THE EFFECT OF SURGICAL APPROACH ON HEARING PRESERVATION IN COCHLEAR IMPLANT PATIENTS

A thesis submitted in fulfilment of the requirement for the degree of

Doctor of Philosophy

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The Faculty of Brain Science, Ear Institute

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Declaration

I, Ibrahim BU SAAD, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated. All participating subjects gave informed consent, and all work was carried out with the approval of the health and research authority, according to guidelines established by the Declaration of Helsinki.

The work was done under the guidance of Professor Shakeel Saeed at the cochlear implant department Royal National Throat, Nose and Ear Hospital and the UCL Ear Institute, and Dr Ghada Almalky, at the Ear Institute- UCL.

Signature:

Date:

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Abstract of the thesis

Background

Preservation of residual hearing (RH) in cochlear implantation is important for speech perception, hearing in noise, and music quality. In addition, preserving intra-cochlear structures may allow patients to benefit from future therapeutic advances. Successful hearing preservation (HP) is multifactorial, and the effects of certain surgical techniques remain subject to debate.

Objectives

i. To review the literature on the effect of electrode array insertion surgery on hearing preservation (HP). ii. Compare the round window (RW) approach to cochleostomy (CY) in terms of HP, speech perception, electrode array dislocations, and insertion depth. iii. Investigate the relationship between electrode dislocation, insertion depth, HP, and speech perception. iv. Evaluate current surgical practice of HP in the United Kingdom.

Methods

The thesis aims were addressed by; i. completing a comprehensive evaluation of the current evidence on the influence of surgical electrode placement on HP; ii. a retrospective study that examined surgical approach, cochlear size, electrode array placement, insertion depth, and HP; iii. a web-based survey that evaluated current surgical practise of HP CI; and iv. a randomised controlled trial (RCT) with double-blinding that compared radiological and audiological outcomes of both approaches and investigated the correlation between insertion accuracy and insertion depth.

Results

The literature showed achievable HP with both approaches, heterogeneity in the inclusion criteria, and quantifying methods of HP. Most CI surgeons in the UK use RW for standard and HP patients, CY as an alternative, use intra-operative corticosteroids and antibiotics. However, there is disagreement on medical regimens and indications for HP protocols. CY approach had superior HP, which was significant at 1 and 3 months. Speech perception, accuracy of insertion, and insertion depth are not significantly different between approaches. Insertion accuracy significantly correlates with depth. Insertion depth, HP, and speech perception scores did not correlate.

Conclusion

This thesis examined HP surgery. Cochlear implant procedures have changed over time. Recent medical literature reports few CY cases, making comparisons difficult. Most surgeons in the UK use RW as the normal treatment and CY as an alternative, which limits retrospective studies. The RCT study overcame previous controversies and limitations in the literature. The RCT provided in this thesis shows that the CY has better HP only in the short term and there is no significant difference between both approaches after that. This allows surgeons to abandon a difficult RW operation and switch to CY. When protecting hearing, insertion depth shouldn't be a priority. Resistance during insertion may suggest trauma. HP surgeries need national and international guidelines to improve surgical outcomes.

Impact statement

Cochlear implants (CIs) are an established treatment option for individuals with severe-to-profound sensorineural hearing loss (SNHL) who obtain little or no benefit from hearing aids. CIs have evolved beyond the phases of concept and benefit demonstration and their applications have been expanded to include patients with some residual hearing (RH). Atraumatic insertion of the electrode array helps to preserve intra-cochlear structures and RH. The benefits of preserving RH include enhanced speech comprehension in challenging environments, enhanced sound localisation, and enhanced music appreciation. Hearing preservation (HP) is feasible and achievable; however, the impact of different surgical procedures is still unclear. Therefore, it is necessary to understand and optimise the effects of surgical procedures to increase and maintain the quality of outcomes.

Despite efforts to enhance HP surgery, the effects of the route of electrode array insertion (round window vs cochleostomy) and the depth of insertion remain open to debate. This may be attributed to the ongoing enhancements and multifactorial nature of this surgery that limit comparability between studies. The majority of the published research on this subject consists of retrospective studies, and the level of evidence is low as most studies have many limitations and include some elements of bias.

The work presented in this thesis assesses the available evidence in the literature, the current practice of CI surgeons in the UK, and bridges the evidence gap by conducting a double-blinded randomised controlled trial (RCT) that overcame the limitations of earlier studies. This study is the first RCT to investigate this topic.

This study randomly assigned participants to one of two surgical procedures to enter the cochlea: round window or cochleostomy. This helped to investigate the effect of surgical approach in an accurate way, as the majority of evidence in the literature compared the outcomes of both approaches when the cochleostomy approach was utilised under unfavourable anatomical conditions. The orientation of the round window influences the electrode trajectory toward the modiolus, which might increase the risk of intra-cochlear trauma with either surgical technique. The randomisation in this study helped us to control for this variable. The findings of this study will assist CI surgeons and improve patient outcomes by addressing some of the limitations in the existing literature.

With regards to the limitations in the literature, it is essential to understand the practice and perspectives of surgeons in the field. The contemporary practise of CI surgeons in the UK was assessed. Assessing the current practice was an important step in linking surgical practice with research. The study was limited to consultant CI surgeons; hence, its findings represent the opinion and depth of experience and constitute an important addition to the existing literature. The findings of our survey and the randomised controlled trial will serve to identify the direction of future HP surgeries, standardise the practice locally and internationally to optimise HP outcomes, and enable future studies to be comparable.

Publications and presentations emanating from this work

- Bu Saad I, Almalki G, Saeed S. 'The effect of surgical approach on hearing preservation using flexible atraumatic moderate length electrode array, a systematic review'. Published as a poster presentation in the BCIG conference, Belfast (17-18 May 2018)
- Bu Saad I, Almalki G, Saeed S. 'Predicting scalar position of electrode array using CBCT and its correlation with the surgical approach, cochlear size and the level of hearing preservation'. Published as Poster presentation in the BAA conference, Liverpool (8-9 November 2018)
- Bu Saad I, Almalki G, Saeed S. 'The effect of surgical approach on hearing preservation using flexible atraumatic moderate length electrode array, a systematic review'. Published as a poster presentation in the BAA conference, Belfast (8-9 November 2018).
- Bu Saad I, silver B, Nash R, Saeed S. 'A survey of cochlear implant surgical practice for hearing preservation in the United Kingdom'. Published as a poster presentation in the BCIG conference, Belfast (11-12 May 2021).
- Bu Saad I, Nash R, Vickers D, Saeed S. 'A randomised controlled trial examining the effect of surgical approach on hearing preservation in cochlear implant surgery: Preliminary Results'. Published as a poster presentation in the BCIG conference, Belfast (11-12 May 2021).

Potential Publications

- A survey of cochlear implant surgical practice for hearing preservation in the United Kingdom.
- A randomised controlled trial examining the effect of surgical approach on hearing preservation in cochlear implant surgery: Preliminary Results.
- A randomised controlled trial examining the relationship between surgical approach and the level of hearing preservation- 12months follow-up.

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Abbreviations

Abbreviations

AB	Advanced Bionics
AB	Antibiotic
BCIG	British Cochlear Implant Group
BKB	Bamford-Kowal-Bench test
CBCT	Cone-beam computer tomography
CI	Cochlear implant
CT	computed tomography
CY	Cochleostomy
EAS	Electro-acoustic stimulus
ECohG	Electrocochleography
HP	Hearing preservation
LW	Lateral wall electrode
IHC	Inner hair cell
MS	Mid-Scala electrode array
SM	Scala media
ST	Scala tympani
SV	Scala vestibuli
OHC	Outer hair cell
PM	Perimodiolar electrode
PST	Possible Scala tympani
PSV	Possible scala vestibuli
PTA	Pure-tone Audiometry
RNTNEH	The Royal National Throat, Nose and Ear Hospital

RW	Round window
RH	Residual hearing
WHO	World Health Organisation
95% CI	95% Confidence Interval
UK	United Kingdom
USA	United State of America

Chapter 1 : Introduction

1.1 Anatomy

1.1.1 The external and middle ear

The ear is one of the most complex organs in the human body and provides the senses of hearing and balance. The ear comprises three parts: the external, middle, and inner ear. The external ear consists of the pinna (auricle) and external auditory canal. The function of the external ear is sound collection and transmission to the tympanic membrane. Moreover, the structure of the external ear aids in its function as a resonator (Wright and Valentine, 2008, Gates and Mills, 2005).

The middle ear is the space located between the tympanic membrane and osseous labyrinth. The middle ear consists of the tympanic cavity, ossicular chain bones and their muscles, the system of mastoid air cells, and the Eustachian tube. The middle ear transmits sound from the tympanic membrane to the inner ear. The tympanic membrane consists of three layers: the squamous epithelial cell layer, middle fibrous layer, and medial mucosal layer. The membrane allows for transmission of acoustic sound waves from the external auditory canal to the ossicular chain in the middle ear. The ossicular chain consists of three bones: the malleus, incus, and stapes. The first bone is the most lateral and is attached to the tympanic membrane; the last bone is attached to the oval window. The ossicular chain helps couple acoustic sound energy through the middle ear to the inner ear (Wright and Valentine, 2008).

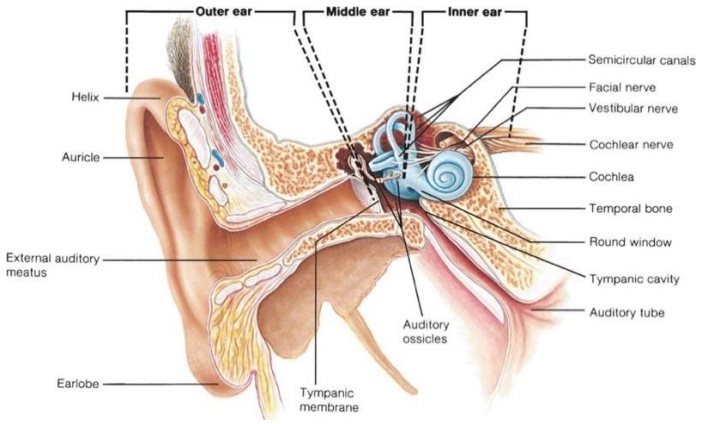

Figure 1-1 The anatomy of the human ear.
Adapted from Wikimedia Commons contributors (2022a)

1.1.2 The inner ear

The inner ear is in the otic capsule, which is located in the petrous part of the temporal bone. The inner ear consists of the cochlea and the vestibular system.

1.1.2.1 The Cochlea

The cochlea is a spiral tubular structure consisting of two and three-fourth turns (Hardy, 1938). Cochlear length varies among humans and can reach up to three turns (Biedron et al., 2009). The length of the human cochlea duct ranges between 25.5 and 35.1 mm (Lee et al., 2010b). The cochlea consists of three tubular compartments known as the scala vestibuli (SV), scala tympani (ST), and scala media (SM). The first two scala (ST and SV) are the outer compartments and are filled with sodium-ion rich peri-lymphatic fluid, while the third scala is filled with potassium-ion rich endolymphatic fluid (Sterkers et al., 1988). The basal part of the cochlea contains the oval window and the round window (RW). The oval window is connected to the footplate of the stapes, which transmits sound to the SV. The SV extends from the oval window to the apex of the cochlea, the helicotrema; the ST begins at the RW and converges with the SV at the helicotrema (Furness and Hackney, 2008, Sterkers et al., 1988).

The scala media is an extension of the membranous labyrinth. Its appearance in cross-section is like a triangle. It is located between both the SV and the ST. It is separated from the SV by Reissner's membrane and from the ST by the basilar membrane (BM). Reissner's membrane extends between the spiral limbus at the SM and the lateral bony wall. It consists of two layers of cells: the epithelial cell layer facing the SM, and the mesothelial layer facing the SV. Reissner's membrane is involved in homeostasis between the two compartments.

The BM forms the floor of the SM and separates it from the ST. It consists of connective tissue and extends medially from the osseous spiral lamina to the spiral ligament. It is stiffer at the basal area and thinner at the apex. This gradual change in stiffness from the base to the apex plays a vital role in tonotopy. At the lateral wall of the cochlear duct, the spiral ligament anchors the BM to the lateral cochlear wall. In addition to the mechanical function of the spiral ligament, it plays an important role together with the stria vascularis in the maintenance of cochlear homeostasis (Furness and Hackney, 2008, Krstic, 1991).

The SM includes endolymph. Endolymph is a potassium (K+)-rich fluid (approximately 140 mM) that is low in sodium ions (Na+) and differs from the majority of extracellular fluids in composition. The endolymph within the cochlea has a strong positive electrical potential (about +80 mV), known as the endocochlear potential. The SM is electrically and chemically insulated from the scala tympani (ST) and scala vestibuli (SV). Both ST and SV are filled with perilymph, a fluid with high sodium (Na+) and low potassium ion (K+) concentrations. Auditory function is dependent on the proper separation of the two fluids at the junctions of the epithelial cells enclosing the endolymphatic space to maintain the endocochlear potential (Forge and Wright, 2002).

