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Invited Review

Development and Clinical Introduction of the Nurotron Cochlear Implant Electrode Array

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As the only medical device used in the treatment for deafness, the cochlear implant has benefited to more than half a million individuals worldwide. However, the device has limited penetration due to its high cost, especially in low- and middle-income countries. China alone has 27.8 million deaf people, but less than 100,000 of them have received a cochlear implant. The Nurotron Venus device was developed to address the need for an affordable yet safe and effective cochlear implant. The present study describes the design, development, and evaluation of the Nurotron intracochlear electrode array. The standard array is 22 mm in length from the round window marker to the apical tip of the carrier and has 24 electrodes, with a surface area of 0.32 mm^2 and center-to-center spacing of 0.85 mm. The Nurotron array has been tested to meet the mechanical, chemical, and electrical requirements specified by the ISO Standard 14708-07. Human temporal bone and clinical trial results showed that the Nurotron array is easy to insert (7.8/10 rating with 10 indicating the highest ease of use) and has a low complication rate (12.5%) of severe insertion trauma while achieving high device stability and reliability (6 array failures in 43,000 patient years of experience). As a critical component, the Nurotron array has contributed to the high level of Nurotron implant speech performance, equivalent to that produced by other existing devices. The Nurotron device has benefited 10,000 deaf people and helped reduce the unit cost from US$25,000 in 2011 to US$4,620 in 2017 through the Chinese Government Tender Program. New, slim, and micromachined electrodes are being developed to further improve performance and accessibility.

KEYWORDS: Auditory prosthesis, cochlear implants, deafness, electric stimulation, electrodes

INTRODUCTION

Hearing loss is a significant health and economic burden that affects the quality of life for about half a billion people worldwide, particularly in low- and middle-income countries where more than 80% of people with hearing loss live [1]. Cochlear implants (CIs) are the only medical intervention that can safely and effectively treat disabling sensorineural hearing loss, but their high cost has limited its market penetration, which is about 20% in developed countries and less than 1% in developing countries [2]. Based on and building upon decades of effort by scientists, engineers, and clinicians [3-5] , the Nurotron Venus® 26-electrode cochlear implant, or the Nurotron device hereinafter (Figure 1), became the first commercially available affordable device that provided high performance equivalent to that of existing devices [6-8]. Since receiving the China FDA approval in 2011 and the European CE marking in 2012, the Nurotron device,has benefited 10,000 individuals, with 95% of them being in China and the rest in other countries in Asia, Africa, South America, and Europe. The Nurotron device has made significant impact on both accessibility and awareness of the overall CI market. For example, the unit cost for the Chinese Government Tender Program has dropped from US$25,000 in 2011 to US$4,620 in 2017, allowing 35,000 deaf children aged 1-6 years to receive the CI to date. Had the unit price stayed at the same US$25,000, which has not significantly changed in the rest of the worldwide market, the number of deaf children benefiting from the CI would have been half of what it is, if not more, in China. The second impact is the benefit to older deaf individuals, who would otherwise not consider cochlear implantation due to financial constraints. Compared with 15% of the Cochlear Corporation's CI recipients being older than 7 years of age [9], 55% of the Nurotron device recipients are in the older age category.

A primary goal of developing the Nurotron device was to design and manufacture an affordable, yet safe and state-of-the-art CI system, responding to the economic and medical environments in low- and middle-income countries. A pragmatic approach has been taken to adopt proven features of electrode design, safe stimulus delivery, advanced speech processing, and effective sys-

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tem integration. As a result, the design of the Nurotron device not only emphasizes ease of surgical implantation, ease of mapping, and ease of use for both clinicians and patients, but is also geared toward developing a manufacturing capability for cost-effective production.

Thanks to 30 years of biomedical engineering expertise, materials science development, neurophysiological research, and clinical experience, a substantial foundation has been laid for the design and development of a new CI system. The specific goals of developing the current Nurotron 24-channel CI electrode include 1) ease of consistent surgical insertion, 2) long-term reliability of the electrode assembly including the wire lead, connection to the implanted stimulator, connection of the lead bundle to the stimulating contact, the contact foils, and the integrated elastomer carrier, 3) minimization of cochlear damage that often results from the insertion of a CI electrode, and 4) optimization of electrode length and contact density.

Ease of Insertion – Straight or slightly curved electrodes are inherently easier to insert into the cochlea than a tightly curved array, particularly without sophisticated insertion tools often used with spiral perimodiolar arrays. These tools add significant cost for each patient if a disposable design is employed or add the risk of complex cleaning and sterilization protocols if tools are designed for multiple uses. This increased ease of use is particularly important in areas that are relatively new to large-scale availability of CIs and face challenges such as the need to train increasing numbers of surgeons and staff to perform this technically advanced procedure.

Electrode Reliability – From a functional standpoint, the failure of one or more individual electrode sites is less critical than that of other implanted components such as the stimulator antenna assembly, hermetic stimulator enclosure, or major stimulator electronic components. The failure of any of these components results in complete device failure and the need for surgical revision. In contrast, the failure of a small number of electrode sites is manageable in most cases with speech processor re-mapping and results in minimal loss of overall performance. With that caveat, it is still the goal of each manufacturer to produce devices with 100% operational capacity throughout the lifetime of the system. To achieve a high level of reliability in the electrode, all materials and manufacturing processes must be carefully designed and diligently controlled.

