. Preoperative radiography and MRI scans revealed normal anatomy of the middle and inner ear. She had no history of bacterial meningitis. The round window was not detected on the right side; thus, cochleostomy insertion was performed. Unexpected oozing of the perilymph was noted. Accordingly, lower impedance and higher NRT values were measured during the intraoperative evaluations. The ESRT, except for electrode 5, could not be triggered. On the following day, postoperative X-ray imaging revealed a tip fold-over at the 18th electrode. Our team decided to perform revision surgery.

Subject#3

A four-year-old male patient with severe bilateral SNHL was referred for sequential bilateral implantation. The first CI on the right side was performed without complication in September 2017; the surgery of the left side was performed in January 2018. Preoperative high-resolution CT and MRI scans showed regular anatomy of the middle and inner ear. He had no history of meningitis. The smooth contralateral insertion suggested the potential for successful surgical insertion. The electrode array was gently inserted via the provided sheath through the round window using a soft-surgery technique. The surgeon reported some unusual resistance during the electrode insertion. The intraoperative tests did not show any abnormalities. The following day, a tip fold-over was detected with X-ray imaging.

Solutions

In the case of Subject #1, our team decided to implant a new device (CI512) with a more rigid and thicker electrode because tip fold-over of the slim perimodiolar electrode may have indicated an obstruction in the membranous labyrinth - which the preoperative CT scan did not reveal. The speech processor was reprogrammed four weeks after the reimplantation. Instead of the whistling and unpleasant sounds, the patient reported a good sound experience. As of this report, she successfully differentiates the sound spectrum and hears sounds in a corresponding tone.

In the second and third cases, early reimplantation was performed on the second postoperative day. The electrode array was gently removed from the cochlea and reinserted into a backup sheath as used in our centre in these cases. Apart from its thin nature and proximity to the modiolus, another advantage of the slim perimodiolar electrode is that it can be reloaded into its external insertion sheath if necessary. Reinsertion was made in both pediatric cases. The intraoperative test results were normal. The following day's postoperative X-ray images showed the correct electrode location. In both cases, we fitted the speech processor four weeks after the surgery. The pediatric patients also demonstrated a good onset of speech perception with babbling and repetition of monosyllables. Speech development in Patient #2 successfully started consciously using disyllabic words one year later. Currently, her passive vocabulary is estimated at approximately 2-300 words. Patient #3 is a perilingual child. Her vocalization has started and, for the time being, she has been producing lallation/unarticulated sounds. She uses her speech processor three hours a day on average. She had not used a hearing aid before, which could cause her dislike towards the speech processor.

DISCUSSION

Preservation of acoustic hearing associated with cochlear implantation improves the postoperatively achievable periodicity and spectral resolution, which improves the patient's speech comprehension and the localization of the tone in, particularly difficult conditions.

The effects of cochlear implantation on residual hearing have been discussed in several studies in which many surgical and technical factors have been identified. There are some surgical techniques of approaching the scala tympani (*i.e.,* RW, ERW, CS) with varying risks of harming the fine structures of the cochlea with prompt or delayed onset. Such late complications, like the appearance of endocochlear connective tissue or new bone formation, may lead to a gradual partial or complete loss of residual acoustic hearing. This is most likely to be seen when the round window is extendedly exposed, where endothelial lesions trigger new tissue proliferation. The slightest is the tendency to harm the endocochlear structures when minimally invasive, soft surgery is applied.

Physical attributes of the electrode profile may also interfere with postoperative cochlear function. Theoretically, the endocochlear hydrodynamics may also be altered, as the vibration of the basilar membrane is restricted due to the presence of an electrode array. At this point, as the travelling waves to the apical region are modified, the basilar membrane would react to sounds differently, leading to an endocochlear "conductive" hearing loss.

The new type of thin-diameter electrode arrays close to the modiolus is expected to have a lower hydrodynamic load since the bony spiral lamina is attached from below, thus the basilar membrane vibrations remain unrestricted. However, the perimodiolar position of the electrode array allows the adjacent nerve elements of the spiral ganglion to be stimulated with a lower electrical intensity and through a smaller surface.

Cadaver experiments demonstrated that a force, applied to the basilar membrane with an average of 88 mN (42 mN to 122 mN) would be sufficient to accomplish the interscalar dislocation of the electrode, of which manual perceptibility is questionable. Studies with large case numbers (n=100) have shown that the probability of the electrode line being located in the scala vestibuli significantly increased during CS, which also manifested itself in the absence of improvement in speech comprehension.