1.1.2.2 The organ of Corti

The organ of Corti is located in the SM and rests on top of the BM. It is the receptor organ of hearing, and it consists of sensory and supporting cells. The sensory cells cover the surface of the organ of Corti and consist of outer hair cells (OHCs) and inner hair cells (IHCs). The supporting cells are attached to the BM and consist of Deiter's cells, Henson's cells, inner phalangeal cells, and Claudius cells.

The organ of Corti consists of 3–4 rows of OHCs and a single row of IHCs. The average number of hair cells in an adult range from 9000 to 10000 OHCs and ~3000 IHCs (Forge and Wright, 2002, Wright, 1983). IHCs are located medially, near the sulcus and modiolus, while OHCs are located at the outer part of the organ of Corti.

Numerous stereocilia bundles project from the top of each hair cell towards the tectorial membrane. The stereocilia of OHCs are organised in rows of 'V'- or 'W'-shaped structures and contact the tectorial membrane. Similarly, IHCs have bundles of stereocilia that project towards the middle of the SM; however, they do not make contact with the tectorial membrane (Furness and Hackney, 2008). The function of IHCs is to sense sound and provide signal output to the spiral ganglion and auditory cortex, while the OHCs are responsible for sound amplification and frequency selectivity (Ashmore and Kolston, 1994, Fettiplace and Hackney, 2006).

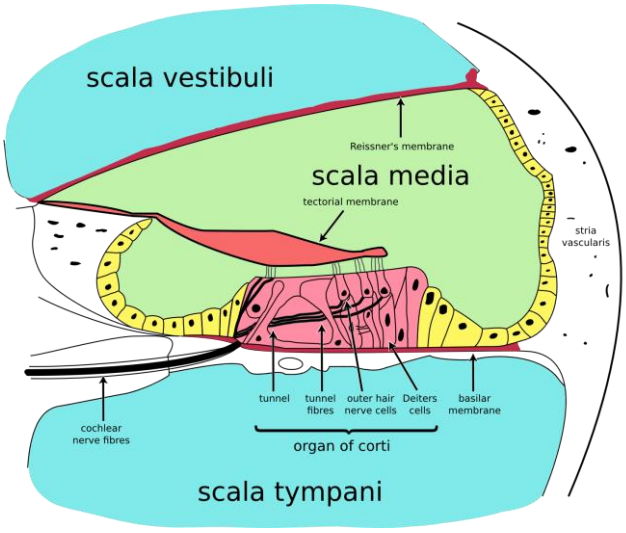

Figure 1-2 The organ of Corti
Adapted from Wikimedia Commons contributors (2021)

1.1.2.2.1 Acoustic hearing

The external ear collects sound waves and transmits them to the tympanic membrane. The vibrations of the tympanic membrane transmit the sound through the ossicular chain in the middle ear to the oval window. When the footplate of stapes moves the oval window, the mechanical compression moves the perilymph in the SV. The magnitude of pressure at the oval window is about 20 times the pressure at the tympanic membrane. This increase in the magnitude of the pressure occurs due to the difference between the surface area of the tympanic membrane and the oval window, as well as the lever effect caused by the length difference between the malleus and incus (Voss et al., 1996).

Perilymph movement is transmitted through the SV to the helicotrema and back through the ST to the RW. The RW baffles out to release the pressure. As the perilymph moves, Reissner's membrane and the BM move on both sides of the SM, transmitting the signal to the organ of Corti (Barrett et al., 2016).

1.1.2.2.2 Cochlear tonotopy

The range of frequencies that the human ear can hear is from 20 Hz to 20,000 Hz (20 kHz), yet most speech frequencies fall between 100 and 4,000 Hz. Frequencies above 20,000 Hz are referred to as ultrasonic, which are outside of human perception, while many animals can hear them (Yost, 2001). The width and rigidity of the BM vary along its length. This variation in these properties leads to stimulation of specific hair cells in relation to the sound frequency (tonotopy) (Voldrich, 1978, Dallos, 1996). The BM at the basal part is narrower and thicker than at the apical turn (Wever et al., 1971, Liu et al., 2015a). Because of this variation, hair cells at the basal turn are activated at high frequencies, and apical hair cells respond to lower frequencies (Echteler et al., 1994, Fettiplace and Fuchs, 1999).

The movement of the BM leads to a shearing effect between the OHCs and their stereocilia, which are impeded in the tectorial membrane. The movement of the stereocilia tips leads to the opening of mechanosensitive channels (Hudspeth and Jacobs, 1979). The hair cells depolarise as potassium ions move from the endolymph into the cells. Hair cell depolarisation triggers voltage-gated calcium channels, with subsequent calcium influx that activates neurotransmitter (mainly glutamate) release and converts the action potentials into neurological signals, which transmit through the

auditory nerve. The neurological action ceases when the stereocilia bend back in the opposite direction to the resting position (Hackney and Furness, 1995, Farris et al., 2006).

1.1.2.2.3 Innervation of the organ of Corti

The cochlear cells are connected to the auditory nervous system with the auditory nerve. The auditory nerve consists of afferent and efferent nerve fibbers, which leaves the organ of Corti leading to the cell bodies in the spiral ganglion in the modiolus and then to the to the internal auditory meatus. The neural fibers that originate from the apex (low frequency fibres) form the trunk of the nerve, where the fibers that originate from the base (high frequency fibres) are at the periphery. Tonotopycity is maintained along the length of the ascending auditory route all the way to the cortex (Gelfand, 2010, Saenz and Langers, 2014).

The afferent nerve fibres form the ascending sensory neurons, which send the signals from the cochlea to the nervous system. The majority of the afferent nerve fibres (90-95 %) arise from the IHC, the remaining 5-10 % arises from the OHC. The IHC are extensively innervated by afferent auditory neurons; each IHC receives approximately 20 inner radial nerve fibres, which continue as type 1 auditory neurons outside of the organ of Corti. Type 1 auditory neurons are bipolar neurons.

In contrast, the neuronal fibres that innervate the OHC are pseudounipolar and send collateral fibres to about ten OHC. Moreover, each OHC revises collateral fibers from many neurons. These neural fibres are known as outer spiral fibres and continue outside the organ of Corti as type 2 auditory neurons (Raphael and Altschuler, 2003). OHCs differ from IHCs in that there is a lack of synaptic ribbons at the presynaptic terminal and far fewer neurotransmitter-containing vesicles present. When stimulated, OHCs do release neurotransmitter in response to transduction currents at the basal ends of the cells, however, there is a relatively poor synaptic transfer compared to IHCs (Gelfand, 2010).

The efferent nerve fibres compose the descending neurons that transmit signals from the central nervous system to the cochlea via the olivocochlear bundle, which is a network of descending pathways from the superior olivary complex to the cochlea. The ending of the efferent neurons has vesicles that contain the chemical transmitter acetylcholine, and they synapse differently with the OHCs and IHCs. The efferent

innervation to the organ of Corti mainly consists of medial olivocochlear efferent fibres connecting directly with OHCs (presynaptically), innervating both the ipsilateral and contralateral cochlea. In contrast, the lateral olivocochlear efferent fibres, which originate in the lateral superior olive, synapses with the afferent neurons below the IHCs of the contralateral cochlea. These configurations reflect the primary functions of the hair cells: the IHCs as receptors and the OHCs as modulators (Forge and Wright, 2002, Gelfand, 2010).

1.2 Hearing loss

1.2.1 Classification of hearing loss

Hearing loss (HL) occurs due to congenital or acquired causes and is classified into conductive, sensorineural, and mixed HL (Kochhar et al., 2007).

Conductive hearing loss (CHL) occurs due to a pathology affecting sound conduction in the external or middle ear. Examples of the former include cerumen impaction, foreign body obstruction of the external auditory meatus, canal atresia, exostoses of the external auditory meatus, and otitis externa with pronounced swelling. In contrast, middle ear disease leads to temporary and fluctuating HL or progressive HL. Examples of middle ear pathologies include otitis media with effusion, tympanic membrane retraction or perforation, otosclerosis, ossicular chain discontinuity or malformation, temporal bone fracture, and cholesteatoma (Kochhar et al., 2007).

Sensorineural hearing loss (SNHL) occurs due to a pathology affecting the cochlea, auditory nerve, or auditory pathway. SNHL can be hereditary or acquired. Examples of acquired SNHL include drug-induced HL (e.g., gentamicin), age-related degeneration (presbycusis), noise-induced HL, and other diseases, like Meniere's disease. Congenital SNHL has been reported in 2-4 in every 1000 births (Ahmed et al., 2018). SNHL might be non-syndromic, such as connexin-26 HL, or syndromic. Examples of syndromic SNHL include Pendred syndrome, Usher's syndrome, and Waardenburg's syndrome. Rubella and pneumococcal meningitis are common infections that can lead to SNHL (Vynnycky et al., 2016, Renauld and Basch, 2021).

Mixed hearing loss (MHL) involves combined conductive and sensorineural pathology. In some cases, a single cause can explain the presence of a mixed loss (such as otosclerosis that begins to invade the cochlea itself). In other instances, it may indicate distinct underlying reasons, such as an infection of the middle with a previous sensorineural hearing loss (Kochhar et al., 2007, Wright and Valentine, 2008).

1.2.2 Severity of HL

There are several classifications for the severity of HL. The quantitative grading of the British Society of Audiology classifies HL into five categories according to the unaided hearing threshold (Table 1-1). The hearing threshold is determined at the lowest level, where patients respond more than 50% of the time. The severity of HL is defined based on the average pure tone threshold at 250, 500, 1000, 2000, and 4000 Hz. The severity of HL ranges from mild HL, where the hearing threshold is higher than 20 dB and lower than 40 dB, to profound HL, where the hearing threshold is higher than 95 dB.

Table 1-1 British Society of Audiology definition of hearing loss.

Severity of hearing loss	Hearing threshold (dB)
Normal	0–20
Mild HL	21–40
Moderate HL	41–70
Severe HL	71–95
Profound HL	>95

British Society of Audiology (2011)

1.3 Cochlear implants as treatment for hearing loss

Management of HL depends on type and severity of the HL. The current available management tools include hearing aids, middle ear implants, bone conduction hearing aids, and cochlear and brainstem implants. Cochlear implants are a globally accepted management for profound SNHL and are considered the most successful implantable prosthesis for sensory organs. According to the National Institute on Deafness and Other Communication Disorders (2019), the current number of registered cochlear implant (CI) devices is more than 736,900 devices worldwide.

The cochlea is the primary lesion site in most SNHL conditions, where the IHCs fail to transduce the acoustic signal and convert it to neural impulses (Cosetti and Waltzman, 2011). The CI converts acoustic sound into a coded electrical signal. The electrode array of the CI is inserted into the cochlea, bypasses the damaged or absent IHCs, and deliver the stimulus directly to the spiral ganglion and auditory nerve (Wilson and Dorman, 2009).

1.3.1 Components of cochlear implants

A CI is a semi-implantable device that has an internal and external component (Figure 1-3). The external component consists of a microphone, sound processor, battery, and coil. In some models, the microphone and speech processor are placed in a small unit that looks like a behind-the-ear hearing aid and has a thin wire that usually connect them to the coil, which is positioned over the internal part of the device. Other models are designed as a single unit processor and are worn on the head directly over the device's internal component. The internal component (i.e., the implant) consists of a receiver and electrode array that is inserted in the cochlea. The electrode array consists of a group of channels ranging between 12 to 22 channels, depending on the manufacturer. The internal part has one or more reference electrodes, depending on the manufacturer.

The function of the CI starts when the microphone receives the sound and sends it to the sound processor. With the use of different speech strategies, the processor converts the sound to frequency-specific channels. The coil uses a radiofrequency to transmit this coded information through the skin to the receiver in the implanted component. The receiver converts the information into pulses of electrical stimuli, which pass through the channels in the electrode array to stimulate the spiral ganglion and the auditory nerve (Wolfe and Schafer, 2015).