Figure 1. The Nurotron Venus® internal receiver and stimulator (Hangzhou, China). The electrode shown is the standard Nurotron array, 22 mm in length with 24 active stimulus contacts. One reference is a ring electrode located near the titanium case and the other reference is a plate electrode located on the surface of the case.

Electrode lead wires and their insulation layer are a critical design component. Several careful assembly and quality control manufacturing steps need to be developed to ensure reliable connection of each contact lead to the stimulator, the spiral winding or other strain relief for the electrode cable, connection of the lead to the stimulating contact, and finally mechanical securing of the contact foil in the elastomer carrier.

Materials – The materials needed to produce a reliable CI electrode include corrosion-resistant lead wire and stimulating contacts, durable insulation to isolate these interconnecting subassemblies, and a biocompatible elastomer to form the electrode carrier and protect the integrated components of the system.

An elastomer carrier holds the lead wires and stimulating contacts. This carrier serves four essential functions. First, the carrier protects the wire leads from damage during surgery and in situ as the very thin Teflon™ insulation on these lead wires is vulnerable both during surgery and throughout the device lifetime. During these years, the electrode lead bundle is in contact with the bone surrounding the mastoid cavity and middle ear space and at the points where the lead is subject to bending stress as it connects to the implanted stimulator or makes the transition from the surface of the skull to the mastoid area. Second, the carrier acts as an insulator, filling a part of the scala tympani (ST). This occupied volume restricts the direct flow of the current between the electrode contacts in the cochlea in bipolar stimulation modes and also shapes the current flow, and thus the region of neural activation, in monopolar stimulus paradigms. Some differences in the spread of excitation with electrical stimulation observed by van den Honert and Stypulkowski [10] and Rebscher [11] can be attributed, at least in part, to the presence or absence of conductive fluid in ST and the presence of a semi-space-filling electrode carrier versus bare electrode contacts. Third, the specific region of activation within the spiral ganglion is determined by the shape of the carrier and the position of the contacts on the surface of the carrier. The effect of contact position, and its interaction with stimulus mode, has been well documented in animal studies and computer modeling [11-14]. Lastly, the physical properties of the electrode array are critical for avoiding trauma during cochlear implantation. The choice of elastomer, pattern of the lead wires in the array, and size and shape of the stimulating contacts on the surface of the array determine the overall stiffness and flex characteristics of the complete electrode.

Current CIs use platinum-based wire as a lead material for the electrode. In most cases, the platinum-iridium alloy Pt90Ir10 or Pt80Ir20 is used because it offers higher strength than pure platinum, yet it is completely compatible with the use of pure platinum stimulating contacts and stimulator feedthrough pins. When wound into an elongated coil, this platinum alloy is resistant to damage from sharp bending and long-term repetitive stresses that may be generated by the movement of the temporalis muscle or other tissues between the stimulator and the entry of the array to the cochlea.

The earliest CI electrodes consisted of small platinum balls melted on the ends of each electrode lead. These simple contacts were relatively small compared with the circumference of the electrode carrier and restricted the overall design of the array by occupying a large portion of the internal volume of the carrier. In this way, the contact balls dictated the location of the wire leads as they traveled along the electrode [15]. This size limitation also limited the amount of stimulus charge that could be safely passed by each contact. The use of thin platinum or PtIr foil contacts, welded or pressed on to the ends of the lead wires, has addressed these fundamental issues and created the opportunity for a wide range of electrode shape, mechanical flexibility, and greater control of charge density. Critical manufacturing considerations in working with these wire leads and contact assemblies include reliable weld or press connections at the stimulator end of the lead and at the contact, strain relief of these connection points, avoidance of damaging stress, bending and abrasion during assembly, and secure holding of the contact foils in the elastomer carrier even when the electrode is subject to repeated bending.

Reduced Intracochlear Damage – Studies to evaluate the frequency of trauma associated with the insertion of CI electrodes indicate that many CI recipients experience significant cochlear damage during this procedure [16, 17]. More recently, studies using high-resolution clinical imaging have demonstrated that this damage has a significant effect on subject performance [18-21]. Thus, a primary goal in the design and clinical application of the Nurotron electrode is to reduce, or eliminate, intracochlear trauma. Several factors contribute to the occurrence and severity of intracochlear trauma: 1) surgical technique-specifically the location of entry into ST, 2) the size and length of the CI electrode, and 3) the mechanical characteristics of the electrode array. The surgical techniques are beyond the scope of the present study, but the use of the round window (RW) approach, modified RW approach allowing reasonable visualization of ST, or cochleostomy that is clearly anterior and inferior to the RW is essential in reducing the rate of trauma resulting from electrode insertion.

The size of a CI electrode is the second critical design parameter affecting the incidence of trauma [22-24]. The cross-sectional dimensions of CI electrodes have gradually decreased over the past decade, and it was a design requirement that the dimensions of the Nurotron array fit within all ST profiles in the UCSF database when the electrode is fully inserted.

The final critical design requirement for an electrode with reduced rate of trauma is defined by the physical properties of the array, specifically how the electrode flexes during insertion into ST [25, 26]. During the past two decades at UCSF, and collaborative centers around the world, we have studied 15 different CI electrode designs provided by four manufacturers in more than 250 temporal bones. To make these studies most relevant to actual clinical experience, we solicited the participation of 23 different surgeons, mostly without extensive CI research experience and mostly with resident-level training in otology. It is our belief that these surgeons best represent the majority of surgeons worldwide, particularly in geographic areas with very rapidly growing application of CI technology. These temporal bone studies, and more recent clinical imaging studies, have demonstrated that electrode arrays that are stiffer in the vertical plane are far less likely to bend upward and pass in to the scala vestibuli (SV) than electrodes without this specific feature [24, 27-30]. This asymmetric stiffness is a key feature of the Nurotron electrode.

