

Cochlear Implantation

Subjects: [Otorhinolaryngology](#)

Contributor: Jennifer J. Lentz , Moises Arriaga ,

Cochlear implants (CIs) are prostheses that electrically stimulate the cochlear nerve to restore not only sound perception, but speech understanding in people with profound sensorineural hearing loss. CIs use a battery-powered sound processor worn at ear level to transmit electrical signals to an electrode array that has been surgically implanted in the inner ear. The first generation of implants was approved by the FDA in 1984. These devices used a single electrode that allowed recipients to perceive the presence or absence of sound, while variably restoring some speech understanding. The FDA approved the first multi-channel implants for adults and children in 1987 and 1990, respectively. Patients who undergo implantation today do so under a growing number of indications and use devices with a tonotopic array of as many as 24 electrodes. These modern CIs promote language acquisition, literacy, and academic performance in pre-lingually deaf children, while restoring meaningful speech recognition and generating better quality-of-life outcomes for adults who are unable to use traditional amplification.

hearing loss

cochlear implantation

deafness

1. Introduction

While Cochlear implant (CI) devices are a successful treatment option for many hearing-impaired individuals, several challenges related to their delivery, use, and access remain. Overcoming these challenges has fueled the investigation and development of biomolecular and pharmacologic therapeutic approaches using gene augmentation, gene-editing, antisense, and other small molecules ^{[1][2][3][4][5][6][7][8][9][10][11][12][13][14]}. Both approaches—CI devices and biomolecular/pharmacological drugs—target the inner ear to improve peripheral function and restore hearing. The CI circumvents defective or absent auditory hair cells to electronically stimulate a subset of spiral ganglion neurons or the nerve fibers of auditory neurons. In contrast, gene and antisense therapies are designed to target defective auditory hair cells directly to restore their function. Recent advances in the design of viral vectors used to deliver gene therapies and the expanding list of chemical modifications made to antisense oligonucleotides have significantly improved the cellular uptake of these drugs, thus demonstrating their potential to reach and treat nearly all inner and outer hair cells for more effective hearing outcomes ^{[14][15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30]}.

2. Hearing with an Implant

CIs are designed to restore speech perception for people with sensorineural hearing loss. They do not, however, replicate people's hearing apparatus. Instead, CIs meet their purpose by layering an array of discrete electrodes

covering the frequency range of human speech into the tonotopic infrastructure upon which people also rely to localize sound and hear music. Unsurprisingly, the extent to which CIs can process complex stimuli such as these is limited.

CIs cover a narrower range of frequencies than the cochlea (200–8500 Hz vs. 20–20,000 Hz), and they do so less accurately. Individual electrodes stimulate broad swaths of territory along the basilar membrane, often falling short of the apical turn [31][32]. As a result, CIs effectively collapse unique signals in a phenomenon called current spread [33]. Due to anatomical variations, such as pathological changes to the hair cells and spiral ganglion cells causing the patient's hearing loss, and the limits of any given manufacturer's device [33], electrodes are commonly misaligned with the cochlea's natural frequency gradient [34]. This place–pitch mismatch underlies characteristic pitch perception deficits among CI users [33][35][36].

CIs also struggle to encode the temporal cues people use to perceive pitch in music, localize sounds, and hear speech in background noise. CIs cannot phase lock as people's cochlea does [33]. Moreover, the basilar membrane can process both the gross waveform of a stimulus, as well as the more rapidly oscillating fine structure upon which it is carried. Historically, CIs have extracted that gross waveform, or the temporal envelope information from stimuli, and presented it in non-simultaneous pulses [37]. This process, called continuous interleaved sampling (CIS), can transmit enough information for a user to understand speech [38][39]. In accomplishing that task while preventing electrodes from distorting the activity of others, implants with enveloped-based strategies such as CIS discard a signal's temporal fine structure processing (FSP) information altogether [33][40].

Along with deciphering speech from background noise, it is with this FSP information that people detect the lower-frequency, bass components of music [41]. A CI user relying exclusively on envelope information is unable to distinguish between samples of music with varying levels of bass. As much as 400 Hz of bass can be removed from musical stimuli before CI users recognize a difference [42]. This performance data pairs with the subjective finding that CI users do not often enjoy listening to music after implantation [43][44][45]. When they do, CI users tend to prefer less complex music with a clear beat and simple lyrics. Users also prefer music to which they were familiar prior to the onset of their deafness.

Novel brain-imaging and sound-processing techniques have allowed people to identify cochlear stimulation and auditory training strategies that may improve music appreciation among this population [46][47][48][49][50]. Some manufacturers have even created and marketed devices that theoretically leverage FSP strategies to allow users to enjoy music and hear better in background noise. While these devices afford clinicians and patients the opportunity to exercise more choice in their hearing care, blinded paired comparisons of implants using both strategies do not consistently show FSP strategies to be superior to CIS in conserving music sound quality or speech recognition [51].

In addition to FSP, there are a variety of other strategies designed to improve the sound quality a CI user can experience when listening to music by stimulating more territory along the basilar membrane. Measuring the extent to which a stimulus must be altered to generate perceived differences in sound quality among CI users [42],

research has shown that stimulation toward the apex via longer electrode arrays and bipolar stimulation that creates “phantom” channels beyond the physical boundaries of an array improves music sound quality perception [52][53].