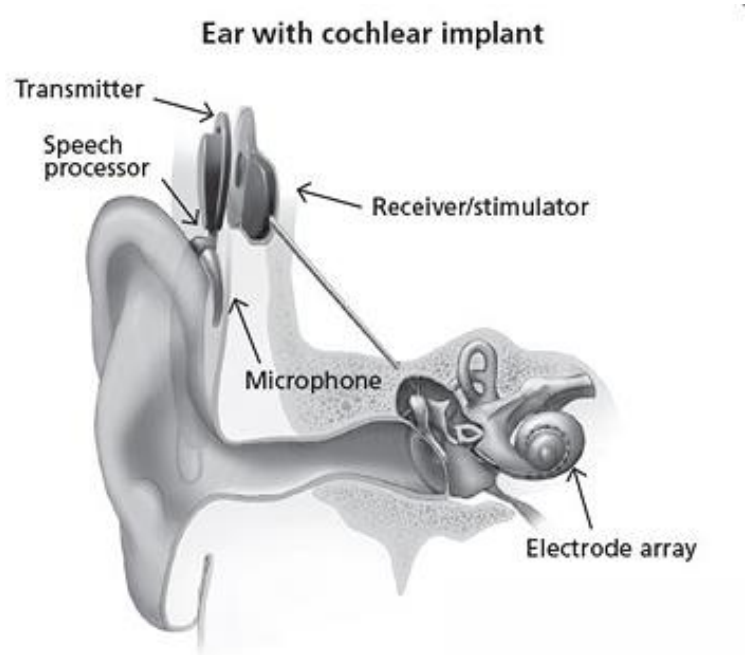

Figure 1-3 Components of the cochlear implant.
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1.3.2 Indication of cochlear implants

The candidacy criteria for CI have gradually changed over the years. In the early days, CI was limited to patients with profound bilateral SNHL, and it was recommended to implant a single side. Over time, the criteria expanded to include patients with residual hearing (RH), and minimal traumatic surgery became the standard of practice in many centres. There are no worldwide candidacy criteria or guidelines for cochlear implantation. However, providing CIs to patients with profound SNHL and speech recognition scores of less than 50% in the best-aided condition is broadly accepted, although signal level varies (70- 90 dBA) (Vickers et al., 2016).

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines (2019) advocate the candidacy criteria for cochlear implantation. The adult criteria include patients with a bilateral unaided hearing threshold equal to or greater than 80 dB HL at two or more frequencies (500–4000 Hz) and who have limited benefit from the hearing aid. The patient's Arthur Boothroyd word test score must be less than 50% in the best-aided condition when the signal is presented at a 70-dBA. In children, other factors are considered, including cognitive ability, developmental stage, and aged-appropriate speech and language skills. Children and adults with dual sensory impairments are offered simultaneous bilateral CIs; other adults are offered single implants (NICE, 2019).

1.3.3 Variability in patient outcomes

Several studies have reported a significant post-implantation improvement in life quality and speech perception ability, especially in noisy environments (Santa Maria et al., 2013, Erixon and Rask-Andersen, 2015). Bilateral cochlear candidates have shown improved speech perception in noisy environments and sound localisation (Gaylor et al., 2013). Although cochlear implantation has been proven to help patients with profound HL, there is unexplained variability in patient outcomes. Many studies reported extensive heterogeneity in hearing outcomes and speech perception scores following unilateral and bilateral cochlear implantation (Blamey et al., 2013, Mosnier et al., 2009, Holden et al., 2013).

Several factors have been identified that affect patient outcomes, including the duration of HL, the use of hearing aids before CI surgery, the preoperative RH score and speech perception score, the percentage of active electrodes, and the coding strategy (Lazard et al., 2012). Other surgical factors that have been investigated in several studies include surgical approach, electrode type, insertion depth, scalar electrode position in relation to the spiral ganglion, and electrode trauma (Finley et al., 2008). The effects of these factors on hearing preservation (HP) are discussed in section 1.4.3).

1.4 Hearing preservation in cochlear implantation

The concept of ‘soft surgery’ was first described by Lehnhardt (1993b). This procedure aims to preserve the intra-cochlear structure; however, patient outcomes have indicated the possibility of preserving some RH (Hodges et al., 1997). Soon after, von Ilberg et al. (1999) presented the idea of hybrid CIs that used electrode-acoustic stimuli. There is continuous improvement in technology and surgical procedures. HP surgery describes the soft surgical procedure used in patients with low-frequency RH. However, research has shown that the benefits of a soft surgical procedure are not limited to patients with RH; it helps to preserve intra-cochlear structures and allows patients to benefit from future innovations (Havenith et al., 2013, Carlson et al., 2011).

There is no standardised protocol for HP surgery. However, the steps of HP surgery include the selection of a thin, atraumatic electrode array, gentle drilling to avoid noise-induced damage, limited suction near the RW, prevention of bone dust and blood entering the cochlea, slow, gentle electrode insertion and stop at resistance, and the

use of intravenous or topical corticosteroids and prophylactic antibiotics (Bruce and Todt, 2018).

1.4.1 The importance of hearing preservation

There are two main advantages to HP. The first advantage is electro-acoustic stimulation for patients with RH at the low-frequency range, where the CI could be used to stimulate the spiral ganglion at basal frequencies, while the apical turn can be stimulated by the acoustic stimulus. Second, the presence of healthy hair cells and neural structures in the cochlea leads to better hearing tonotopicity and temporal response (Bas et al., 2012), which improves hearing in noisy environments and music appreciation (Gantz et al., 2005, Gfeller et al., 2006). Fraysse et al. (2006) reported that patients with RH performed better in the sentence recognition test (5 dB SNR) than patients who did not have RH.

Music perception has been evaluated in patients with RH and uses electro-acoustic stimulation (EAS). These patients performed better than patients who did not have a RH in recognising songs and melody; however, their recognition was less than normal listeners (Gfeller et al., 2008, Gfeller et al., 2012). Brockmeier et al. (2010) evaluated pitch discrimination in patients with RH and used EAS with long electrodes (Med EL, Combi40+); they found that the performance of these patients was better than patients with no RH. Moreover, the ability of EAS users did not change significantly when the EAS was turned off, which highlighted the importance of HP surgery and preserving intra-cochlear structures in patients who use EAS implants and those with conventional implants. Furthermore, preserving the cochlear structure allows patients to benefit from future inventions.

1.4.2 Aetiology of loss of residual hearing

Loss of RH might occur at an early or late stage after cochlear implantation. Several factors might trigger the loss of residual functional hair cells during or after cochlear implantation surgery. These factors can occur before electrode insertion, like noise trauma due to drilling, or during electrode insertion, including electrode trauma and insertion of blood or bone fragments. The long-term factors that occur after cochlear implantation include fibrosis and new bone formation (osteoneogenesis).

1.4.2.1 Early loss of RH due to trauma

Physical damage to intra-cochlear structures due to electrode array insertion results in early loss of RH, which can be measured shortly after the operation. During the electrode insertion stage, direct trauma may occur to the BM or hair cells, displacement of the electrode array through the SM to the SV, and damage to the osseous spiral lamina or modiolus. Surgical trauma leads to early RH loss, which is triggered by cell apoptosis, necrosis, and a necrosis-like reaction (Eshraghi, 2006, Dinh and Van De Water, 2009, Van De Water et al., 2010a). The exact pathophysiological mechanism of this process is not known (Jia et al., 2013); however, one of the mechanisms includes trauma that leads to the creation of free radicals of oxygen and other elements, which leads to cell apoptosis. Eshraghi (2006) reported a progressive increase in cellular apoptosis during the first 12, 24, and 36 hours after cochlear implantation surgery. The reactive oxygen species (ROS) pathway is considered the main contributing factor to RH loss after electrode trauma (Do et al., 2004, Eshraghi, 2006).

1.4.2.2 Delayed RH loss due to fibrosis and osteoneogenesis

Fibrosis and osteoneogenesis might occur after implantation and lead to delayed loss of RH. The effects of these processes might not be measurable for several months (Bas et al., 2012, Adunka and Kiefer, 2006, Nadol and Eddington, 2006, Li et al., 2007). Osteoneogenesis might develop over time due to the presence of bone fragments in the ST (Bas et al., 2012, Gstoettner et al., 2000), or due to trauma of the lateral wall (Li et al., 2007) or the spiral lamina (O'Leary et al., 2013).

Kamakura and Nadol (2016) reported that damage of the lateral wall or the spiral lamina was not correlated with new bone formation, while damage of both tended to lead to new bone formation. Moreover, they reported that the volume of new bone formation correlated with the severity of intra-cochlear trauma and the electrode length located in the SM, SV, or spiral ligament.

In contrast, Kamakura and Nadol (2016) found no significant correlation between the volume of fibrous tissue and intra-cochlear trauma, which suggests that fibrosis is not a result of electrode trauma, and that it might be a result of a foreign body reaction (Seyyedi and Nadol Jr, 2013). The exact mechanism of fibrosis in the cochlea is unknown; however, high levels of tumour-necrosis factor alpha (TNF-α) and interleukin

1β (IL-1β), ischemia, and presbycusis have been observed after acoustic trauma (Menardo et al., 2012).

The relationship between RW scarring and delayed HL has been studied in previous studies. As it is well-known that occluding the RW impedes the cochlear mechanics and the fluid motions within ST, occluding the RW may cause hearing loss. The impact of RW sealants and its relationship with delayed HL was investigated in previous animal studies (Rowe et al., 2016b, McLean et al., 2021, Rowe et al., 2016a). Rowe et al. (2016a) compared post-operative HL between cases that had RW insertion and cases that had RW incision without insertion. All cases were sealed with a muscle graft. The study reported delayed HL in both groups. This highlights the impact of any intervention on the RW membrane, which could affect the function of RW and the level of HP.

Another study conducted by Rowe et al. (2016b) investigated post-surgical changes in cochlear mechanics, related to the material used to seal the cochlea after round window implantation, which may contribute to this loss. The study reported that sealing the RW after CI leads to delayed loss in low-frequency threshold. All groups had delayed HL at 200Hz. The muscle graft group experienced the greatest deterioration in hearing threshold, followed by the periosteum group and finally the fibrine glue group. A more recent study investigated the effects of RW incision and sealing between four groups (McLean et al., 2021). The study included four groups, three of which had different sealant materials (muscle, fascia and fibrin sealant), and the fourth was a control. The control cases were incised but left unsealed. The study reported that the effect on the cochlear mechanics in all groups was not statistically significant. In addition, the study reported a significant drop in hearing over time but no significant difference between groups. Histological analysis showed more fibrosis in the fascia group and minimal difference in the OHC count between groups (McLean et al., 2021).

In the absence of clinical studies comparing the effects of various types of sealants in human studies, there is no standard procedure for RW sealing in clinical settings. Nevertheless, because prior research indicated that the RW's sealant may affect the outcomes of patients. It is suggested to avoid materials that result in the most severe scarring after surgery and to instead use fibrin glue or preferably no sealing (Rowe et al., 2016b), as some meta-analyses have questioned the safety of fibrin glue (Santa Maria et al., 2014).

1.4.3 Factors affecting hearing preservation

1.4.3.1 Surgical

1.4.3.1.1 History of surgical procedures

Lehnhardt (1993b) was the first to describe the soft surgical approach. This approach was initially used to preserve the cochlear structure and later for HP cases using EAS electrode arrays. A few years later, (Kiefer et al., 2004) improved the approach by using smaller drill size and slower drilling speed, cochleostomy (CY) instead of the RW, CY inferior to the mid-line of the RW to avoid any damage of the BM, and limiting the insertion depth to 20 mm (Campbell et al., 2013). To minimise trauma to the BM and spiral ganglion and for more reliable insertion into the ST, the approach was modified by Roland and Wright (2006) to have the CY anteroinferior to the RW.

1.4.3.1.2 Surgical approach: cochleostomy and round window

1.4.3.1.2.1 Histological studies

The RW acts as a permanent landmark for the ST that helps in the correct placement of the electrode array (Roland et al., 2007, Kang and Kim, 2013). However, the RW does not provide straight access to the ST and its visualisation is not clear in all patients, which might result in trauma (Bae et al., 2019, Pringle and Konieczny, 2021). This disadvantage was more obvious with old rigid arrays. In contrast, CY anteroinferior to the RW allows for direct access to the ST (Figure 1-4). It was thought that electrode insertion via the CY procedure might damage the BM and spiral ganglion. However, Addams-Williams et al. (2011) conducted a histological study on guinea pigs who had been implanted via a CY approach. At 4 weeks post-surgery, they found no evidence of spiral neuronal ganglion loss.

The orientation and visualisation of the RW and anatomical configuration of this narrow area significantly impacts the surgery, whether it uses a RW or CY approach (Campbell et al., 2013). Previous studies showed that the RW membrane cannot be visualised in 8% of patients, and it is partially (50% of the membrane) visualised in 20% of patients (Jiang and Fitzgerald O'Connor, 2007). Unfavourable orientation and decreased visualisation increase the risk of trauma due to electrode bending (Addams-Williams et al., 2011) or inaccurate placement of CY.

Electrode insertion through the CY approach requires drilling through the cochlear wall. The noise level generated by drilling during the CY might reach 110 dB when the

bony layer is very thin, and 130 dB when the membranous layer is fully exposed. Therefore, it is advised at this stage of the CY to stop drilling and use a needle to open the membranous labyrinth of the cochlea (Pau et al., 2007, Cipolla et al., 2012). Although drilling might lead to reactive inflammation (Roland, 2005, Nadol and Eddington, 2004), it was found that this inflammation was limited to the site of the CY (Addams-Williams et al., 2011). The use of corticosteroids and antibiotics might help in these conditions (Jia et al., 2013).