Electrode Length and Number of Contacts – In most CI candidates, the hair cells in the organ of Corti (OC) are damaged, leading to the degeneration of dendrites from the spiral ganglion cells. This degeneration implies that the normal 35-mm cochlear tonotopic map [31], representing the functional length of the normal OC, does not apply to most patients receiving a CI. Instead, a more appropriate mapping for CI subjects is the 14-mm ganglion cell map developed by Stakhovskaya et al. [32]. To accommodate the possible survival of apical neurons or patient-specific insertion issues related to an ossified cochlea, etc., the Nurotron device has designed electrodes with length ranging from 17.5 to 25.5 mm covering most of the length of the spiral ganglion encountered in the CI patient population. Within these arrays, we placed as many contacts as possible to improve spectral resolution, which is the single most significant factor limiting CI performance [33]. The 17.5-mm Slim short array, with 22 contacts and 0.7-mm spacing, is the most densely populated electrode currently in clinical trial and potentially provides even greater spectral resolution using bipolar, tripolar, or virtual channel stimulation supported by the Nurotron system.

Nurotron Electrodes

The Nurotron 24 channel intracochlear electrode array has the following features: 1) Size – an ideal array must fit within ST of all anatomically normal cochleae when inserted to its intended depth, 2) stiffness – an electrode that is stiffer in the vertical plane is less likely to deviate upward into the scala vestibule, and 3) insertion depth and distribution of stimulating contacts – for optimum performance, stimulus channels must be inserted to a depth that corresponds to the cochleotopic locations critical for speech discrimination.

Standard electrodes – Figure 2 shows the Nurotron standard electrode array, which is 22.0 mm in length from the RW marker to the apical tip of the carrier and has 24 foil contacts with a center-to-center contact spacing of 0.85 mm. The array is slightly curved toward the modiolus with the contacts located on the inner surface.

Figure 3 illustrates the cross-sectional outlines of the Nurotron electrode modeled within a series of profiles of the human ST. The dimensions of the standard array clearly fit within the volume

Figure 2. The standard Nurotron electrode array. The electrode holds 24 Pt90Ir10 foil contacts in an elastomer carrier. The round window marker is shown as the ring on the left. The mean insertion depth for the array was 426° (n=60, initial Nurotron clinical trial data).

of the ST, achieving the design goal for this electrode. Additionally, the silicone elastomer selected for the Nurotron array is stiff enough to avoid buckling during insertion and allows the tapered tip of the array to be easily directed into the RW or cochleostomy, yet flexible enough to conform to the inner surface of ST without damage. The lead wires in the electrode are assembled into a vertically oriented rib to increase stiffness in the vertical plane and reduce the incidence of trauma. The 22.0-mm length and densely located 24 stimulus sites allow the delivery of a spectrally detailed signal into the second turn of the cochlea, where lower frequency speech components can best be interpreted by the central auditory system.

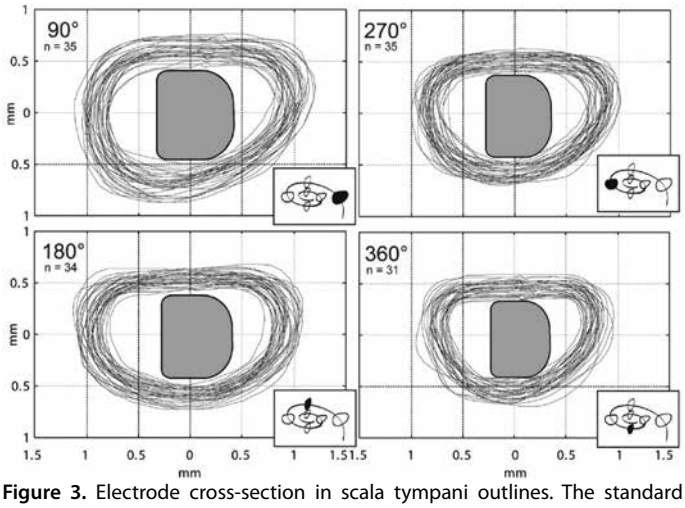

Figure 3. Electrode cross-section in scala tympani outlines. The standard Nurotron electrode array was designed to fit within the range of dimensions observed in the normal human cochlea. The cross-sectional profiles of the Nurotron array are modeled above in the scala tympani outlines (n=35) assembled at the UCSF [24].

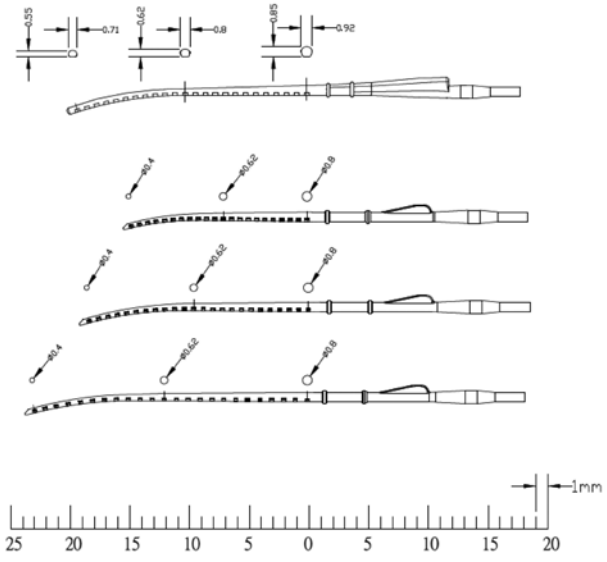

Figure 4. Drawings of four Nurotron electrode arrays. The overall shape and cross-sectional dimensions of each electrode array are shown above. The standard Nurotron array is shown at the top of this illustration with the short, medium, and long versions of the Slim arrays shown below. The apical section of the Slim arrays is 30% smaller than that of the standard array.