In many studies, intraoperatively performed electro-cochleography is used to track the electrode insertional trauma, furthermore to postoperative residual hearing follow-ups.

For the implementation of Electro-Acoustic (EAS) or hybrid speech processors, the long-term preservation of residual acoustic hearing is inherently inevitable, thus the application of atraumatic surgical techniques and electrode arrays is essential.

Our study cohort demonstrates that the application of appropriate soft surgery techniques and atraumatic electrodes can retain residual hearing in a long run. The positive experience gained with the new type of CI532 Slim Modiolar electrode predicts the possibility for the preservation of structural and functional integrity of all cochlear regions. Furthermore, a prompt, definitive solution could be provided for a possible late hearing loss progression, where only a psychophysical reprogramming of the implant would be enough.

Based on our results, if the acoustic hearing loss can be preserved with the assurance and efficacy of the initial experience, we will be able to provide sustained prominent hearing rehabilitation even in the indication of EAS that results in significant improvement in the life quality of many implantees.

Besides, long-term residual hearing loss may be of crucial importance in the subsequent feasibility of regenerative procedures and medical treatments.

Intracochlear trauma due to electrode insertion may be as follows: (1) the trauma to the lateral wall tissues, (2) the translocation from scala tympani to scala vestibuli, (3) the basal fracture of the osseous spiral lamina, etc. As for the lateral wall electrodes, many studies have been conducted with the stylet-based perimodiolar electrodes (e.g. Contour and Contour Advance (Cochlear Ltd., Sydney, Australia.)) to reveal their impact on cochlear microstructure and residual hearing. Lateral wall electrodes evidently contact lateral wall structures of the scala tympani, resulting in various degree of trauma to them. On the other hand, the impact of stylet-based perimodiolar electrodes varies, depending on the surgical technique applied (standard insertion technique vs advanced off stylet; SIT vs AOS). Perimodiolar electrodes implanted with SIT resulted in similar trauma profile to that with lateral wall electrodes; while with the AOS technique the lateral wall forces were minimized or negated such that they remain below the threshold for trauma or rupture of the intrascalar partition.

Up to date, only a few studies have been published with the sheath-based, slim-perimodiolar electrode and on its impact on cochlear microstructure and hearing preservation, that is the object of this present study.

Our results have proved the Nucleus CI532 Slim Perimodiolar® electrode array to be safe and effective in preserving residual hearing over three-years long follow-up period. This long-term preservation of residual hearing refers to that the endocochlear trauma during electrode insertion is negligible or even absent.

There is always some risk of losing residual hearing due to cochlear implantation. In this study, all of the subjects retained residual hearing within 9.73 dB(HL) on average at the measured 125-4000 Hz frequency range. These results are similar to a previous single-centre study outcome with the Hybrid L24 where the median threshold increase was 10 dB(HL).

Electrical stimulation can be optimized by proper intrascalar positioning of the slim-perimodiolar electrode array in proximity to the neuronal structures of the cochlea. Due to this reduced distance, the CI can deliver stimulation at a lower electrical intensity and through a smaller electrode surface, which has been proved to provide greater neural specificity, reduced stimulation levels, and improved hearing performance.

There were no surgery-related complications, the slim perimodiolar electrode was suitable for round window approach in all case, that would improve the compliance of many surgeons.

A wide range of cochlear implants with different electrodes is available for rehabilitation of hearing impaired patients with severe to profound SNHL. Hearing rehabilitation outcomes may be influenced by optimizing device and electrode choice for the individual. Several comparative studies have been conducted including electrophysiological (ESRT, NRT) test methods to evaluate the influence of straight and perimodiolar electrode designs and their in-situ characteristics on clinical outcomes. Our study is unique in that it measured the influence of various electrode designs combined with a common receiver stimulator upon electrophysiological assessments for a relatively large routinely treated multicentre study cohort. As such, it is the first study to report on the influence of electrode design while using consistent implant receiver-stimulator electronics. The cooperation of the two clinics was established in 2017 with the aim to compare the perimodiolar and the straight electrode arrays. The study clinics followed a standard protocol enabled by the manufacturer's software, thus a conclusion from their individual results can be made. The results of Hey et al. from their multicentre study on CI532 are in good correlation with our results which proves that our methodology and results are reliable.