In contrast, the RW approach requires less drilling and the insertion happens through the natural opening of the RW, which minimises acoustic trauma. However, inserting the electrode array through the RW sacrifices the function of the RW membrane. Some studies found that the RW membrane might play a role in the immune defence (Addams-Williams et al., 2011) and the equilibrium of inner ear fluid, absorption and secretion (Goycoolea and Lundman, 1997). Therefore, damaging this membrane might affect its biological functions.

1.4.3.1.2.2 Clinical studies

Most articles investigating the relationship between surgical approaches and HP are retrospective, use a small sample size, and use variable electrodes. Two systematic reviews and two meta-analyses evaluated the effects of RW and CY approaches on HP (Havenith et al., 2013, Santa Maria et al., 2014, Causon et al., 2015, Snels et al., 2019), see Table 1-2. Havenith et al. (2013) concluded that there was no significant difference between both approaches, and further research is needed to produce more robust evidence. Santa Maria et al. (2014) found that the CY approach was superior to the RW approach. Both studies included a variety of electrodes, and they tried to be specific in their results by investigating HP across manufacturing companies, dates of publication, and electrode length. Results could be more accurate when variation is absolute. The third study was conducted by Causon et al. (2015) and investigated HP in EAS electrodes only, including both straight and pre-curved electrodes. Causon et al. (2015) reported that the RW approach was superior for HP. The last and the most recent systematic review and meta-analysis was conducted by Snels et al. (2019) and reported superiority of the RW approach during the first 6 months and found no significant difference between both approaches after that time. Considering the conflicting findings of these studies, it is difficult to reach a conclusion (Table 1-2). Santa Maria et al. (2014) suggested that the final shift in practice from CY to RW

happened quickly, with insufficient evidence. A shift in practice has been linked to the innovation of electrode arrays, as explained in the next section (1.4.3.1.2.3)

Table 1-2 A summary of previous systematic reviews and meta-analyses

Study	Study type	No. studies	Any RCT	No. cases	Age group	Age range	No. RW	No. CY	Main conclusion
Havenith et al. (2013)	SR	16	No	170	Not specific	N/A	103	67	No difference
Santa Maria et al. (2014)	MA	24	No	507	Adults and paediatrics	N/A	?	?	CY is better
Causon et al. (2015)	SR	12	No	200	Not specific	N/A	?	?	RW is better
Snels et al. (2019)	MA	26	No	936	Adults and paediatrics	N/A	699	237	The RW approach during the first 6 months and found no significant difference between both approaches after that time.

SR= systematic revive, MA= Meta-analysis, RCT= randomised controlled trials.
N/A= not available.
RW= round window, CY= cochleostomy

1.4.3.1.2.3 Electrode stiffness and the surgical approach

In the early days of cochlear implantation, electrode arrays were thick and caused cochlear trauma during insertion. Numerous studies suggest a correlation between the stiffness of these electrodes and the incidence of trauma, especially with the RW approach (Rebscher et al., 2008). At that stage, CY was superior to the RW approach regarding protection of the inner structures. The stiffness of the electrode array was one of the motivations for changing the practice of electrode insertion from the RW to the CY approach. Inserting the electrode array through the RW requires bending of the array, which damaged cochlear structures, Figure 1-4. In contrast, the CY approach provides more straight access and showed better outcomes while using the old stiff arrays (Clark et al., 1984). Souter et al. (2012) evaluated the safety of RW insertion utilizing the Cochlear Contour Advanced array in a human temporal bone study. According to the study, this region causes deflection toward the modiolus and/or buckles the array, resulting in an elevated risk of trauma. The trajectory of RW insertion could be affected by variation in the anatomy and orientation of the RW (Souter et al., 2012). Another animal study assessed the impact of electrode trajectory between the RW and CY approaches and reported that all groups presented similar hearing loss when averaged across the cochlea; however, the RW groups presented more hearing

loss at 2000Hz. Moreover, the RW group showed lower OHC and pillar cell counts and SGN densities. Even though the RW incision is the least traumatic, the RW insertion was found to be the most traumatic (Rowe et al., 2016a).

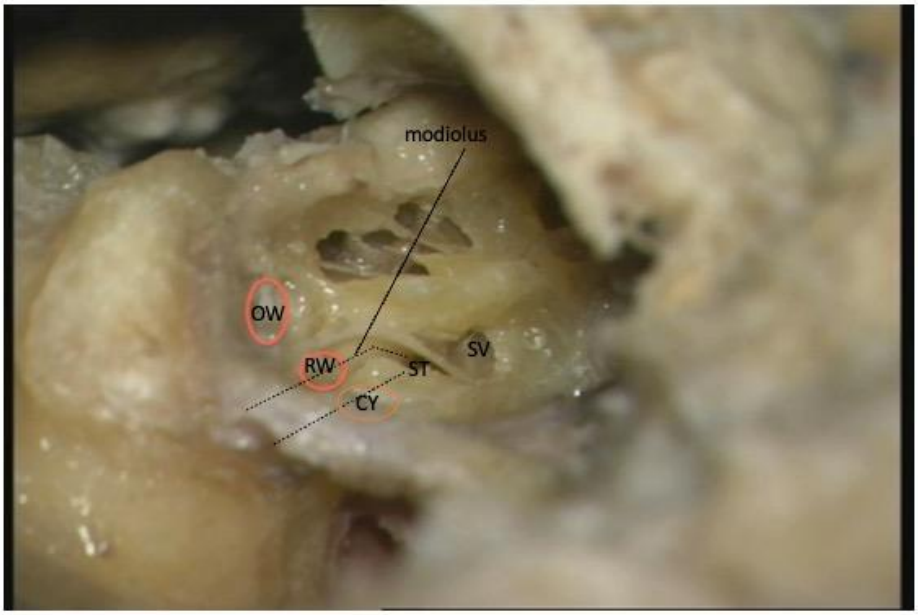


Figure 1-4 Right cochlear dissection diagram showing the trajectory of electrode array when inserted into the basal ST with CY and RW.
Abbreviations in the diagram; OW= oval window, RW= round window, CY= cochleostomy, ST= scala tympani, SV= scala vestibuli.

Over time, CI manufacturers improved the electrode arrays and produced flexible, atraumatic arrays. The use of these arrays had better outcomes when paired with the RW approach (Hassepass et al., 2015). As a result of this improvement and the recommendations of several manufacturers, the practice shifted back from the CY to the RW approach. This shift happened over a brief period and did not allow enough time to compare both approaches with the same atraumatic arrays (Santa Maria et al., 2014).

Sun et al. (2015) compared HP in patients who had been implanted with modern electrodes via the RW approach with patients who had been implanted with older electrodes via the CY approach during the period from 2008 to 2013. Although this study had some biases in the comparison between both approaches, they reported no significant difference between the approaches. This study highlighted the advantage of using the new atraumatic electrodes. Moreover, it showed several advantages of

the CY approach. However, unbiased comparison between both approaches is needed for a better understanding of the influence of surgical approach on HP.

1.4.3.2 Electrode scalar placement

Electrode scalar placement affects patient outcomes. Placing the electrode array in the ST is superior to placing it in the SV (Aschendorff et al., 2007). Studies show that electrode placement in ST reduces electrical impedance between the electrode and surrounding tissue. While dislocated electrodes to SV requires a higher electrical signal than ST electrode placement and can increase the spread of excitation, which might lead to interaction between adjacent channels (Jones et al., 2013). Furthermore, the maximum comfortable loudness level (charge units) is higher in patients with dislocated electrodes (Fischer et al., 2015).

Electrode arrays crossing from the ST to the SV occurs through the BM or osseous spiral lamina. This dislocation damage to the BM and spiral ganglion (Finley et al., 2008). Patients with full electrode placement in the ST have better HP than those with dislocated arrays into the SV (Wanna et al., 2015). Fischer et al. (2015) showed that the mean threshold of patients who had crossed electrodes to the SV placement was within the extremes of those with full electrode placement in the ST. ST electrode placement has been associated with better speech perception performance than SV electrode placement (O'Connell et al., 2016d, Tan et al., 2015, Finley et al., 2008, Holden et al., 2013, Skinner et al., 2007)

Many factors might lead to electrode dislocation, including the length of the electrode array and the insertion depth, stiffness, and curvature of the electrode array. The effect of electrode type should be considered when assessing scalar placement (this will be discussed in the following sections). Finally, the causative relationship between electrode displacement and surgical approach has been studied for a long time and there was no substantial evidence to support the relationship (Havenith et al., 2013).

1.4.3.3 Electrode effect

1.4.3.3.1 Electrode array design

There are broad variations in electrode models. Electrodes vary in length and thickness of the array and can be straight or pre-curved. Each of these properties

influences HP. Currently, the most commonly used electrode array in HP surgeries are atraumatic lateral wall [LW] moderate-length electrodes.

1.4.3.3.2 Straight, pre-curved and mid-scalar

Electrodes can be classified as straight LW and perimodiolar. The latter is pre-curved and tends to be close to the modiolus. Perimodiolar electrodes generally have a higher likelihood of dislocating from the ST to the SV (Boyer et al., 2015, James et al., 2006), which results in decreased HP (Causon et al., 2015). Some designs, like Advance Contour from Cochlea Corp., have a higher likelihood for ST placement than the old Nucleus Contour electrode arrays (Aschendorff et al., 2007). The mid-scalar electrode array is another pre-curved array that was created to improve cochlear placement. The design of the mid-scalar electrode reduces the likelihood of lateral wall and modiolus trauma. This electrode array was reported to have a low incidence of intracochlear trauma when implanted through the RW and cochleostomy techniques (Hassepass et al., 2014). LW electrodes are used in most HP surgeries as they are less traumatic and are associated with better HP outcomes.

1.4.3.3.3 Electrode length

Electrode arrays are manufactured in various lengths. The effect of electrode length on HP has been investigated in previous studies, and the findings are inconsistent. Some studies have shown that HP decreases with deeper insertion (Jurawitz et al., 2014, Adunka et al., 2004b, Adunka and Kiefer, 2006, Suhling et al., 2016). Suhling et al. (2016) studied the effect of three electrodes (20 mm, 24 mm, and 28 mm) on HP. The results showed a negative correlation between HP and electrode length. A more recent study by the same author used six electrode arrays to study this relationship and showed that HP was achieved in all patients; however, patients with shorter arrays had increased levels of HP (Suhling et al., 2019).

In contrast, other studies showed no significant relationship between electrode length and HP (Kisser et al., 2016, Skarzynski et al., 2009, Nordfalk et al., 2016). Kisser et al. (2016) reported that complete HP at the low-frequency range was possible even with long electrode arrays.

In a meta-analysis conducted by Santa Maria et al. (2014), they noticed a mixed trend depending on the definition of HP, and there was no significant relationship between HP and length of the electrode. The current literature does not support the use of very long electrodes; however, it is essential to have an electrode length that is sufficient for adequate cochlear coverage (Gantz et al., 2009, Soda-Merhy et al., 2008, Skarzynski et al., 2012).

1.4.3.4 The importance of full insertion

Cochlear implants can be used to manage patients with partial HL and RH in the low-frequency range; short electrodes have been designed to fit the needs of this clinical condition (Ye et al., 2007, Wanna et al., 2014, Adunka et al., 2004a, Skarzynski et al., 2007). Short electrodes aim for shallow insertion, providing electrical stimulus for the basal part of the cochlea while using acoustic stimulus to stimulate the viable auditory neurons in the apical part. These devices are known as Electroacoustic stimulation (EAS) (von Ilberg et al., 1999), hybrid stimulation (Gantz and Turner, 2003), or partial-deafness CIs (Skarzynski et al., 2003). EAS has the advantage of improving the quality of speech perception, hearing in noise, and music appreciation (Nguyen et al., 2016). EAS users report better speech discriminate than patients who have electrical stimulus alone (Helbig et al., 2011b).

While using a short electrode array is effective for HP (Rader et al., 2013), loss of RH can occur several months after the surgery (Helbig et al., 2016) and requires re-implantation of a longer electrode array. A second surgery exposes patients to the additional risks of cochlear trauma and general anaesthesia. It was reported that patients implanted with longer electrodes had better speech discrimination than those who had shorter electrodes after the loss of RH (Friedmann et al., 2015). Therefore, using longer electrodes and deeper insertion in the first operation might be a better option to convert to complete electrical stimulation in case of late-onset HL (Eshraghi et al., 2016, Nguyen et al., 2016).