The individual stimulus contacts in the Nurotron electrode are fabricated from Pt90Ir10 and welded to the terminus of each electrode lead. The geometric surface area of each contact is 0.32 mm^2. An adhesive silicone coating is applied to the rear surface of each contact before the electrode is assembled to prevent separation of the contact foil on repeated flexing of the array.

Slim Series Electrodes – Figure 4 and Table 1 detail the dimensional differences incorporated in the Slim series Nurotron electrodes currently undergoing clinical trial. This set of arrays will offer three lengths to suit the preference of surgeons and anatomic constraints of individual subjects. The medium and long Slim arrays will share the same number of stimulus sites (24) distributed along a carrier of 22.0 mm and 25.5 mm in length. The short Slim array will hold 22 stimulating contacts. All Slim arrays incorporate increased vertical stiffness found in the current standard array. To accommodate the varied length of these electrode carriers, the contact spacing has been adjusted. The center-to-center spacing is 0.7 mm in the 17.5-mm short Slim array, 0.85 mm in the 22.0-mm medium Slim array, and 1.0 mm in the 25.5-mm long Slim array.

To accommodate the smaller profile of the Slim series arrays, the foil contact dimensions are reduced to 0.28 mm^2 in the basal region of the inserts, 0.22 mm^2 in the center of the arrays, and 0.16 mm^2 in the apical portion of the electrodes. Based on measured charge per phase data from the current standard Nurotron electrode, these contact sizes will allow stimulus pulses well within the safe limits across the length of the arrays.

Electrode Testing and Validation

The Nurotron electrode has been thoroughly tested to meet all requirements under the ISO International Standard 14708-07 (Implants for surgery-Active implantable medical devices-Part 7: Particular requirements for cochlear implant systems. First edition, 2013). To ensure both high reliability and long-term patient safety, the Nurotron system has been evaluated mechanically, electrically, and in human temporal bones. All components of this system have met or exceeded the international standards for CIs.

Table 1. Summary of the Nurotron Electrode Dimensions

Electrode Type	Electrode length-Stimulator to RW marker (mm)	Electrode length-RW marker to tip (mm)	Distance between contacts (mm)	Number of Contacts+Grounds	Exposed area (mm^2)
Standard	80.0	22.0	0.85	24+2	0.32
Slim-short	80.0	17.5	0.70	22+2	0.16-0.22-0.28 (Apical-Middle-Basal)
Slim-medium	80.0	22.0	0.85	24+2	0.16-0.22-0.28 (Apical-Middle-Basal)
Slim-long	80.0	25.5	1.0	24+2	0.16-0.22-0.28 (Apical-Middle-Basal)

RM: round window; Distance between contacts: the center-to-center spacing

Mechanical testing for the electrode includes 1) an elongation test to ensure that the array is able to withstand tensile forces, which may be encountered during or after implantation, 2) a flexural stress test to measure the ability to withstand bending stresses, 3) a fatigue test to assess the resistance to repeated micro-movements after implantation, 4) an insulation test to evaluate the function and stability of the electrode and lead wire insulation following repeated elongation, and 5) an insertion test to validate the mechanical stability of the silicone carrier, wire electrode leads, lead wire to stimulating contact connection, and adhesion of the contact foil to the silicone carrier during repeated insertion cycles.

Elongation Test – The electrode array was held in a clamp fixture at the RW marker, while the lead between the electrode and the stimulator was elongated to a minimum of 15 mm for 60 seconds. Following this step, a load of 100 g was applied to the electrode lead for 60 seconds, creating a stretch of approximately 25%. Lastly, the cable was stretched to 110% of its resting length and fixed in that position, while the stimulator was rotated 360° in each direction. This process was repeated 10 times. Prior to each of these stress tests, the array was preconditioned by soaking in a 0.9% saline bath at 37±2°C for 10 days. After the mechanical test, all samples were returned to the saline bath for 1 hour before impedance testing. Following the second saline immersion, all sample impedances were within the normal range.

Flexural Test – The electrode was held in a soft-surfaced clamp 10 mm behind the RW marker, and the stimulator was dropped from the level of this clamp (repeated 5 times). Impedance and shorting tests confirmed electrode performance in saline following this test.

Fatigue Test – To evaluate the resistance to repeated bending, the stimulator was held in a fixture attached to a rotational oscillator. The electrode lead exiting the stimulator was tensioned with a load of 3 g and 10 mm from the most proximal electrode. Two guides, each 2 mm in diameter, constrained the electrode leads, while the stimulator was rotated to an angle of 15° on each side at a rate of 2 Hz for 100,000 repetitions. Physical inspection of the electrode cable and impedance measurements indicated no failures in the lead cable following this test protocol.