3. Current Surgical Approaches to Implantation into the Cochlea

Modern cochlear implantation is a relatively routine and safe procedure. Nonetheless, operations can generate trauma, inflammation, fibrosis, obstructive hydrops, or synaptic changes in the inner ear that can manifest as residual hearing loss and vertigo [54][55][56][57][58].

For patients who have some residual hearing, threshold shifts are almost inevitable after implantation [59]. Today, modern technology and surgical techniques permit ‘softer’ approaches to implantation that can both treat a patient’s hearing loss and better preserve their residual hearing by protecting the structural integrity of the inner ear [58][60][61]. Early success with hybrid devices placed via the round window (RW) approach have encouraged clinicians and scientists to continue pursuing new and minimally invasive operative techniques [31][59]. Robot-assisted operations informed by advanced imaging that implant steerable [62][63][64], drug eluting devices may become the standard in cochlear implantation [65]. Currently, there are just three active operating systems that deploy robotics to access the middle ear [66]. The surgical approach and hardware in an implant remain tangible, significant contributors to patient outcomes [58].

Electrode arrays are most commonly implanted via the transmastoid facial recess approach with RW or cochleostomy insertion [67]. Some centers avoid the facial recess by employing a ‘suprameatal’ technique [68]. The ‘soft’ surgical approaches to implantation pioneered at the end of the 20th century were oriented around neural preservation via the use of perioperative systemic and topical steroids, meticulous avoidance of bone dust and surgical debris entering the cochlea, and slow, gentle insertion of more delicate electrode arrays. Early hearing preservation ‘soft’ surgical techniques relied on cochleostomies [58][61]. Today, RW insertion is more common, and most surgeons use ‘soft’ surgery techniques in all cochlear implantation surgeries, regardless of the length of the electrode being placed or a patient’s residual hearing status [69]. To date, cochleostomies are still a comparatively unstandardized set of procedures that rely on loosely defined anatomical landmarks [69]. Just 10% of neurotologists prefer cochleostomy to round window or extended round window approaches for electrode placement [70]. Even fewer choose cochleostomy when a patient has residual hearing to preserve.

The RW itself presents a reliable landmark for a surgeon placing an electrode array [69], and RW insertions are associated with lower rates of electrode misplacement than cochleostomies [71]. This anatomical reliability is paramount given the considerable variability in ideal insertion vectors among different patients [72]. Computed tomography (CT) data indicate that RW insertions can place electrodes closer to the modiolus, and thus the spiral ganglion cells in the cochlea’s basal turn [67]. It is hypothesized that closer placement could mitigate current spread and generate better speech comprehension for the patient. Still, when electrodes are placed successfully, neither approach consistently results in better postoperative outcomes [71][73][74].

RW approaches are perhaps especially suited to placing shorter electrode arrays, such as those used for patients with substantial residual low frequency hearing. They are doubly favorable here, as histopathologic evidence indicates cochleostomies can seed an ossification process causing endolymphatic hydrops that characteristically costs a patient the low frequency hearing the operation aims to preserve, while treating their hearing loss [54]. These findings are consistent with others that demonstrate that the RW approach may be less traumatic [75], but trials comparing the approaches remain underway [76].

The design of a CI's electrode array also impacts hearing preservation after implantation. The two major categories of array are straight lateral wall (LW) and curved peri-modiolar (PM) [31]. PM arrays are curved to closely hug the modiolus along the medial wall of the cochlea; however, this perimodiolar position may mitigate interference between electrodes by directly stimulating spiral ganglion cells [31][58]. LW arrays lie some distance farther from the modiolus and must stimulate the nerve fibers of the auditory neurons, as opposed to the neurons themselves. Accepting potentially more crosstalk between electrodes but limiting trauma with the delicate structures of the inner ear, LW arrays are preferred for hearing preservation in hybrid implant candidates.

Pure hybrid implants have electrodes that are roughly a third the length of typical arrays. There are also longer, short-LW arrays that offer slightly more coverage in the cochlea, while appearing to preserve hearing in the lower frequencies [77], though not at the rates of the truly short electrodes. Currently, many surgeons prefer to implant patients with longer electrodes even if they meet criteria for a hybrid implant [70]. Longer electrodes are thinner than ever before, and with modern surgical techniques, they can allow for the preservation of a patient's residual hearing while covering more of the cochlea. Patients with even substantial residual low frequency hearing at the time of implantation can lose it as their underlying hearing loss progresses, or because of surgical sequelae such as that of cochlear fibrosis or endolymphatic hydrops [54]. If a patient who was originally implanted with a short electrode loses their residual hearing, they may need to undergo re-implantation with a longer electrode. Revisions and re-implantations are notoriously challenging.

The growing use of cone beam CT imaging has allowed for intraoperative and postoperative evaluation of electrode placement. CT scans can show electrode dislocation, tip fold-over, and mispositioning. This allows for real time visualization of the electrode and revision of the insertion at the time of initial surgery [78]. When combined with expected electrical distribution of charge from an electrode, postoperative cone beam CT facilitates the deactivation of interfering electrodes, which can improve speech recognition [79][80][81].