1.4.3.5 Medical regimens

1.4.3.5.1 Use of corticosteroids

Corticosteroids are known for their anti-inflammatory effect and suppression of autoimmune reactions by preventing cellular reactions like apoptosis, necrosis, and

necrosis-like reactions (Jia et al., 2013). Corticosteroids are used intraoperatively to help minimise the loss of RH that results from surgical trauma and cellular changes. Dexamethasone is considered one of the best glucocorticoids for intraoperative use due to its long-acting half-life of 36–72 hours and its strong anti-inflammatory potency (Liu et al., 2015b, Cho et al., 2016).

Corticosteroids have been used to salvage hearing in sudden sensorineural hearing loss (SSHL). Topical intraoperative corticosteroids have a positive effect on HP in CI patients (Causon et al., 2015). Despite the positive short-term effect of corticosteroids, the long-term effects of corticosteroids are debated (Kuthubutheen et al., 2018, O'Leary et al., 2021). Previous studies showed that corticosteroids did not prevent fibrosis and long-term loss of RH in an animal model (Yang et al., 2000, Huang et al., 2007). Moreover, local intraoperative corticosteroid administration might have a limited benefit as it does not reach the apical turn of the cochlea, which might limit its action in the low-frequency range (Nguyen et al., 2016).

Several studies have investigated the positive effect of corticosteroids on HP after cochlear implantation (Causon et al., 2015, Chang et al., 2009, Rajan et al., 2012). Santa Maria et al. (2014) conducted a meta-analysis that included 507 patients and reported a positive effect of intraoperative corticosteroids only in conjunction with postoperative oral corticosteroids. A similar result was reported by (Cho et al., 2016), who compared two groups of patients: the first group received systematic oral preoperative and topical intraoperative corticosteroids, while the second group did not receive oral corticosteroids. Rajan et al. (2012) compared combined preoperative and intraoperative corticosteroids with a control group and reported more stabilisation of HP in the corticosteroids group. Another study by Sweeney et al. (2015) administered only preoperative tapered corticosteroids for 3 days and reported significant improvement in the level of HP.

The benefit of preoperative transtympanic corticosteroids application has been investigated in several studies. A recent randomised controlled trial (RCT) investigated the effect of single preoperative transtympanic corticosteroids application and reported a significant benefit in the short term and minimal benefit on the long term (Kuthubutheen et al., 2018). Even though topical intraoperative corticosteroids are administered in most soft CI surgeries, there is no standardised protocol or regimen

for their use. This topic is still under investigation to determine the optimal timing, dose, and delivery route.

1.4.3.5.2 Use of hyaluronic acid as a lubricant

Hyaluronic acid has been used in CI surgeries to facilitate smooth electrode insertion and to avoid electrode trauma (Lehnhardt, 1993a). Moreover, it acts as a sealant to prevent contamination of the perilymph (Garcia-Ibanez et al., 2009, Laszig et al., 2002), and it might have an anti-inflammatory effect after implantation (van de Water et al., 2010b). Interestingly, Ramos et al. (2015) reported that HP level was significantly improved when dexamethasone was combined with hyaluronic acid than when dexamethasone was used alone. The authors believed that hyaluronic acid helped in prolonging exposure to dexamethasone and maintaining its high concentration in the perilymph, as demonstrated in previous animal studies (Chandrasekhar et al., 2000, Bjurström et al., 1987).

1.4.3.5.3 Use of antibiotics

CI surgery is considered clean surgery. Infections that might occur in CI users include wound infection, skin breakdown, meningitis, and device-related infection, which leads to device rejection (Farinetti et al., 2014). Some of these acute infections can be treated with antibiotics and delay device activation and usage, while other conditions require device removal and re-implantation of a new device after treating the infection (Francis et al., 2008, Cohen and Hoffman, 1991).

Anne et al. (2016) conducted a systematic review of the efficacy of using a perioperative prophylactic antibiotic in CI patients. This systematic review showed that the incidence of infection in CI patients ranged between 3% and 5%. The evidence for using a prophylactic perioperative antibiotic to protect from postoperative infection is weak. The three articles included in this systematic review reported a low rate of infection using a single dose of perioperative antibiotic (Garcia-Valdecasas et al., 2009, Basavaraj et al., 2004, Hirsch et al., 2007). Garcia-Valdecasas et al. (2009) reported that the rate of infection was lower in patients who had a single perioperative dose and a 6-week postoperative course of antibiotics.

Verschuur et al. (2004) conducted a systematic review of perioperative antibiotic use in ear surgeries. This systematic review did not focus on CI surgery and was general for clean and clean-contaminated otologic surgeries. This systematic review

concluded that there was no firm evidence for using prophylactic antibiotics to protect from infections after surgery. However, complications that might occur after CI infection are expensive and expose the patient to the subsequent risks of anaesthesia and cochlear trauma due to electrode re-insertion (Verschuur et al., 2004). A survey conducted by Barker and Pringle (2008) found that prophylactic antibiotics were used in most CI centres in the UK.

Verschuur et al. (2015) conducted a meta-analysis involving 106 patients on the effect of antibiotics and corticosteroids on HP concluded that corticosteroids impacted HP, but antibiotics did not. Causon et al. (2015) reported the same results in their systematic review. Both studies included any form of antibiotic administration route (pre-, peri-, or postoperative) as one category to measure its effect on HP.

1.5 Outcome measures of hearing preservation

1.5.1 Pure-tone average

The pure-tone audiometry test is the most commonly used test to assess HP (Causon et al., 2015). The hearing assessment is conducted in two stages: preoperative and postoperative. The degree of HP can be determined based on changes in the degree of the pure-tone average (PTA). There has been no reported uniform method in the literature to define and classify the degree of HP, which is considered one of the difficulties of this topic.

The most common definitions and classifications of HP were summarised by Santa Maria et al. (2014); the first definition uses the PTA of 250, 500, 750, and 1000 Hz. If the difference between preoperative and postoperative PTA is less than 10 dB, it is considered complete HP. If the difference is between 10 dB and 20 dB, it is considered partial HP. If the difference is more than 20 dB, it is considered unsuccessful HP. The second definition is similar to the first, except it replaces the 750-Hz data point with 2000 Hz. The final classification was described by the HEARRING Group (Skarzynski et al., 2013). In (2013) Skarzynski et al. published a universal definition and classification system for HP. Skarzynski et al. (2013) described a formula to calculate relative changes in the preoperative dynamic range (Figure 1-5). The results of this calculation are reported as percentages (S value), which is translated to a categorical scale. Table 1-3 shows the degree of HP according to the difference between the preoperative and postoperative hearing thresholds.

The first two methods have some limitations in that they cannot be used to assess HP in patients who have a high hearing threshold (minimal RH). In contrast, Skarzynski's method is able to calculate changes more accurately. We used the HEARING Group method in this thesis as it is the most commonly used at present and it provides more accurate results, especially in detecting minimal changes in the level of hearing.

Figure 1-5 The HEARRING GROUP formula for hearing preservation.

$$S = \left[1 - \left(\frac{(PTApost - PTApre)}{(PTAmax - PTApre)} \right) * 100 \right] [\%]$$

Figure 1.1 Skarzynski formula of HP classification system. PTAmax is the limit of the audiometer (see Table 1-4). PTApost is pure-tone average (PTA) measured postoperatively, while PTApre is the PTA measured before the operation (Skarzynski et al., 2013).

Table 1-3 The scale of HEARRING Group's classification system of hearing preservation (Skarzynski et al., 2013).

Percentage of preserved residual hearing (S value)	Classification
>75%	Complete HP
26–75%	Partial HP
0–25%	Minimal HP
No measurable hearing	Loss of hearing/No hearing

Table 1-4 Maximum detectable hearing (MDH) measurable for each frequency (PTAmax).

Hz	125	250	500	750	1000	1500	2000	3000	4000	6000	8000
MDH	90	105	110	120	120	120	120	120	115	100	95

1.5.2 Speech perception test

The speech perception test is one of the main assessments that CI candidates must undergo before and after surgery. PTA scores reflect the level of RH; they do not reflect functionality, which requires including speech testing in the assessment battery of patients with RH (Balkany et al., 2006).

The Bamford-Kowal-Bench (BKB) sentence test is the most commonly used test in the UK as it is one of the main elements used in assessing CI patients. This test consists of 21 lists, 16 sentences, and 50 keywords (Bench et al., 1979). The test is conducted in a double-walled, soundproof booth by playing male or female voice recordings. The intensity level of the stimulus is 70 dB. If the test is conducted in noise, the signal-to-noise ratio (SNR) is +10 dB.

1.5.2.1 The effect of HP on speech perception

Preservation of RH at low frequencies helps patients to discriminate speech in noisy environments. Gantz et al. (2009) reported a significant relationship between the level of HP and patients' ability to discriminate speech in noise but not in quiet. Acoustic low-frequency cues are an advantage of EAS users (Golub et al., 2012, Campbell et al., 2013). The advantage of the RH was measured in patients who used EAS in comparison to patients with no RH who used conventional electrodes. Rader et al. (2015) reported that speech perception scores of binaural EAS users were significantly better than the scores of conventional binaural CI.

Another study found that the result of speech in noise test testing for patients who used EAS was equal to those who had mild to moderate HL, and that the results were more favourable than the results of patients who used only electrical stimulation (Gantz et al., 2005). Gantz et al. (2009) believed that this benefit was related to the level of RH, and that it might be lost in cases of unsuccessful HP.

1.5.3 Imaging and cochlear implantation

1.5.3.1 The importance of radiological assessment

1.5.3.1.1 Preoperative

Imaging plays a crucial role in identifying abnormalities of the cochlea in addition to postoperative confirmation of electrode array placement. Computed tomography (CT) and magnet resonance imaging (MRI) are used in most centres to provide detailed pictures of the anatomy of the cochlea. CT scans are essential in identifying the bony structure of the cochlea, while MRI is necessary to study soft tissues, like the presence of the 7th and 8th cranial nerve, and to rule out any central conditions, like acoustic neuroma, in older patients (Helbig et al., 2009, Trotter and Briggs, 2010). Moreover, it is essential to identify the course of the facial nerve by CT to avoid injury to the nerve during surgery. Previous studies showed that up to 20% of paediatric candidates had inner ear malformations that were diagnosed by CT or MRI (Papsin, 2005, Aschendorff, 2011).

Moreover, there is a wide variation in cochlear anatomy, size (Franke-Trieger and Murbe, 2015), length (Wurfel et al., 2014a), and orientation, even in patients who have normal cochlear morphology (Avci et al., 2014). Therefore, it is essential to clarify the anatomy of the cochlea before the operation, as it helps in selecting device type and surgical procedure.

1.5.3.1.2 Intraoperative

Intraoperative imaging is important in patients with abnormal anatomy and difficult electrode insertion to ensure the correct placement of electrodes inside the cochlea and to avoid unnecessary postoperative imaging, revision operations, and re-exposing the patient to general anaesthesia. Intraoperative imaging includes plain-film x-ray, three-dimensional rotational x-ray, fluoroscopy, and CT scan (Appachi et al., 2018, Aschendorff, 2011).

1.5.3.1.3 Post-implantation

Postoperative imaging is used to confirm electrode placement and to exclude kinking, bending, or migration of the electrode. Immediate postoperative imaging can be used as a reference for potential future complications, such as electrode migration. In the early days of cochlear implantation, x-rays (trans-orbital or modified Stenver's views) were sufficient for this purpose. In recent years, different imaging modalities have been

used for more accurate imaging, such as CT scan, digital volume tomography (DVT) (Aschendorff, 2011), micro-CT (O'Connell et al., 2016a), and cone-beam CT (CBCT) in some centres (Boyer et al., 2015, Cerini et al., 2008, De Seta et al., 2016).

1.5.3.2 Imaging modalities and cochlear implantation

A wide range of radiological modalities have been used to assess CI patients, ranging from x-ray (modified Stenver's view), intraoperative fluoroscopy, conventional CT scans, high-resolution CT scans, multi slices CT (MS-CT) scan, and CBCT scan (Boyer et al., 2015). Plain x-ray is a useful tool to assess electrode location and the angle of insertion (Boyer et al., 2015); however, it cannot detect displaced electrodes inside the cochlea (Cohen et al., 1996). CT scan is the standard procedure to assess CI candidates in most CI centres. Despite the superior resolution of high-resolution CT compared with conventional CT scan in predicting the location of the electrode array inside the cochlea, the presence of metallic artefacts is challenging in many cases.

CBCT scan is a modern modality that has been used for maxillofacial assessment (Boyer et al., 2015) and has been developed to be able to assess bony structures in the head and neck. The main advantage of CBCT is the low dose of radiation (Cushing et al., 2012, Faccioli et al., 2009, Guldner et al., 2012b, Ruivo et al., 2009, Bartling et al., 2006), short procedure duration, (Saeed et al., 2014) and better resolution of bony structures than MSCT (Hodez et al., 2011). Furthermore, CBCT can be more accurate in predicting the location of the electrode array in the cochlea (Ruivo et al., 2009). CBCT has been used in some centres as it provides more accurate visualisation, especially when assessing the location of electrodes after surgery in HP conditions (Saeed et al., 2014, Ruivo et al., 2009, Boyer et al., 2015).