The Contour Electrode was the first perimodiolar electrode from Cochlear. As reported by researchers, some intracochlear trauma has been associated with its insertion, with a more reliable and less traumatic insertion achieved when deployed using the recommended advance off-Stylet technique. This is largely due to an inherent reduction in intracochlear outer wall force generation when using this technique for this electrode.

The Slim Modiolar Electrode is designed for insertion with minimal cochlear trauma. It has the advantage of taking 60% less volume in the scala tympani compared to the Contour Advance Electrode and is therefore placed in a position close to the modiolus. Perimodiolar proximity is an important clinical consideration as Holden et al. concluded, observing that total insertion depth was not associated with better speech discrimination outcomes, however, the distance from the electrodes to the modiolus did indicate a significant influence. The Slim Modiolar electrode array takes a closer position to the modiolus than the Contour Advance electrode array as confirmed by a comparative radiological evaluation.

In this retrospective study the data from recipients with the three main types of electrode arrays used in each of the two author implant centres were included. Although the electrode of CI522 was known to take the lateral wall position within the cochlea, the authors' decided to enroll those subjects who were implanted with CI522 to gain a more detailed overview. Although results of two different implant centres were combined for evaluation, upon review, the authors considered the routine clinical practices employed and device parameters used at each site as sufficiently comparable.

Results from the objective intraoperative measurements indicated that the electrode contacts of the CI532 array were located closer to the modiolus than those of CI512. A previous study found that withdrawal of the stylet in the Contour Advance Electrode resulted in better NRT and ESRT responses, than with the stylet in place. They concluded that this is most probably due to a more favourable position of the electrode array towards the modiolus within the scala tympani once the stylet is removed.

In our study, although the mean ESRT was only slightly lower with CI532, the difference was statistically significant at the basal most electrodes tested. However, the mean T-NRT for CI532 was significantly lower than for CI512, especially in the apical-middle section, which is considered to be indicative of closer positioning towards the modiolus. An expected rate of scalar dislocations could be 26% with precurved electrode (i.e. CI512) and 3% with straight electrode (i.e. CI522) with round window insertion technique and this dislocation should have a significant impact on the NRT threshold in the apical part of the electrode. In order to minimize scalar dislocation, the extended round window insertion technique was used. Although the institutional protocols did not include postoperative computed tomography, the results from T-NRT and ESRT, both being constantly higher for CI512 when compared with CI532 and T-NRT being constantly lower for CI512 when compared with CI522 are not indicative of significant dislocations between scalae tympani and vestibuli. The sizeable reduction in both T-NRT and ESRT observed in our study are considered sufficiently large to potentially influence differences in clinical outcomes as observed for subjective comfort level.

The surface area of an electrode is inversely proportional with the resistance, thus current is proportional with the surface area. If the electrode with a smaller surface is capable of eliciting the same response it means that it is closer to the stimulated structure. The lower objective electrophysiological thresholds of CI532 suggest that the electrodes are capable of eliciting reflex responses with lower stimulation intensity, resulting from closer proximity to the modiolus.

In our experience, the CI532 with its Slim Modiolar electrode profile provides a relatively easy and low trauma insertion procedure. However, implantation of this delicate electrode array was associated with tip fold-over at a rate of 3.19% that is comparable with the reported rates found in the literature, but immediate intraoperative identification based on tactile feedback of the operating surgeon and standard intraoperative telemetry failed. Radiography definitively detected tip fold-over. Based on our experience and measurement results, we are unable to determine the exact location of electrode array along its full length. International literature provides reference to the use of Spread of Excitation measurements to detect tip-fold-over. However, our department has not had the availability to perform such measurements yet.

Based on our clinical protocol, X-ray imaging is performed the day after surgery. If the radiologist detects a suspected abnormality in the electrode position, fluoroscopy, cone-beam CT or low dose CT scans can be performed. Our recommendation is revision surgery, reloading the electrode array, if intact into a backup insertion sheath, and reinsertion of the array. In an ideal situation, abnormalities of the electrode position would be detected in real time or shortly after insertion in order to spare a second procedure. Reliable electrophysiological methods or real-time imaging in the operating room (cone-beam CT, fluoroscopy, or X-ray imaging) are encouraged. It is important to put special emphasis on preoperative imaging and 3D reconstruction. The more frequent use of fine and pre-curved electrodes necessitates rigorous routine postoperative radiological control of electrode array position.

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