4. Technology in Development

4.1. Optical Cochlear Implants

Basic research on the feasibility of an Optical Cochlear Implant (oCI) using photonic stimulation of the hair cells or spiral ganglion cells rather than electrical current as used in the current Electrical Cochlear Implant (eCI) suggests a theoretical possibility of improving the dynamic range of current eCI stimulation strategies (which could enhance understanding in background sound and music appreciation) and more focused neural stimulation than eCI (which

could limit electrode “cross talk”). Recent reviews provide an excellent summary of the major issues related to oCI [82][83].

Two basic strategies are under investigation: Infrared Neural Stimulation (INS), which encodes sound by creating heat with an implanted laser to initiate neural stimulation; and Optogenetic Stimulation, which expresses photosensitive ion channels to neurons. Despite the potential, investigators have several significant obstacles to overcome. With INS, the challenge of balancing the heat generation to create enough to stimulate without damaging the cells is formidable. There is still controversy as to whether or not such INS stimulation is producing direct neural stimulation from the localized thermal effect or if there is an optoacoustic event stimulating surviving neurons from the stress-relaxation waves following confined heating within the cochlea in animal experiments [82]. With Optogenetic Stimulation, the blue–green stimulation of light-sensitive ion channels such as Chronos-mediated stimulation risked phototoxic damage to cells and the newer strategies emphasize red-shifted stimulation with ChrimsonR which avoids the ototoxicity and offers improved firing rates in experimental designs. These optogenetic strategies rely on viral gene transfer with Adeno-associated Viruses as the main candidate for future application. Such optogenetic strategies open the possibility of Active oCI and Passive oCI stimulation with either implantation of a micro-LED (light-emitting diode) arrays versus passive waveguide-based implantation with emitter arrays spread through the area of implantation [83]. However, there are still formidable challenges in designing such arrays for safe implantation, such as understanding the neural effects of prolonged stimulation, current requirements, and durability. While the concept of oCI merits further investigation, clinical application of an oCI is not imminent.

4.2. Electrode Coating and Drug Elution

The placement of the CI electrode array within the scala tympani necessarily disrupts the microenvironment of that delicate inner ear structure. A silicone carrier delivers the electrodes from the receiver–stimulator to the cochlea. Recent developments have allowed special grafting and coating of materials onto the silicone electrode carrier. Materials which reduce friction and insertion trauma have already been implemented in animal models with some success [84]. The preservation of acoustic hearing in the setting of cochlear implantation will likely be facilitated by further developments and improvements in electrode delivery.

Development of coating materials not only allows for atraumatic electrode insertion, but may also enable the delivery of drugs and other biologically active compounds directly to the inner ear. Animal studies evaluating the safety of steroid-eluting electrode arrays are well underway. The ability to deliver steroids to the scala tympani provides an exciting opportunity to further advance acoustic hearing preservation and reduce vertigo in the setting of cochlear implantation [85]. Finally, research teams are investigating the use of biologically active particles grafted to the electrode that would allow the on-growth of new spiral ganglion cells within the inner ear [86].

4.3. Intraoperative Monitoring

Intraoperative facial nerve monitoring has long been the practice for CI surgeons to preserve facial motor function during the delicate surgical procedure. Within the last decade, there have been significant developments of additional intraoperative monitoring procedures to evaluate the electrode insertion process and final placement prior to closure. Impedance measurements and neural response telemetry can be obtained after electrode placement and prior to closure to partially evaluate device integrity and placement.

To further preserve acoustic hearing in patients undergoing CI, new intraoperative monitoring techniques have been developed to evaluate cochlear trauma and direct the surgeon to more gentle insertion. While a full discussion of these techniques is beyond the scope of this manuscript, intraoperative electrocochleography measures electrical potentials generated within the cochlea and can be used to evaluate preservation of function during insertion. The results of large reviews on the efficacy of this type of monitoring in the clinical setting are largely mixed [87]. More recently, the use of transimpedance matrices allows for the detection of tip fold over and fine details of electrode positioning, such as proximity to the lateral wall [88][89]. These intraoperative monitoring techniques are not yet in wide clinical use but may prove to be a useful adjunct for plain-film X-ray prior to wound closure.