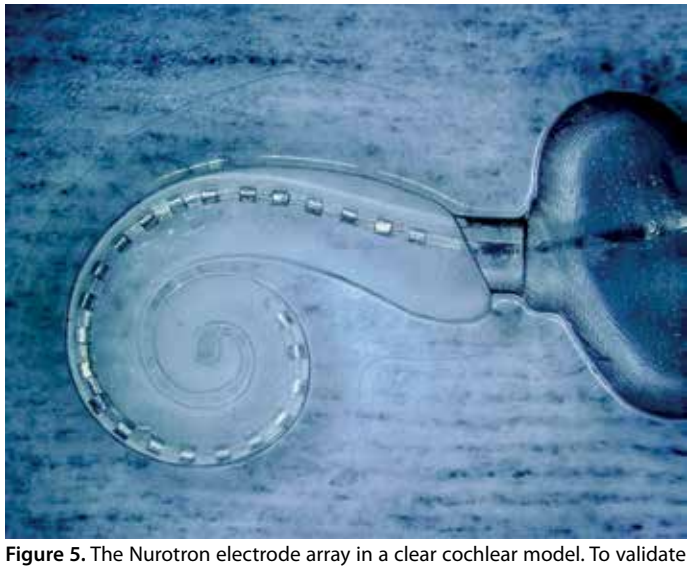

Figure 5. The Nurotron electrode array in a clear cochlear model. To validate the reliability of the electrode carrier, leads, and contacts when subjected to repeated insertions. Test electrodes were mechanically inserted into a clear plastic model of the cochlea. Each electrode was tested 50 times and evaluated for physical damage and electrical performance.

*Insulation Test*_– Electrode samples were preconditioned in saline (0.9%, 37±2°C, 10 days). Each electrode lead cable was clamped at the RW marker and at the normal location of the stimulator (not attached in this test). An elongation to 15 mm was applied for 60 seconds and a 1-kHz square wave signal (20 V p-p) was applied to each conducting pair along the array for 15 seconds. Electrodes were rinsed in deionized water, immediately wiped dry, and impedances were tested. The measured impedance of all conducting pairs exceeded 100 KΩ.

Insertion Test – Insertion test designed to evaluate the effects of repeated insertion on the electrode array was performed in an acrylic model of the human ST developed at Nurotron Biotechnology (Figure 5). The model ST cavity was filled with solution (water with a small amount of soap added) and the electrode tip was positioned just inside the lumen representing the RW. The insertion was driven by a constant speed linear actuator at a velocity of approximately 1 mm/second. Insertion of the array was stopped when the tip of the electrode reached a depth of 425–450° from the round window. The electrode was then slowly withdrawn and the operation was repeated 50 times for electrode. Each electrode was visually inspected at a magnification of 20× and electrode impedances were measured following each of the 10 insertions. Observations revealed that there was no damage to the silicone carrier, all stimulating contacts were intact, and all contacts had normal impedance values at each of these intervals and after completion of the test protocol.

Electrochemical Testing – Effective electrical stimulation of auditory neurons relies on safely depolarizing the membranes of excitable cells through a voltage gradient across the semi-permeable cell membrane. This gradient is established between stimulation electrode(s) and a ground or reference electrode [34]. The voltage gradient is achieved by applying constant current pulses to generate the injectable charge required to excite neural cells. If charge, or charge density on the electrode contact surface, is too high for a given electrode, irreversible electrochemical reactions may occur. These reactions include metal corrosion or dissolution, gas evolution, or production of toxic chemical reaction products [35]. These irreversible electrochemical reactions during charge transfer not only cause electrode damage but also result in tissue or nerve damage. Shannon developed a model to predict the point at which damage occurs based on a combination of total charge and charge density [36]. According to this model, safe charge and charge density is linked in the formula: log (D)=k–log (Q), where D is the charge density in $\mu C/cm^2$/phase, Q is the charge delivered per phase to the electrode in μC/phase, and k is a dimensionless constant used to set the boundary. For neural stimulation in a CI, using k=1.75 is appropriate (American National Standard, ANSI/AAMI CI86 Cochlear implant systems: Requirements for safety, functional verification, labeling and reliability reporting, p79. 2017). The safe charges and charge densities calculated at various exposed contact areas are listed in Table 2.

As shown, the safe charge limit increases with from 300 to 424 nC for increases in electrode exposed areas from 0.16 to 0.32 mm^2. This range of areas covers both the contact sizes in the standard Nurotron electrode array and the Slim series of electrodes currently in trial (Table 1). More importantly, the Nurotron stimulator has a maximal hardware charge limit of 250 nC, which is lower than the safe charge limits for all electrodes in the Nurotron system.

The maximum charge densities at 250 nC were also calculated (charge divided by the electrode geometric surface area) and were compared with the safe charge density limits predicted by the Shannon model. Figure 6 shows that all electrodes have charge densities much lower than the safe limits to ensure safe electrical stimulation.

Temporal Bone Testing – The Nurotron 24 channel electrode array, and pending Slim versions of the Nurotron electrode, were tested in human cadaver temporal bones at the University of Miami under the supervision of Drs. Adrien Eshraghi, Simon Angeli, and Xue-Zhong Liu. To simulate the real-world performance of the Nurotron electrode, resident and attending level surgeons from seven independent hospitals in China performed the cochlear implantation. These surgeons had little or no actual cochlear implantation experience at the time of the study. Three types of electrodes were inserted in eight temporal bones, including the standard Nurotron 22-mm electrode array, 25.5-mm Slim array, and 17.5-mm Slim array. The type of array was randomized among the surgeons. Surgeons prepared each specimen exactly as they would in the clinical setting. Accordingly, the mastoid bone was drilled to the middle ear space observing the boundaries common in clinical practice, the facial nerve was fully preserved, and the size and location of the opening into the ST was created with the limited view and instrument access commonly experienced. Insertions were performed via the RW, modified RW, or cochleostomy based on the preference of each surgeon and the anatomy of each specimen.