1.5.3.3 The role of cone-beam CT in the assessment of HP

As described earlier, loss of HP might occur either in the short or long term. The primary cause of short-term loss of RH is electrode trauma due to electrode dislocation from the ST. Several temporal bone studies have suggested that CBCT is a sensitive method to predict the scalar location of CI electrodes (Saeed et al., 2014, Ruivo et al., 2009). Adunka et al. (2005) found that electrode location was a predictor for HP;

therefore, CBCT could be an effective tool in predicting HP. Therefore, this thesis will utilise CBCT in the retrospective study and the RCT to determine electrode location, insertion depth, and cochlear size.

1.6 Conclusion

HP is related to preserving intra-cochlear structures; therefore, it is not limited to patients with substantial RH. HP has a positive impact on patients' ability to discriminate speech and appreciate music. The topic of HP is multifactorial as it includes factors related to the patient, device, surgery, and medications. The exact effect of each of the factors is not well understood. The surgical approach is one of the factors that has undergone many changes over time. The current evidence in the literature is weak and shows conflicting results, which highlights the need for further research and stronger evidence.

1.7 Rational and knowledge gap

Hearing preservation (HP) and preservation of intra-cochlear structures is one of the key targets for improving the outcomes of cochlear implant surgery. The importance of this has increased with the expansion of inclusion criteria to allow patients with a greater amount of residual hearing. Many factors are thought to influence HP outcomes, including the type and length of the electrode array (Suhling et al., 2016, Adunka et al., 2004b), depth and speed of insertion, use of corticosteroids (Chang et al., 2009, Rajan et al., 2012), antibiotics (Anne et al., 2016), and accuracy of electrode insertion into the scala tympani through the round window (RW) or cochleostomy (CY) (Aschendorff et al., 2007, Adunka and Kiefer, 2006).

The effect of the surgical approach of electrode insertion on HP has been extensively discussed in the literature, and there is strong disagreement surrounding this topic. Even systematic reviews have not reached a concise conclusion. Two systematic reviews and two meta-analyses had investigated this research question: Havenith et al. (2013), Causon et al. (2015), Santa Maria et al. (2014), and Snels et al. (2019) respectively (Table 1-2). The systematic review conducted by Havenith et al. (2013) showed no significant relationship between surgical approach and HP. Causon et al. (2015) found that HP was better in patients who had electrode insertion through the RW. Snels et al. (2019) reported that the RW exhibited superior HP for just the first six months, after which there was no significant difference. In contrast, Santa Maria et al.'s (2014) meta-analysis reported that HP was better in the CY group than in the RW group.

Studying HP is challenging because of the nature of CI surgery and the large number of factors that might affect HP. This research attempted to elucidate the effect of the surgical approach while controlling for other factors. The research was explicitly focused on post-lingual adults implanted with the modern atraumatic LW electrode array.

This project can enhance several areas. First, it will help to identify the current practice of surgeons regarding HP. Second, this project will contribute novel findings as we conducted the first double-blinded RCT investigating this research question. Finally, the findings of this study will help to establish a standardised surgical protocol for HP in CI patients.

1.8 The overall hypothesis of this thesis

This thesis will test the following hypothesis:

- H1: The level of postoperative HP is correlated with the surgical approach of electrode insertion in adult patients.
- H0: The level of postoperative HP is not correlated with the surgical approach of electrode insertion in adult patients.

1.9 Aims and objectives

This thesis aims to assess the current practice of HP in the UK and to study the effects of surgical approach on HP in adult CI recipients implanted with modern atraumatic LW electrode arrays. To address these aims and test the hypothesis that the level of postoperative HP is correlated with the surgical approach of electrode insertion in adult patients, the following four studies were conducted:

The first project (Chapter 2) is a systematic review of the literature. The objective of this chapter is:

- To review the literature and compare HP outcomes between both surgical approaches (RW versus CY) among patients implanted with modern LW electrode array.

The second project (Chapter 3) was a retrospective study that was conducted to address the following objectives:

- To compare the incidence of electrode trauma among adult CI patients who were implanted through the RW and CY approaches.
- To investigate the relationship between electrode position and the degree of HP.
- To identify cochlear size based on the diameter of the basal turn, as described by Escude et al. (2006).
- To investigate the relationship between insertion depth and cochlear size.
- To examine the relationship between electrode position and each of insertion depth and cochlear size.

The third project (Chapter 4) was a survey study that was conducted to address the following objective:

- To assess the current surgical practice for HP in cochlear implantation among the consultant surgeons in the UK.

The fourth project was a double-blinded RCT. The RCT consisted of two parts (Chapters 5 and 6). The objectives of the RCT are grouped into two themes. The first theme aims to compare the outcomes of the surgical approach, while the second theme correlates the audiological and radiological outcomes.

The objectives of the first part (Chapter 5) were:

- To determine if there is a significant difference in preservation of RH between both surgical approaches within the first 6 months after surgery.
- To compare long-term HP over 12 months between both surgical approaches.
- To compare the results of the BKB speech perception tests in quiet between both surgical approaches.
- To compare the accuracy of electrode insertion into the ST between both surgical approaches.
- To compare electrode distance to the modiolus between both surgical approaches.

The objectives of the second part of the RCT were presented in Chapter 6:

- To investigate the relationship between the depth of insertion and the accuracy of electrode insertion into the ST.
- To investigate the relationship between the depth of insertion and BKB scores in quiet.
- To investigate the relationship between the depth of insertion and PTA scores.
- To investigate the relationship between the accuracy of electrode insertion into ST, PTA scores, and BKB scores in quiet.

1.10 Thesis outline

This thesis is organised into nine chapters, starting with the introduction, systematic review, retrospective study, a survey study, RCT part 1, RCT part 2, and ending with a general discussion, limitations, and future work. A detailed description of the population, sample size, study design, outcome measures, and statistical analysis will be presented in each chapter.

Chapter 1

This chapter introduces this research project. It discusses the history of CI surgery, the importance of HP, and factors influencing the success of HP.

Chapter 2

This chapter presents a systematic review that evaluates and compares the effect of surgical approach on HP outcomes among patients implanted with modern atraumatic LW electrode arrays. This review critically appraised the literature and was beneficial in identifying the current level of evidence surrounding this topic, identifying the knowledge gap, and helping to design the prospective study.

Chapter 3

This chapter describes a retrospective study that was conducted to evaluate intra-cochlear trauma. The study utilised CBCT scans to determine electrodeposition in CI recipients with atraumatic LW electrode array. Moreover, the study investigated the relationship between electrode scalar position, HP, surgical approach, insertion depth, and cochlear size.

Chapter 4

This chapter describes a survey study that was conducted to explore the current surgical practice of HP in cochlear implantation in the UK. The survey represents the views of consultant surgeons regarding device choice, surgical techniques of electrode insertion, medications, and audiological follow-up. The findings of this survey are

beneficial as they represent the views of expert surgeons and help in the development of a standardised HP protocol.

Chapter 5

This chapter presents the first part of the double-blinded RCT. This study compared patients' outcomes after being randomised between the RW and CY approach. The level of HP and speech perception scores of the BKB test were compared between both approaches. The CBCT scan was used to assess and compare electrode scalar placement and the insertion depth between both approaches. The study presents novel findings as it is the first double-blinded controlled trial investigating this topic.

Chapter 6

This chapter presents the second part of the RCT. This chapter investigates the relationship between the angular depth of insertion and each of HP, speech perception scores, and electrode position. Moreover, this chapter investigates the relationship between electrode scalar location, insertion depth and HP and speech perception scores.

Chapter 7

This chapter represents a summary and general discussion of the main findings of this thesis.

Chapter 8

This chapter represents the strengths and limitations of this thesis.

Chapter 9

This chapter represents the implications and future work of this thesis.

Chapter 2 : The Effect of Surgical Approach on Hearing Preservation Using Modern Atraumatic Lateral-Wall Electrode Arrays: A SYSTEMATIC REVIEW

Abstract

Introduction

The inclusion criteria for cochlear implantation have been widened to include patients with residual hearing (RH). Preservation of RH improves the patients' ability to discriminate sound. Many factors might affect hearing preservation (HP), include the surgical approach, type of electrode array, corticosteroid use, and the usage of hyaluronic acid and antibiotics (Ramos et al., 2015). The aim of this systematic review is to study the effect of surgical approach on HP among patients who have modern atraumatic lateral wall (LW) electrodes.

Method

Three databases (PubMed, Embase, and Midline) were searched for relevant articles published in the period between 1980 and 1st of April 2017. The inclusion criteria were strict for studies that used atraumatic lateral wall (LW) electrodes. The PRISMA approach was used to identify the articles, and the Downs and Black (1998) checklist was used to assess their quality and bias.

Results

This search resulted in 1396 unique articles; 25 of these studies satisfied our inclusion criteria, which included 591 patients. The number of cases in the included studies ranged from 5 to 120. There were 14 adult studies, 2 paediatric studies, and 9 combined adult and child studies among the 25 papers. Most of the studies reported HP outcomes within the first year after surgery. There was heterogeneity in the inclusion criteria, the definition of HP, and the method of quantifying the success of HP. The reviewed studies revealed that HP could be achieved with both the RW and CY approaches in the short to mid-term. HP can be achieved with electrodes that are less than 25 mm and greater than 25 mm in length.

Conclusion

There was no significant difference in the degree of HP between either surgical approach using atraumatic LW electrodes. All studies used the CY approach as an alternative approach if the RW approach was not feasible, which may have skewed the results. Most of the current literature is represented by retrospective studies that lack reporting on confounding factors and have variability in their methods of quantifying HP. There is a need for well-structured prospective studies that consider all factors and produce validated evidence. Future research should quantify HP using the relative change method (the HEARRING Group method) to ensure more precise results and more comparability between studies.

2.1 Introduction

Cochlear implantation has become standard management for patients with severe to profound HL. The inclusion criteria for cochlear implantation have been widened to include patients with RH in the low-frequency range (Cullen et al., 2004). The National Institute on Deafness and Other Communication Disorders (2019) reported that there are currently over 736,900 registered cochlear implant (CI) devices globally.

Although this management is routine practice, the audiological outcomes of patients with CI are not equal. This variation can be related to many factors, such as age, rehabilitation, patient contribution (Fu and Galvin, 2007), type of device, surgical approach, preservation of inner ear structures, insertion depth (Suhling et al., 2016), speed of insertion (Rajan et al., 2013, Esquia Medina et al., 2013, Tamir et al., 2012), and electrode location inside the cochlear structure (Aschendorff et al., 2007). Moreover, the duration of deafness and aetiological causes affect the quality of audiological outcomes (Wilson and Dorman, 2008, Blamey et al., 1996, Blamey et al., 2013).

The two main surgical approaches for cochlear implantation are RW and CY. Both approaches have advantages when it comes to HP. In the CY approach, the electrode array is inserted through a hole drilled into the cochlea. Minimal CY is positioned anteroinferior to the RW. It is known as ‘soft surgery’ and was first described by Lehnhardt (1993b). The location of the CY provides direct access for the arrays and limits the incidence of insertion trauma. In contrast, electrode insertion through the RW approach requires less drilling and occurs through the natural opening of the RW.

Some surgeons use the CY approach as an alternative when the RW is not accessible, while others use it as a standard procedure. There is extensive debate on the superiority of one approach over the other. Several studies have been conducted to compare histological and clinical outcomes of both approaches (Addams-Williams et al., 2011, Santa Maria et al., 2014). Previous systematic reviews and meta-analyses investigated the effect of surgical approach on outcomes, and their findings were inconsistent, as discussed in Section 1.4.1.2.2. The discrepancy between the results of these studies could be attributed to the use of a variety of electrode types (rigidity, length and straight versus. pre-curved) or manufacturers, or differences in surgical techniques or the treatment regimen, which includes pre-, post-, and intraoperative protocols (i.e., use of corticosteroids, antibiotics, and hyaluronic acid lubricant).

Another reason for this conflict is the variation between definitions and classification systems of preserved hearing (Skarzynski et al., 2013).

2.2 Aim and objectives of the study

This review aimed to investigate the relationship between HP and surgical approach (RW versus CY) when controlling for the electrode array type. All included studies in this review used modern atraumatic LW electrode arrays with a minimum length of 20 mm. These electrodes were selected as they are the most widely used in current practice. An electrode specification was used in this study to ensure the inclusion of homogeneous electrode arrays and to minimise their effect.