References

1. de Joya, E.M.; Colbert, B.M.; Tang, P.-C.; Lam, B.L.; Yang, J.; Blanton, S.H.; Dykxhoorn, D.M.; Liu, X. Usher Syndrome in the Inner Ear: Etiologies and Advances in Gene Therapy. *Int. J. Mol. Sci.* 2021, 22, 3910.
2. Géléoc, G.G.S.; El-Amraoui, A. Disease mechanisms and gene therapy for Usher syndrome. *Hear. Res.* 2020, 394, 107932.
3. Mirian, C.; Ovesen, T. Intratympanic vs. Systemic Corticosteroids in First-line Treatment of Idiopathic Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis. *JAMA Otolaryngol. -Head Neck Surg.* 2020, 146, 421.
4. Omichi, R.; Shibata, S.B.; Morton, C.C.; Smith, R.J.H. Gene therapy for hearing loss. *Hum. Mol. Genet.* 2019, 28, R65–R79.
5. Ma, Y.; Wise, A.K.; Shepherd, R.K.; Richardson, R.T. New molecular therapies for the treatment of hearing loss. *Pharmacol. Ther.* 2019, 200, 190–209.
6. Pendse, N.D.; Lamas, V.; Pawlyk, B.S.; Maeder, M.L.; Chen, Z.-Y.; Pierce, E.A.; Liu, Q. In Vivo Assessment of Potential Therapeutic Approaches for USH2A-Associated Diseases. *Adv. Exp. Med. Biol.* 2019, 1185, 91–96.
7. de Vrieze, E.; Martín, J.C.; Peijnenborg, J.; Martens, A.; Oostrik, J.; van den Heuvel, S.; Neveling, K.; Pennings, R.; Kremer, H.; van Wijk, E. AON-based degradation of c.151C>T mutant COCH

- transcripts associated with dominantly inherited hearing impairment DFNA9. *Mol. Ther.-Nucleic Acids* 2021, 24, 274–283.
8. Lentz, J.J.; Jodelka, F.M.; Hinrich, A.J.; McCaffrey, K.; Farris, H.E.; Spalitta, M.J.; Bazan, N.G.; Duelli, D.M.; Rigo, F.; Hastings, M.L. Rescue of hearing and vestibular function by antisense oligonucleotides in a mouse model of human deafness. *Nat. Med.* 2013, 19, 345–350.
 9. Gao, X.; Tao, Y.; Lamas, V.; Huang, M.; Yeh, W.-H.; Pan, B.; Hu, Y.-J.; Hu, J.H.; Thompson, D.B.; Shu, Y.; et al. Treatment of autosomal dominant hearing loss by in vivo delivery of genome editing agents. *Nature* 2018, 553, 217–221.
 10. Yeh, W.-H.; Shubina-Oleinik, O.; Levy, J.M.; Pan, B.; Newby, G.A.; Wornow, M.; Burt, R.; Chen, J.C.; Holt, J.R.; Liu, D.R. In vivo base editing restores sensory transduction and transiently improves auditory function in a mouse model of recessive deafness. *Sci. Transl. Med.* 2020, 12, eaay9101.
 11. Ahmed, H.; Shubina-Oleinik, O.; Holt, J.R. Emerging Gene Therapies for Genetic Hearing Loss. *J. Assoc. Res. Otolaryngol.* 2017, 18, 649–670.
 12. Hastings, M.L.; Jones, T.A. Antisense Oligonucleotides for the Treatment of Inner Ear Dysfunction. *Neurotherapeutics* 2019, 16, 348–359.
 13. Ding, N.; Lee, S.; Lieber-Kotz, M.; Yang, J.; Gao, X. Advances in genome editing for genetic hearing loss. *Adv. Drug Deliv. Rev.* 2021, 168, 118–133.
 14. Noh, B.; Rim, J.H.; Gopalappa, R.; Lin, H.; Kim, K.M.; Kang, M.J.; Gee, H.Y.; Choi, J.Y.; Kim, H.H.; Jung, J. In vivo outer hair cell gene editing ameliorates progressive hearing loss in dominant-negative Kcnq4 murine model. *Theranostics* 2022, 12, 2465–2482.
 15. Taiber, S.; Cohen, R.; Yizhar-Barnea, O.; Sprinzak, D.; Holt, J.R.; Avraham, K.B. Neonatal AAV gene therapy rescues hearing in a mouse model of SYNE4 deafness. *EMBO Mol. Med.* 2021, 13, e13259.
 16. Wu, J.; Solanes, P.; Nist-Lund, C.; Spataro, S.; Shubina-Oleinik, O.; Marcovich, I.; Goldberg, H.; Schneider, B.L.; Holt, J.R. Single and Dual Vector Gene Therapy with AAV9-PHP.B Rescues Hearing in Tmc1 Mutant Mice. *Mol. Ther.* 2021, 29, 973–988.
 17. Lentz, J.J.; Pan, B.; Ponnath, A.; Tran, C.M.; Nist-Lund, C.; Galvin, A.; Goldberg, H.; Robillard, K.N.; Jodelka, F.M.; Farris, H.E.; et al. Direct Delivery of Antisense Oligonucleotides to the Middle and Inner Ear Improves Hearing and Balance in Usher Mice. *Mol. Ther.* 2020, 28, 2662–2676.
 18. Wang, L.; Kempton, J.B.; Jiang, H.; Jodelka, F.M.; Brigande, A.M.; Dumont, R.A.; Rigo, F.; Lentz, J.J.; Hastings, M.L.; Brigande, J.V. Fetal antisense oligonucleotide therapy for congenital deafness and vestibular dysfunction. *Nucleic Acids Res.* 2020, 48, 5065–5080.