Table 2. The safe charge limits calculated at various exposed contact areas and the maximum charge delivered by the stimulator

Exposed contact area (mm^2)	Safe charge limit (nC)	Maximum charge stimulator delivered (nC)
0.16	300.0	250.0
0.22	351.7	250.0
0.28	396.8	250.0
0.32	424.2	250.0

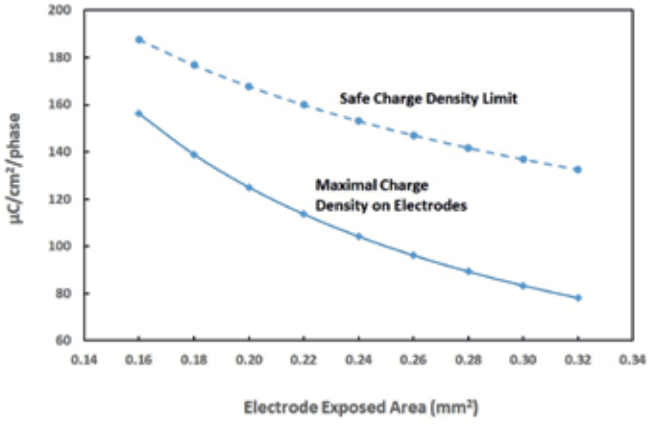

Figure 6. Safe charge density limits and maximal charge densities on electrodes as determined by processor and stimulator hardware limits.

After consultation with supervising surgeons, each electrode was inserted a single time until resistance was met or until the electrode was fully inserted as indicated by the molded marker ring on the electrode array. After insertion, a small drop of cyanoacrylic cement was placed near the RW to secure the array during subsequent processing and the remaining electrode lead was amputated near the facial recess to reduce the possibility of damage.

In each specimen, the cochlea was exposed by drilling to the "blue line" and removing all surrounding bone and soft tissue. A silk suture was tied tightly around the electrode and secured through a small tunnel drilled in the underlying bone immediately distal to the facial recess. This step is required because the dehydrating agent used to prepare the specimen for epoxy embedding will dissolve the temporary cyanoacrylic fixation of the array near the RW.

After isolation of the cochleae, the temporal bones were dehydrated in acetone, which was changed multiple times over a period of 7 days, infiltrated with epoxy resin (EpoFix, Electron Microscopy Sciences, Hatfield, PA, USA), and cured (48 hours). After full curing, each temporal bone was sectioned at 1.5-mm intervals using an ultra-fine diamond wafering blade (Buehler, Lake Bluff, IL, USA). In most cases, this resulted in 8–10 slices representing the complete cochlea from RW to the lateral extent of the basal turn adjacent to the carotid artery.

Individual slices were mounted on glass slides using epoxy resin, polished with 600 grit abrasive sheet, stained, cover slipped, and imaged at a magnification of 2-5× with 50 MP resolution. Trauma was evaluated using these images and by viewing the mounted sections at 10-50× magnification. Damage, when seen, was scored using a scale of 0-4 developed by Eshraghi (0=no visible damage, 1=elevation of the basilar membrane, 2=rupture of the basilar membrane, 3=electrode in the scala vestibule, and 4=fracture of the osseous spiral lamina).

Figure 7 illustrates typical temporal bone cross-sections from the temporal bone study. In this series, no significant damage (a damage score of 0 or 1) was observed in 7 of the 8 specimens evaluated. Figure 8 illustrates a case of significant damage (a damage score of 3) in the right temporal bone. The electrode was well positioned without damage in the region between the RW and the first turn. However, as the array passes through the lateral first turn, approximately 170° from the RW, the tip of the array deviates from ST into SV, remaining in the SV throughout the remainder of the cochlea.

Overall, the rate of severe trauma observed with the Nurotron electrode arrays is 12.5%, which is significantly lower than the rates reported in similar studies of electrode designs that did not incorporate specific features to limit upward bending of the electrode tip [37-39]. The 12.5% rate of severe trauma is comparable to that seen with other electrode designs that incorporated increased vertical stiffness, for example, the family of electrodes manufactured by Advanced Bionics, LLC [24, 25, 28].