2.3 Methods

2.3.1 Data sources

A protocol for the systematic review was created and registered to PROSPERO, the international prospective register of systematic reviews (2019: CRD42019141368). A systematic search of the PubMed, Embase, and Medline databases was performed. The search terms that were used were ‘cochlear implant’, ‘cochlear implantation’, ‘cochlear prosthesis’, ‘hearing preservation’, and ‘residual hearing’. The exact terms and synonyms that were used are listed in Appendix 1. In addition, the bibliography of relevant articles and reviews was checked.

2.3.2 Study selection

The PRISMA model was followed to filter the results and include relevant articles (Figure 2-1). The literature search was undertaken by one reviewer. The screening process included titles, abstracts, and full-text screening. To construct inclusion and exclusion criteria, the Participants, Intervention, Control, Outcomes, and Study Designs (PICOS) technique was employed (Richardson et al., 1995), Appendix 2.

The inclusion criteria of this systematic review were restricted to studies published in the English language. The designs of the included studies were randomised, non-randomised, repeated measures, or cohort studies. All CI studies aimed for HP and

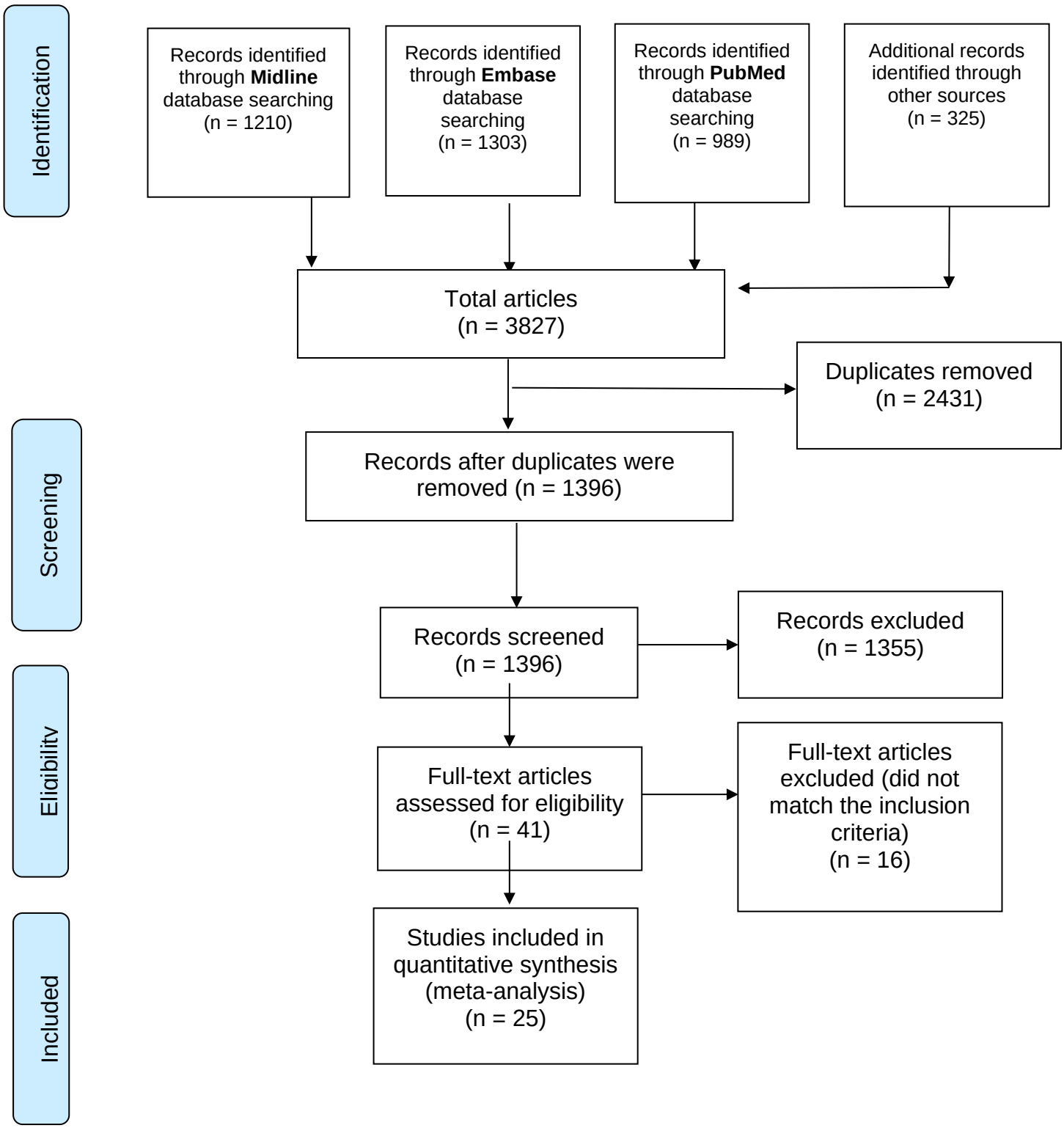
use modern atraumatic LW electrodes for the majority of subjects in the included studies. The length of the electrodes had to be >20 mm. Comparing the RW versus CY approach did not have to be the study's main aim.

The exclusion criteria that were used were duplicate articles, in vitro, temporal bone studies, animals, histopathology, case reports, conference abstracts, title only, reviews, and systematic reviews. All studies that used pre-curved or short electrodes (<20 mm) were also excluded.

2.3.3 Article appraisal (quality of articles)

The quality of evidence of the included articles was assessed using the Downs and Black (1998) checklist, which is widely used in many previous systematic reviews. The checklist included 27 questions and can be used to assess the level of evidence in randomised and non-randomised studies. The checklist assesses articles from multiple aspects: reporting, external validity, internal validity (bias), and confounding factors (selection bias), and sample power. The scoring was divided into ranges and given corresponding quality levels, as described by Hooper et al. (2008): excellent (26–28), good (20–25), fair (15–19), and poor (≤14).

Figure 2-1 PRISMA Flow Diagram



2.3.4 Synthesis of results

All extracted data, including study design, participant characteristics, HP inclusion criteria, method of HP quantification, electrode type, surgical approach and protocol, outcome measures, and primary findings, was collected in a Microsoft Excel spreadsheet. A series of tables were created to summarise the studies, help to answer the research questions, and to assess the levels of evidence, research quality, and bias. A meta-analysis was not possible due to the heterogeneity among studies regarding the definition and classification of HP and the duration of follow-up. However, some of the included studies provided raw audiogram data, and it was possible to pool the available raw data and investigate the correlation between HP and surgical approach.

2.4 Results

The results of the systematic search yielded 1396 unique titles from three databases (Midline, Embase, and PubMed) after removing 2431 duplicate articles. As a result of title and abstract screening, 1355 articles were excluded. The remaining 41 articles were assessed by reading the whole text, and 16 of them did not meet the inclusion criteria and were excluded. The PRISMA flow chart (Figure 2-1) illustrates the filtering process. The total number of included articles was 25. Of the 25 articles, there were 14 adult studies, 2 paediatric studies, and 9 mixed studies with adults and children. The number of cases in the included studies ranged from 5 to 120. The total number of cases in all studies was 591.

The included studies were summarised with their findings in three tables. Table 2-1 summarises articles in terms of study type, sample size, age group, mean follow-up time, inclusion criteria, and method of calculating HP. Table 2-2 summarises the surgical aspects of each study and includes the type of electrode array, surgical approach, reason for choosing the CY approach, insertion depth, speed of insertion, and use of corticosteroids, antibiotics, or hyaluronic acid. Table 2-3 summarises the primary and secondary outcomes. The findings of all are presented in detail in the following sections.

Table 2-1 Studies characteristics and outcomes measures.

No	Author	Study type	No. pt.	Age group (A/P)	Mean Age (years)	Mean Follow up (month)	HP inclusion criteria	Method of calculating HP	Secondary outcome
1	(Adunka et al., 2013)	RS	18	A	55 (SD=15.25)	12m	"Each subject had normal to moderate hearing loss in the low- to mid-frequencies and sloping severe to profound hearing loss in the mid- to high frequencies bilaterally".	Change in the hearing threshold at (250, 500, 750, 1000, 1500, 2000 HZ).	Speech perception
2	(de Carvalho et al., 2013)	RS	6	A	47y	12m	Patients have pure tone thresholds of ≤60 dB hearing loss in at least 1 frequency between 250 and 500 Hz and of ≥80 dB in frequencies above 1000 Hz	"-**Complete HP =** 0-10dB loss of RH - **Partial HP=** loss of >10dB while indices≤80 dB, at least at frequencies between 250 and 1000 Hz. - **No HP=** no benefit with the use of an EAS, post-operative threshold > 80dB."	Speech perception
3	(Erixon et al., 2012)	RS	21	A	59y	13m	Patients who fulfilled the MED-EL criteria for EAS, defined as pure tone hearing thresholds less than 65 dB at frequencies of 125–750 Hz.	Change in hearing threshold at 125-1000Hz.	Insertion angle
4	(Gstoettner et al., 2009)	RS	9	A and P	46.13y (7-71)	9.72m (6-15m)	Bilateral sensorineural hearing loss with pure-tone thresholds<60 dB HL in at least two frequencies 125, 250 and 500 Hz and of >60 dB at frequencies >1 kHz and stable hearing loss for at least 2 years before surgery.	**Complete HP =** PTA threshold shift less than 10dB, **Partial HP=** greater shift than 10dB.	Speech perception
5	(Lee et al., 2010)	RS	10	A	55.5 y (SD= 15.6)	22.3m (SD= 23.2)	Patients with profound high frequency hearing loss and acoustically aidable low frequency hearing	"We define the **total loss of acoustic hearing as** (i) no response obtained at the maximal level of the audiometer or (ii) a total loss of RH. **A substantial increase in acoustic hearing loss** was defined as increased hearing thresholds across the low frequencies (125–750 Hz) of >20 dB".	Speech perception, insertion depth
6	(Brown et al., 2015)	RS	9	A and P	52.9y (3-83)	6-12m	Functional preoperative acoustic hearing (defined as low-frequency pure tone average thresholds e90 dB).	< 10 dB average change at low-frequency PTA measures (125, 250, 500, and 1,000 Hz)	--
7	(Mahmoud et al., 2014)	RS	5	A	(48-69)	12m	Mild-to-moderate low-frequency hearing loss and severe-to-profound sensorineural high-frequency hearing loss.	**- Significant hearing loss** was defined as greater than 20-dB reduction in air conduction across the entire low-frequency range (250- 3000 Hz)	Speech perception
8	(Usami et al., 2011)	RS	5**	A	50y	9.4m	-	Change in PTA at low-frequency range (125-1000Hz).	Vestibular evoked myogenic potential (VEMP) and caloric response
9	(Usami et al., 2014)	RS	31	A	(21-71)	12m	Pure tone hearing levels bilaterally at 65dB for (125-250, and 500Hz), 80dB for (2000Hz) and 85dBHL for (4000 and 8000Hz).	Change in PTA at low-frequency range (125-1000Hz).	Speech perception
10	(Radeloff et al., 2012)	RS	6**	A	46.5y (35-57)	1 week	Patients with pre-operative residual hearing	**- Complete HP =** PTA threshold shift less than 10dB - **Partial HP=** greater shift than 10dB.	Cochlear microphonics
11	(Arnoldner et al., 2010)	RS	11	P and A	(7.6- 71.3y)	7.85 m (0.95– 15.65 m)	Bilateral SNHL with pure-tone thresholds of <60 dB HL in at least two frequencies (125, 250 and 500 Hz) and of >60 dB at frequencies >1 kHz	**- Complete HP=** PTA threshold shift less than 10dB at low-frequency (125–750 Hz). **- Partial HP=** PTA shift >10dB at low frequency.	Monosyllabic words test and Hochmair-Schulz- Moser (HSM) sentence test in quiet and in noise.
12	(Guimaraes et al., 2015)	RS	19	A	48 y (19-70)	23.6m (4.5-81m)	"Pure tone thresholds better than 65 dB at frequencies of125, 250 and 500 Hz, and worse than 80 dB at frequencies above 1000 Hz"	**-Complete HP =** 0-10dB loss of RH **- Partial HP=** loss of >10dB while indices≤80 dB, at least at frequencies between 250 and 1000 Hz. **- No HP=** no benefit with the use of an EAS, post-operative threshold > 80dB.	Speech test
13	(Bruce et al., 2014)	RS	16	P	13y (10- 17y)	34m (4- 57m)	Recordable hearing at 125, 250 and 500 Hz	**Complete HP=** change in threshold < 10dB	Speech perception

Table 2-1 Studies characteristics and outcomes measures.