19. Lee, B.; Kim, Y.R.; Kim, S.J.; Goh, S.H.; Kim, J.H.; Oh, S.K.; Baek, J.I.; Kim, U.K.; Lee, K.Y. Modified U1 snRNA and antisense oligonucleotides rescue splice mutations in SLC26A4 that cause hereditary hearing loss. *Hum. Mutat.* 2019, 40, 1172–1180.
20. György, B.; Meijer, E.J.; Ivanchenko, M.V.; Tenneson, K.; Emond, F.; Hanlon, K.S.; Indzhykulian, A.A.; Volak, A.; Karavitaki, K.D.; Tamvakologos, P.I.; et al. Gene Transfer with AAV9-PHP.B Rescues Hearing in a Mouse Model of Usher Syndrome 3A and Transduces Hair Cells in a Non-human Primate. *Mol. Ther.-Methods Clin. Dev.* 2019, 13, 1–13.
21. Ponnath, A.; Depreux, F.F.; Jodelka, F.M.; Rigo, F.; Farris, H.E.; Hastings, M.L.; Lentz, J.J. Rescue of Outer Hair Cells with Antisense Oligonucleotides in Usher Mice Is Dependent on Age of Treatment. *J. Assoc. Res. Otolaryngol.* 2018, 19, 1–16.
22. Isgrig, K.; Shteamer, J.W.; Belyantseva, I.A.; Drummond, M.C.; Fitzgerald, T.S.; Vijayakumar, S.; Jones, S.M.; Griffith, A.J.; Friedman, T.B.; Cunningham, L.L.; et al. Gene Therapy Restores Balance and Auditory Functions in a Mouse Model of Usher Syndrome. *Mol. Ther.* 2017, 25, 780–791.
23. Pan, B.; Askew, C.; Galvin, A.; Heman-Ackah, S.; Asai, Y.; Indzhykulian, A.A.; Jodelka, F.M.; Hastings, M.L.; Lentz, J.J.; Vandenberghe, L.H.; et al. Gene therapy restores auditory and vestibular function in a mouse model of Usher syndrome type 1c. *Nat. Biotechnol.* 2017, 35, 264–272.
24. Shibata, S.B.; Ranum, P.T.; Moteki, H.; Pan, B.; Goodwin, A.T.; Goodman, S.S.; Abbas, P.J.; Holt, J.R.; Smith, R.J.; Shibata, S.B.; et al. RNA Interference Prevents Autosomal-Dominant Hearing Loss. *Am. J. Hum. Genet.* 2016, 98, 1101–1113.
25. Kaur, T.; Mukherjea, D.; Sheehan, K.; Jajoo, S.; Rybak, L.P.; Ramkumar, V. Short interfering RNA against STAT1 attenuates cisplatin-induced ototoxicity in the rat by suppressing inflammation. *Cell Death Dis.* 2011, 2, e180.
26. Mukherjea, D.; Jajoo, S.; Whitworth, C.; Bunch, J.R.; Turner, J.G.; Rybak, L.P.; Ramkumar, V. Short Interfering RNA against Transient Receptor Potential Vanilloid 1 Attenuates Cisplatin-Induced Hearing Loss in the Rat. *J. Neurosci.* 2008, 28, 13056–13065.
27. Maeda, Y.; Fukushima, K.; Nishizaki, K.; Smith, R.J. In vitro and in vivo suppression of GJB2 expression by RNA interference. *Hum. Mol. Genet.* 2005, 14, 1641–1650.
28. Shubina-Oleinik, O.; Nist-Lund, C.; French, C.; Rockowitz, S.; Shearer, A.E.; Holt, J.R. Dual-vector gene therapy restores cochlear amplification and auditory sensitivity in a mouse model of DFNB16 hearing loss. *Sci. Adv.* 2021, 7, eabi7629.
29. Nist-Lund, C.A.; Pan, B.; Patterson, A.; Asai, Y.; Chen, T.; Zhou, W.; Zhu, H.; Romero, S.; Resnik, J.; Polley, D.B.; et al. Improved TMC1 gene therapy restores hearing and balance in mice with genetic inner ear disorders. *Nat. Commun.* 2019, 10, 236.