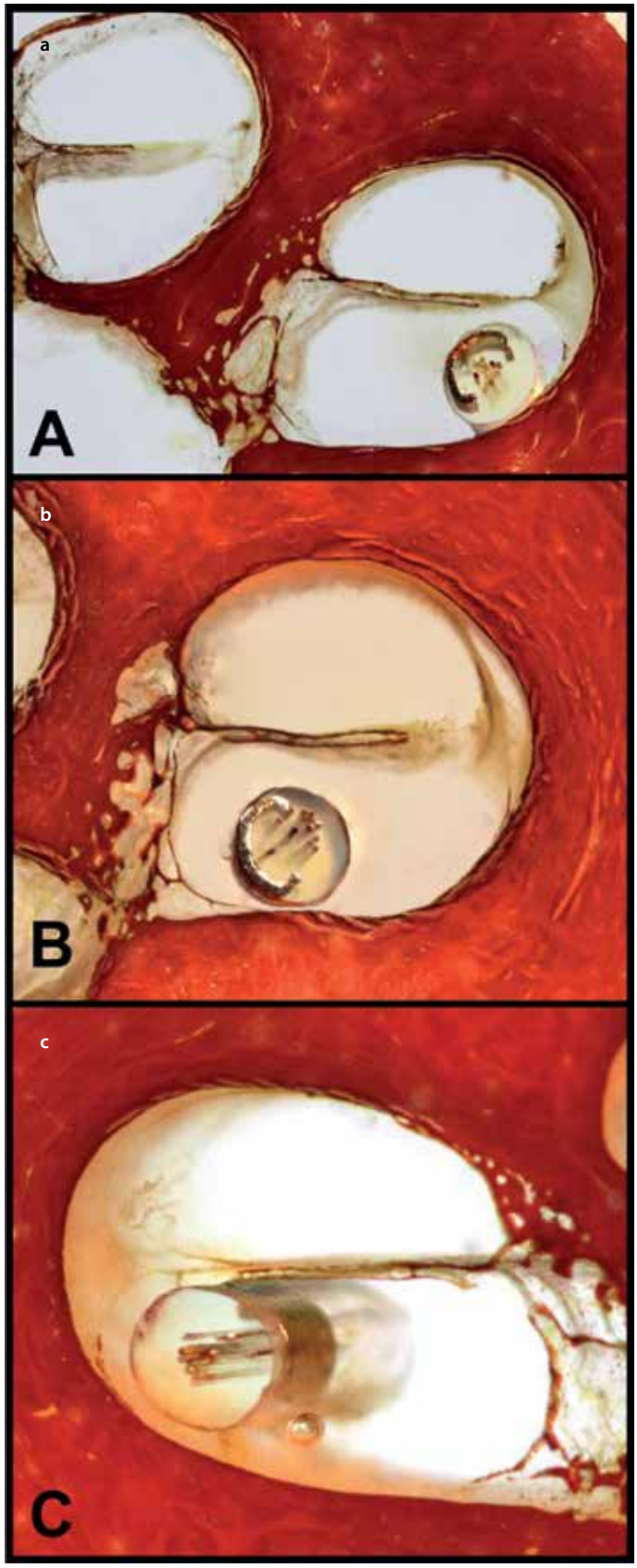

Figure 7, a-c. Histology without insertion trauma in three human temporal bones. Sections A and B show the standard Nurotron electrode array in the basal first turn of the scala tympani. Section C illustrates a standard array in the ascending first turn. The stimulating contacts can be clearly seen in each cross-section. No trauma was noted in any section.

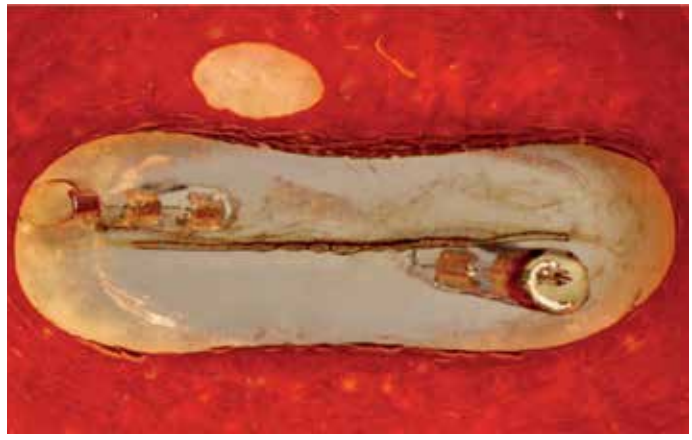

Figure 8. Histology with trauma. Translocation of the electrode from the scala tympani into the scala vestibuli (trauma grade 3) was seen in one specimen in this temporal bone series. This specimen showed the histological slice from the lateral wall region of the first turn: The electrodes were correctly located in the scala tympani (with two contacts being visible in the lower-right part of the picture), then incorrectly moved into the scala vestibule (with three contacts being visible in the upper-left part of the picture.

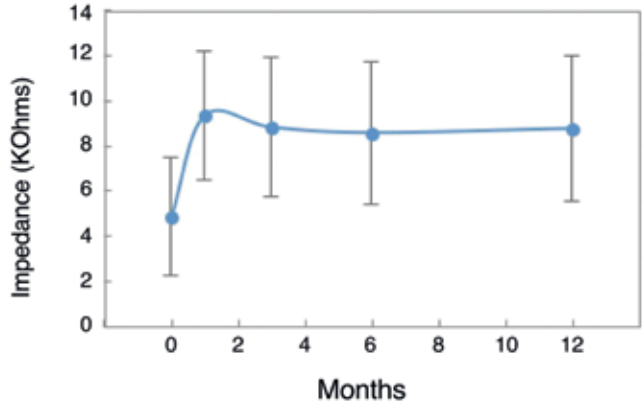

Figure 9. Electrode impedance as a function of post-implantation time. Average impedance was calculated from data collected from 100 Nurotron CI patients, with error bars representing ± one standard deviation.