30. Al-Moyed, H.; Cepeda, A.P.; Jung, S.; Moser, T.; Kügler, S.; Reisinger, E. A dual-AAV approach restores fast exocytosis and partially rescues auditory function in deaf otoferlin knock-out mice. *EMBO Mol. Med.* 2019, 11, e9396.
31. Dhanasingh, A.; Jolly, C. An overview of cochlear implant electrode array designs. *Hear. Res.* 2017, 356, 93–103.
32. Würfel, W.; Lanfermann, H.; Lenarz, T.; Majdani, O. Cochlear length determination using Cone Beam Computed Tomography in a clinical setting. *Hear. Res.* 2014, 316, 65–72.
33. Caldwell, M.T.; Jiam, N.T.; Limb, C.J. Assessment and improvement of sound quality in cochlear implant users. *Laryngoscope Investig. Otolaryngol.* 2017, 2, 119–124.
34. Jiam, N.T.; Gilbert, M.; Cooke, D.; Jiradejvong, P.; Barrett, K.; Caldwell, M.; Limb, C.J. Association Between Flat-Panel Computed Tomographic Imaging–Guided Place-Pitch Mapping and Speech and Pitch Perception in Cochlear Implant Users. *JAMA Otolaryngol.-Head Neck Surg.* 2019, 145, 109–116.
35. Landsberger, D.M.; Svrakic, M.; Roland, J.T., Jr.; Svirsky, M. The Relationship Between Insertion Angles, Default Frequency Allocations, and Spiral Ganglion Place Pitch in Cochlear Implants. *Ear Hear.* 2015, 36, e207–e213.
36. Gilbers, S.; Fuller, C.; Gilbers, D.; Broersma, M.; Goudbeek, M.; Free, R.; Başkent, D. Normal-Hearing Listeners' and Cochlear Implant Users' Perception of Pitch Cues in Emotional Speech. *i-Percept.* 2015, 6, 0301006615599139.
37. Kiefer, J.; Von Ilberg, C.; Hubner-Egner, J.; Rupprecht, V.; Knecht, R. Optimized speech understanding with the continuous interleaved sampling speech coding strategy in patients with cochlear implants: Effect of variations in stimulation rate and number of channels. *Ann. Otol. Rhinol. Laryngol.* 2000, 109, 1009–1020.
38. Shannon, R.V. Speech and Music Have Different Requirements for Spectral Resolution. *Int. Rev. Neurobiol.* 2005, 70, 121–134.
39. Zeng, F.-G.; Rebscher, S.; Harrison, W.V.; Sun, X.; Feng, H. Cochlear Implants: System Design, Integration, and Evaluation. *IEEE Rev. Biomed. Eng.* 2008, 1, 115–142.
40. Limb, C.J.; Roy, A.T. Technological, biological, and acoustical constraints to music perception in cochlear implant users. *Hear. Res.* 2014, 308, 13–26.
41. Heng, J.; Cantarero, G.; Elhilali, M.; Limb, C.J. Impaired perception of temporal fine structure and musical timbre in cochlear implant users. *Hear. Res.* 2011, 280, 192–200.
42. Roy, A.T.; Jiradejvong, P.; Carver, C.; Limb, C.J. Assessment of Sound Quality Perception in Cochlear Implant Users During Music Listening. *Otol. Neurotol.* 2012, 33, 319–327.

43. Jiam, N.T.; Caldwell, M.T.; Limb, C.J. What Does Music Sound Like for a Cochlear Implant User? *Otol. Neurotol.* 2017, 38, e240–e247.
44. Gfeller, K.; Driscoll, V.D.; Looi, V. Music Appreciation and Training for Cochlear Implant Recipients: A Review. *Semin. Hear.* 2012, 33, 307–334.
45. Migirov, L.; Kronenberg, J.; Henkin, Y. Self-Reported Listening Habits and Enjoyment of Music among Adult Cochlear Implant Recipients. *Ann. Otol. Rhinol. Laryngol.* 2009, 118, 350–355.
46. Chari, D.A.; Barrett, K.C.; Patel, A.D.; Colgrove, T.R.; Jiradejvong, P.; Jacobs, L.Y.; Limb, C.J. Impact of Auditory-Motor Musical Training on Melodic Pattern Recognition in Cochlear Implant Users. *Otol. Neurotol.* 2020, 41, e422–e431.
47. Gilbert, M.L.; Deroche, M.L.D.; Jiradejvong, P.; Barrett, K.C.; Limb, C.J. Cochlear Implant Compression Optimization for Musical Sound Quality in MED-EL Users. *Ear Hear.* 2021, 43, 862–873.
48. Jiam, N.T.; Gilbert, M.; Mo, J.; Jiradejvong, P.; Limb, C.J. Computed Tomography–Based Measurements of the Cochlear Duct: Implications for Cochlear Implant Pitch Tuning. *Ear Hear.* 2021, 42, 732–743.
49. Jiam, N.T.; Limb, C. Music perception and training for pediatric cochlear implant users. *Expert Rev. Med. Devices* 2020, 17, 1193–1206.
50. Limb, C.J. Cochlear implant-mediated perception of music. *Curr. Opin. Otolaryngol. Head Neck Surg.* 2006, 14, 337–340.
51. Magnusson, L. Comparison of the fine structure processing (FSP) strategy and the CIS strategy used in the MED-EL cochlear implant system: Speech intelligibility and music sound quality. *Int. J. Audiol.* 2011, 50, 279–287.
52. Roy, A.T.; Penninger, R.T.; Pearl, M.S.; Wuerfel, W.; Jiradejvong, P.; Carver, C.; Buechner, A.; Limb, C.J. Deeper Cochlear Implant Electrode Insertion Angle Improves Detection of Musical Sound Quality Deterioration Related to Bass Frequency Removal. *Otol. Neurotol.* 2016, 37, 146–151.
53. Munjal, T.; Roy, A.T.; Carver, C.; Jiradejvong, P.; Limb, C.J. Use of the Phantom Electrode strategy to improve bass frequency perception for music listening in cochlear implant users. *Cochlear Implant. Int.* 2015, 16, S121–S128.
54. Ishiyama, A.; Doherty, J.; Ishiyama, G.; Quesnel, A.M.; Lopez, I.; Linthicum, F.H. Post Hybrid Cochlear Implant Hearing Loss and Endolymphatic Hydrops. *Otol. Neurotol.* 2016, 37, 1516–1521.
55. Li, Q.; Lu, T.; Zhang, C.; Hansen, M.R.; Li, S. Electrical stimulation induces synaptic changes in the peripheral auditory system. *J. Comp. Neurol.* 2020, 528, 893–905.

56. O'Leary, S.; Monksfield, P.; Kel, G.; Connolly, T.; Souter, M.; Chang, A.; Marovic, P.; O'Leary, J.; Richardson, R.; Eastwood, H. Relations between cochlear histopathology and hearing loss in experimental cochlear implantation. *Hear. Res.* 2013, 298, 27–35.
57. Scheperle, R.A.; Tejani, V.D.; Omtvedt, J.K.; Brown, C.J.; Abbas, P.J.; Hansen, M.R.; Gantz, B.J.; Oleson, J.J.; Ozanne, M.V. Delayed changes in auditory status in cochlear implant users with preserved acoustic hearing. *Hear. Res.* 2017, 350, 45–57.
58. Tarabichi, O.; Jensen, M.; Hansen, M.R. Advances in hearing preservation in cochlear implant surgery. *Curr. Opin. Otolaryngol. Head Neck Surg.* 2021, 29, 385–390.
59. Usami, S.-I.; Moteki, H.; Tsukada, K.; Miyagawa, M.; Nishio, S.-Y.; Takumi, Y.; Iwasaki, S.; Kumakawa, K.; Naito, Y.; Takahashi, H.; et al. Hearing preservation and clinical outcome of 32 consecutive electric acoustic stimulation (EAS) surgeries. *Acta Oto-Laryngol.* 2014, 134, 717–727.
60. Friedland, D.R.; Runge-Samuelson, C. Soft Cochlear Implantation: Rationale for the Surgical Approach. *Trends Amplif.* 2009, 13, 124–138.
61. Lehnhardt, E. Intracochlear placement of cochlear implant electrodes in soft surgery technique. *HNO* 1993, 41, 356–359.
62. Wang, Z.; Li, J.; Wu, Y.; Zhu, R.; Wang, B.; Zhao, K. Optimal path generation in scala tympani and path planning for robotic cochlear implant of perimodiolar electrode. *Proc. Inst. Mech. Eng. Part H J. Eng. Med.* 2020, 234, 578–589.
63. Yasin, R.; Dedmon, M.; Dillon, N.; Simaan, N. Investigating variability in cochlear implant electrode array alignment and the potential of visualization guidance. *Int. J. Med. Robot. Comput. Assist. Surg.* 2019, 15, e2009.
64. Zhang, J.; Wei, W.; Ding, J.; Roland, J.T., Jr.; Manolidis, S.; Simaan, N. Inroads Toward Robot-Assisted Cochlear Implant Surgery Using Steerable Electrode Arrays. *Otol. Neurotol.* 2010, 31, 1199–1206.
65. Dexamethasone-Eluting Cochlear Implant Electrode (CIDEX). Available online: <https://clinicaltrials.gov/ct2/Show/NCT04450290> (accessed on 6 March 2022).
66. De Seta, D.; Daoudi, H.; Torres, R.; Ferrary, E.; Sterkers, O.; Nguyen, Y. Robotics, automation, active electrode arrays, and new devices for cochlear implantation: A contemporary review. *Hear. Res.* 2022, 414, 108425.
67. Jiam, N.T.; Jiradejvong, P.; Pearl, M.S.; Limb, C.J. The Effect of Round Window vs. Cochleostomy Surgical Approaches on Cochlear Implant Electrode Position: A Flat-Panel Computed Tomography Study. *JAMA Otolaryngol.-Head Neck Surg.* 2016, 142, 873–880.