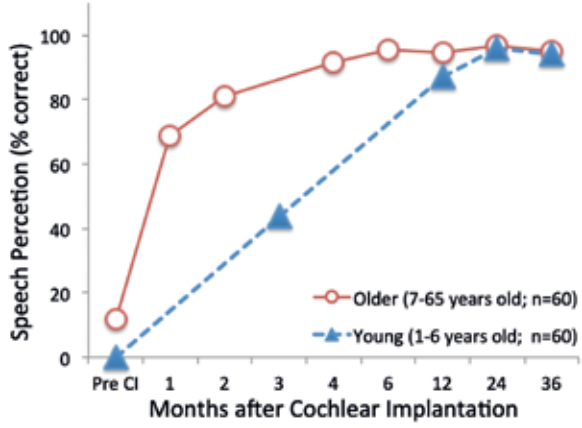

Figure 10. Speech perception from Nurotron adult and child clinical trials. Disyllabic word recognition in % correct is plotted as a function of time from pre-cochlear implantation to 36 months after cochlear implantation. The data from older individuals are from Gao et al. [41], while those from younger subjects are from Yu [40]. The present data helped Nurotron 26-device receive approval from China Food and Drug Administration for adults in 2011 and children in 2013.

Ease of Insertion – Surgeons with all levels of experience have been trained to insert both the standard Nurotron electrode array and the three Slim array models in human temporal bones and anatomically accurate 3D plastic models of the human cochlea (Phacon GmbH, Germany). As a part of these training sessions, surgeons were asked to evaluate the ease of insertion on a scale of 1–10 with 10 representing the highest ease of use. Ninety-one surgeons participated in this survey with a mean score of 7.8, indicating that the Nurotron intracochlear electrode is straightforward to insert. No differences were noted between the standard and Slim arrays. Intraoperative comments from more experienced surgeons reflect the comments from the formal temporal bone survey. These surgeons agree that the mechanical characteristics of the Nurotron electrodes do not present any challenges to insertion outside of those experienced with other clinically available CI electrodes.

Electrode Impedance Monitoring – Impedance variation after implantation was monitored in 100 patients. The data were collected at the time of surgery and at 1, 3, 6, and 12 months. As seen from Figure 9, the average impedance sharply increased after implantation and peaked at approximately 1 month post-operatively. After this, impedance stabilized at approximately 9 kΩ at 3 months post-operatively, indicating the establishment of a stable electrode–tissue interface. The Nurotron electrode has demonstrated a high level of reliability with failure in only 6 patients in 43,000 patient years of experience to date.

Subject Performance – Electrode reliability is critical to CI performance. Figure 10 shows Nurotron CI performance from the adult and child clinical trials conducted between 2009 and 2013 [8, 40, 41]. Due to the requirements set by the China FDA and the Chinese Government Tender Program, two independent trials were conducted for 60 young deaf individuals aged between 1 and 6 years and for an additional 60 older individuals aged between 7 and 65 years. The pre-implantation baseline performance was 0% for the young group and 12% for the old group. The young group's performance increased to 44% at 3 months after implantation and to an asymptotic level of ~90% after 1 year of implantation. The performance of the old group improved at a more rapid rate than that of the young group, reaching the same high-level asymptotic performance at 4 months after implantation.

Future Direction

Although contemporary CI electrodes have evolved from balls and rings to foil plates, with the electrode array being either curved or straight, hugging or not hugging the modiolus in the last 30 years, their fundamental design has remained the same with the electrodes being inserted in ST. This fundamental design is now the most significant constraint limiting further improvement in CI performance [2]. One future direction is to address the mismatch between the limited number of electrodes (12-24) and the thousand times more independent neurons, perhaps through a penetrating electrode array. A second future direction is to convert the labor-intensive manual assembly methods into an automated manufacturing of cochlear electrodes. We are developing a Parylene thin-film electrode array and a micro-fabrication method to make a high-density and automated CI electrode array [42].

CONCLUSION

The need for cochlear implants is urgent and universal. In China alone, the number of deaf individuals is a staggering 27.8 million, but only ~50,000 of them have received a CI so far [43]. The Nurotron device was developed to address this unmet need by offering an affordable yet safe and effective CI. The present study describes the design, development, and evaluation of the Nurotron electrode array:

- The Nurotron array is 22 mm in length from the RW marker to the apical tip of the carrier and contains 24 intracochlear electrodes with a 0.85-mm center-to-center electrode spacing. The electrode contact is made of Pt90Ir10 and has a 0.32-mm^2 surface area.
- The Nurotron array has been thoroughly tested to meet the ISO Standard 14708-07 requirements, having undergone elongation, flexural, fatigue, insulation, insertion, and electrochemical tests.
- The human temporal bone and clinical trial studies have demonstrated that the electrode array can be easily inserted without the use of complex insertion tools (7.8/10 rating with 10 indicating the highest ease of use), produces a low incidence (12.5%) of severe insertion trauma, stable electrode–tissue interface (asymptotic impedance 1 month after implantation), and high reliability (6 failures in 43,000 patient years of experience).
- Since receiving the China FDA approval in 2011 and the European CE marking in 2012, the Nurotron device has benefited 10,000 individuals worldwide. Their speech performance is equal to the reported performance with other major CI devices.
- The Nurotron device has helped reduce the device unit cost from US$25,000 in 2011 to US$4,620 in 2017 through the Chinese Government Tender Program. The low cost has resulted in the delivery of tens of thousands of CIs to both adults and children that would not have received cochlear implantation at the existing worldwide pricing.

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Conflict of Interest: S.R. is a consultant for Advanced Bionics LLC and Nurotron Biotechnology and has an equity interest in Nurotron Biotechnology. D.Z. is an employee of Nurotron Biotechnology. F.Z. has an equity interest in Nurotron Biotechnology.

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