68. Kronenberg, J.; Migirov, L.; Baumgartner, W.D. The Suprameatal Approach in Cochlear Implant Surgery: Our Experience with 80 Patients. *ORL J. Otorhinolaryngol. Relat. Spec.* 2002, 64, 403–405.
69. Luers, J.C.; Hüttenbrink, K.; Beutner, D. Surgical anatomy of the round window-Implications for cochlear implantation. *Clin. Otolaryngol.* 2018, 43, 417–424.
70. Carlson, M.L.; O'Connell, B.P.; Lohse, C.M.; Driscoll, C.L.; Sweeney, A.D. Survey of the American Neurotology Society on Cochlear Implantation: Part 2, Surgical and Device-Related Practice Patterns. *Otol. Neurotol.* 2018, 39, e20–e27.
71. Wanna, G.B.; Noble, J.H.; Carlson, M.L.; Gifford, R.; Dietrich, M.S.; Haynes, D.S.; Dawant, B.M.; Labadie, R.F. Impact of electrode design and surgical approach on scalar location and cochlear implant outcomes. *Laryngoscope* 2014, 124 (Suppl. 6), S1–S7.
72. Breinbauer, H.A.; Praetorius, M. Variability of an Ideal Insertion Vector for Cochlear Implantation. *Otol. Neurotol.* 2015, 36, 610–617.
73. Adunka, O.F.; Dillon, M.T.; Adunka, M.C.; King, E.R.; Pillsbury, H.C.; Buchman, C.A. Cochleostomy Versus Round Window Insertions: Influence on functional outcomes in electric-acoustic stimulation of the auditory system. *Otol. Neurotol.* 2014, 35, 613–618.
74. Hassepass, F.; Aschendorff, A.; Bulla, S.; Arndt, S.; Maier, W.; Laszig, R.; Beck, R. Radiologic Results and Hearing Preservation With a Straight Narrow Electrode via Round Window Versus Cochleostomy Approach at Initial Activation. *Otol. Neurotol.* 2015, 36, 993–1000.
75. Adunka, O.; Unkelbach, M.H.; MacK, M.; Hambek, M.; Gstöettner, W.; Kiefer, J. Cochlear implantation via the round window membrane minimizes trauma to cochlear structures: A histologically controlled insertion study. *Acta Oto-Laryngol.* 2004, 124, 807–812.
76. Jwair, S.; Boerboom, R.A.; Versnel, H.; Stokroos, R.J.; Thomeer, H.G.X.M. Evaluating cochlear insertion trauma and hearing preservation after cochlear implantation (CIPRES): A study protocol for a randomized single-blind controlled trial. *Trials* 2021, 22, 895.
77. Moran, M.; Dowell, R.C.; Iseli, C.; Briggs, R.J.S. Hearing Preservation Outcomes for 139 Cochlear Implant Recipients Using a Thin Straight Electrode Array. *Otol. Neurotol.* 2017, 38, 678–684.
78. Labadie, R.F.; Schefano, A.D.; Holder, J.T.; Dwyer, R.T.; Rivas, A.; O'Malley, M.R.; Noble, J.H.; Dawant, B.M. Use of intraoperative CT scanning for quality control assessment of cochlear implant electrode array. *Acta Oto-Laryngol.* 2020, 140, 206–211.
79. Jia, H.; Torres, R.; Nguyen, Y.; De Seta, D.; Ferrary, E.; Wu, H.; Sterkers, O.; Bernardeschi, D.; Mosnier, I. Intraoperative Conebeam CT for Assessment of Intracochlear Positioning of Electrode Arrays in Adult Recipients of Cochlear Implants. *Am. J. Neuroradiol.* 2018, 39, 768–774.

80. Labadie, R.F.; Noble, J.H.; Hedley-Williams, A.J.; Sunderhaus, L.W.; Dawant, B.M.; Gifford, R. Results of Postoperative, CT-based, Electrode Deactivation on Hearing in Prelingually Deafened Adult Cochlear Implant Recipients. *Otol. Neurotol.* 2016, 37, 137–145.
81. Widmann, G.; Dejaco, D.; Luger, A.; Schmutzhard, J. Pre- and post-operative imaging of cochlear implants: A pictorial review. *Insights Imaging* 2020, 11, 93.
82. Littlefield, P.D.; Richter, C. Near-infrared stimulation of the auditory nerve: A decade of progress toward an optical cochlear implant. *Laryngoscope Investig. Otolaryngol.* 2021, 6, 310–319.
83. Dombrowski, T.; Rankovic, V.; Moser, T. Toward the Optical Cochlear Implant. *Cold Spring Harb. Perspect. Med.* 2019, 9, a033225.
84. Bennion, D.M.; Horne, R.; Peel, A.; Reineke, P.; Henslee, A.; Kaufmann, C.; Guymon, C.A.; Hansen, M.R. Zwitterionic Photografted Coatings of Cochlear Implant Biomaterials Reduce Friction and Insertion Forces. *Otol. Neurotol.* 2021, 42, 1476–1483.
85. Astolfi, L.; Simoni, E.; Giarbini, N.; Giordano, P.; Pannella, M.; Hatzopoulos, S.; Martini, A. Cochlear implant and inflammation reaction: Safety study of a new steroid-eluting electrode. *Hear. Res.* 2016, 336, 44–52.
86. Wey, K.; Schirrmann, R.; Diesing, D.; Lang, S.; Brandau, S.; Hansen, S.; Epple, M. Coating of cochlear implant electrodes with bioactive DNA-loaded calcium phosphate nanoparticles for the local transfection of stimulatory proteins. *Biomaterials* 2021, 276, 121009.
87. Yin, L.X.; Barnes, J.H.; Saoji, A.A.; Carlson, M.L. Clinical Utility of Intraoperative Electrocochleography (ECochG) During Cochlear Implantation: A Systematic Review and Quantitative Analysis. *Otol. Neurotol.* 2021, 42, 363–371.
88. Hans, S.; Arweiler-Harbeck, D.; Kaster, F.; Ludwig, J.; Hagedorn, E.; Lang, S.; Meyer, M.; Holtmann, L.C. Transimpedance Matrix Measurements Reliably Detect Electrode Tip Fold-over in Cochlear Implantation. *Otol. Neurotol.* 2021, 42, e1494–e1502.
89. Söderqvist, S.; Lamminmäki, S.; Aarnisalo, A.; Hirvonen, T.; Sinkkonen, S.T.; Sivonen, V. Intraoperative transimpedance and spread of excitation profile correlations with a lateral-wall cochlear implant electrode array. *Hear. Res.* 2021, 405, 108235.

Retrieved from <https://encyclopedia.pub/entry/history/show/55706>