No	Author	Study type	No. pt.	Age group (A/P)	Mean Age (years)	Mean Follow up (month)	HP inclusion criteria	Method of calculating HP	Secondary outcome
14	(Erixon et al, 2015)	RS	19	P and A	58 years (10-82)	24m	"Unaided pure-tone threshold ≤65 dB HL at frequencies ≤500 Hz and >80 dB HL at frequencies ≥2000 Hz"	Change at low frequency range (125, 250 and 500Hz)	Speech perception, patients' satisfaction survey
15	(Fischer et al, 2015)	RS	63	P and A	57y (7-85)	6m	--	Change in low frequency threshold (250, 1000, 4000, 8000Hz)	CBCT scan, Maximum comfortable level (charge unit)
16	(Hassepass et al., 2015)	RS	41	A	49.2y	8m	--	**- Hearing preservation=** stability in PTA at low frequencies (250, 500 and 1000Hz). **- Complete loss of HP=** PTA at low-frequencies >130dB HL.	Speech test, radiological assessment of electrode positior
17	(Helbig et al., 2011)	RS	22	P and A	52y (14-81y)	(4-33m)	Subjects with measurable preoperative residual hearing and at least 1 postoperative unaided audiogram were included in the study	**Complete HP =** PTA threshold shift less than 10dB, **Partial HP=** greater shift than 10dB.	Speech perception
18	(Santa Maria et al., 2013)	RS	13	A	51y (32-72)	24m	<= 65 dB in the low frequencies at 500 Hz) and > 80 dB at higher frequencies >2 kHz)	Skarzynsky's Formula	Speech perception, patients' satisfaction survey (APHAB, and GHABP Scales)
19	(Skarzynski et al., 2014)	Prospective	35	P and A	44y (15-84)	12m	--	They used the median change at low frequencies (125,250, 500Hz) as described by (Fraysse,2006). - **Complete HP=** PTA shift within 10dB **- Partial HP=** PTA shift within 40dB. Also looked at change cross-time was measured at single frequency 500Hz.	Speech perception
20	(Skarzynski et al., 2016)	?	19	P	11.9y (6-18)	24m	Profound SNHL for frequencies over 750 Hz	Skarzynsky's Formula	Insertion depth and hearing at contralateral ear.
21	(Suhling, et al., 2016)	RS	120	A	57y	12m	Preoperative air conduction thresholds better than or equal to 80 dB between 125 and 1500 Hz,	Change of median hearing loss at (125-1500Hz). The degree of HP was classified as follow: PTA shifts 15 dB, >15 to 30 dB, and PTA shift >30 dB.	CBCT scan to determine electrode position
22	(Sun et al., 2015)	Case-control	40	A	33.8y (SD= 14.55)	3m	"Preoperative three-frequency pure-tone average (PTA) hearing at 250 Hz, 500 Hz, and 1,000 Hz of better than 75 dB".	"The residual hearing was considered as preserved when the audiometric changes were <10 dB hearing loss for each variable".	-
23	(Bruce, et al., 2011)	RS	14	P and A	32y (6-79)	1m	Patients who had recordable hearing thresholds that were outside our current criteria for hearing preservation using the FlexEAS electrode (FlexEAS electrode criteria better than 65 dB HL at 250 and 500 Hz).	"Currently, no consensus has been reached on what exactly defines ''successful'' hearing preservation. Present our results in the format of change in hearing levels measured in decibels. PTA was measured at 125, 250, 500, 1,000, and 2,000 Hz".	-
24	(Moteki et al., 2016)	RS	17pt (19 ears)	A	46y (SD= 9.8)	01-May years	All patients had severe high frequency hearing loss and relatively residual low frequency hearing.	Skarzynsky's Formula	Speech perception
25	(adunka et al., 2014)	RS	20	A	55.1y (SD=14.81)	14m	Normal to moderate hearing in the low to mid frequencies and severe-to-profound hearing in the mid to high frequencies.	Chane in the mean pure tone thresholds for 250, 500, 750, and 1,000 Hz	Speech perception

Table 2-2 Implants and surgical details.

No	Author	Electrode array	Comparing RW vs CY	Surgical approach	CY if RW is not accessible	Insertion Depth	Insertion speed	Steroid	Antibiotic	HA
1	(Adunka et al., 2013)	Flex24	No	RW= 10 CY= 8	Yes	Around 20mm	?	Yes	?	Yes
2	(de Carvalho et al., 2013)	Flex24	NO	RW= 5 CY= 1	Yes	?	Slow	Yes	Yes	?
3	(Erixon et al., 2012)	Flex24 FlexSoft (pt.5)	No	RW=21 CY= 0	NA	Mean= 384 degrees (300–540) Mean linear = 21.1mm (17.5–28.5) Stop at resistance	Slowly	Yes	Yes	?
4	(Gstoettner et al., 2009)	Flex24	NO	RW= 7 CY= 2	Yes	Mean = 19.8mm	Slow over a period of approximately 3 min.	Yes	Yes	Yes
5	(Lee et al., 2010)	FlexEAS24(7), Medium (3)	No	RW= 8 CY= 2	?	Mean= 330 degrees (SD= 80)	Slow	?	Yes	?
6	(Brown et al., 2015)	CI422	No	RW= 9 CY= 0	NA	20mm	Slow	Yes	Yes	No
7	(Mahmoud et al., 2014)	Flex24	No	RW= 5 CY= 0	NA	10 of 12 electrodes of the FLEXEAS array were inserted into the cochlea.	?	Yes	Yes	Yes
8	(Usami et al., 2011)	Flex24, FlexSoft, Combi40+(1 case, excluded)	No	RW= 4 CY= 0	NA	Full insertion	?	Yes	?	?
9	(Usami et al., 2014)	Flex24 FlexSoft	No	RW= 31 CY= 0	NA	Full insertion (24mm, and 31.5mm)	?	Yes	?	?
10	(Radeloff et al., 2012)	FlexSoft FlexEAS20	No	RW= 2 CY= 4	?	Full insertion	?	?	?	?
11	(Arnoldner et al., 2010)	FLexEAS24	NO	RW= 8 CY= 3	Yes	18–22 mm, corresponding to 360°	Slow	Yes	Yes	Yes
12	(Guimaraes et al., 2015)	Flex24	No	RW= 16 CY= 3	Yes	Full insertion	slow	Yes	Yes	No
13	(Bruce et al., 2014)	Flex20(1), Flex24(4), Flex28(1), FlexSoft(10)	No	RW= 2 CY= 14	NO	10 full insertion, 6 partial insertion.	Slow	Yes	Yes	?

Table 2-2 Implants and surgical details.

No	Author	Electrode array	Comparing RW vs CY	Surgical approach	CY if RW is not accessible	Insertion Depth	Insertion speed	Steroid	Antibiotic	HA
14	(Erixon et al, 2015)	Flex24(18), MED-EL custom made (1)	No	RW= 19	NA	?	Slow	Yes	?	?
15	(Fischer et al, 2015)	Flex24(24), Flex28(28), FlexSoft(31), Standard (31)	No	RW= 60 CY= 3	?	Mena Depth 451°	?	?	?	?
16	(Hassepass et al., 2015)	CI422	Yes	RW= 27 (22 with RH) CY= 14 (13 with RH)	Yes	- Mean 21.5mm (SD= 1.1) - Mean 388 degrees (SD= 34.7) - Stop at first resistance was felt	Slowly without excessive force.	Yes	Yes	?
17	(Helbig et al., 2011)	FlexSoft(22)	No	RW= 16 CY= 6	Yes	To the first point of resistance. Full insertion (31mm) in 13/22, the depth of the other 9 cases range between 26-29mm.	?	?	Yes	?
18	(Santa Maria et al., 2013)	Flex24	NO	ERW	NA	?	?	Yes	?	?
19	(Skarzynski et al., 2014)	CI422	No	RW	NA	?	?	?	?	?
20	(Skarzynski et al., 2016)	CI422	NO	RW	NA	Full insertion (20-25mm)	?	Yes	?	?
21	(Suhling, et al., 2016)	Flex20(46), Flex24(34), Flex28(40)	NO	RW	NA	Full insertion	?	?	?	?
22	(Sun et al., 2015)	FlexSoft, Standard	Yes	RW= 20 CY= 20	? (Old retrospective sample)	Full insertion	Slow	Yes	?	Yes
23	(Bruce, et al., 2011)	FlexSoft	NO	CY= 14	?	To the first point of resistance. Full insertion (31mm) in 9/14, other 4 cases have one extra-cochlear electrode.	Slow	Yes	Yes	Yes
24	(Moteki et al., 2016)	Flex24	NO	RW= 17 CY= 0	NA	?	Slow	Yes	?	?
25	(adunka et al., 2014)	Flex24	Yes	RW= 12 CY= 8	Yes	Mean= 19.4 (SD=0.92) mm	slowly without the use of any excessive force	Yes	Yes	?

Table 2-3 Primary outcomes (HP success) and secondary outcomes.

NO	Author	Short-term (1-6m)	Mid-term HP (6-12m)	Long-term HP (>12m)	Other outcome measures
1	(Adunka et al., 2013)	"HP was achieved with CY and RW surgical approaches in 17 of the 18 pt.". At activation: PTA at low frequencies (250–1,000 Hz) dropped from 44.7 (SD= 16.5) dB to 60.6 (SD= 16.1) dB. - **2 months after surgery:** 35.3% had complete HP "within 10 dB**".**	- Minimal change at 12 months review. - 23.5% demonstrated a progressive deterioration of pure-tone thresholds over time. - Mean PTA decrease to 68.5 (SD= 21.7) dB at the 12-month interval.		- "The added benefit of hearing preservation on speech perception is of special interest". - "Combined EAS offers excellent speech perception abilities in quiet and in noise". - EAS offers speech perception abilities than conventional CI. - The progressive loss was observed in a small subset of subjects but remains problematic.
2	(deCarvalho et al., 2013)		At 12 months: HP was possible in 4/6 patients. - Complete HP= 1 patient (RW=1) - Partial HP= 3 patients, (RW=2, CY=1) - Total loss of RH= 2 patients (RW=2) - The pt. who had CY had partial HP.		Postoperative speech perception scores improved in all subjects.
3	(Erixon et al., 2012)	At 1 month following surgery: - Mean hearing loss shift at 125–500 Hz was 14.4 dB - All patients had HP. - No total loss was reported.		At 13 months: - PTA shift between 1 and 13m was not significant (16dB).	- Insertion angle (300–540) and depth (17.5–28.5 mm) were **not statistically correlated to hearing loss.** - Anatomic variations of the RW can influence insertion resulting in hearing loss.
4	(Gstoettner et al., 2009)		After a mean follow-up of 9.73 months: - All patients had hearing preservation: - Complete HP (<10db elevation of threshold) = 44.4% - Partial HP= 55.6% - Total loss of RH= 0%		- "Mean monosyllabic test scores improved from 9% correct with the HA alone to 48% with the CI and to 65% in the EAS mode". - EAS offers speech perception abilities than conventional CI.
5	(Lee et al., 2010)	At the fitting time: - 8 out of 10 patients showed sufficient post-operative residual hearing to facilitate EAS.		At the most recent PTA testing (mean= 22.3months): - Substantial increase in acoustic hearing loss= 3 patients (30%) -Complete HP in 5 patients - Total loss of hearing= 2 patients (20%)	- The angular depth varied among patients (180–390°). - HP does not correlate significantly with the angular depth. - "All patients investigated in this study reported benefits from EAS and CI use compared to pre-operative results with conventional HA."
6	(Brown et al., 2015)		At 6 and 12 months: - Low-frequency HP was achieved in all 9 cases (Less than 10 dB average change at low frequencies).		

Table 2-3 Primary outcomes (HP success) and secondary outcomes.

NO	Author	Short-term (1-6m)	Mid-term HP (6-12m)	Long-term HP (>12m)	Other outcome measures
7	(Mahmoud et al., 2014)	**-Immediately after implantation,** patients experienced worsening of between 0 and 40 dB in pure-tone thresholds at isolated low frequencies. -All participants showed preserved hearing after implantation. - No patients met criteria for significant postoperative hearing loss.	-Over the subsequent 12 months: - minimal further changes were observed.		- EAS conditions show significant improvement in speech perception sores sooner than CI alone.
8	(Usami et al., 2011)		"Hearing at low frequencies was well preserved in all 5 cases.		- **Full insertion** of the electrodes showed that hearing at low frequencies was well preserved in all 5 cases. - VEMP were well preserved postoperatively. - **Caloric response** was well preserved in all cases.
9	(Usami et al., 2014)	"Low-frequency (250–1000 Hz) pure-tone thresholds dropped at the initial cochlear implant activation. In particular, hearing deterioration at 500 Hz was evident compared with 250 Hz or 1000 Hz".	- Pure- tone thresholds were maintained until the 12-month evaluation.		- HP was preserved with **full insertion** in all ears - Speech perception results improved over the time. - Speech perception results of EAS results were significantly better than ES only.
10	(Radeloff et al., 2012)	- One week after surgery: - All patients that received a **deep insertion** electrode (**FlexSoft**) array lost their residual hearing. - Patients that received the **Flexeas20-array**, HP was achieved (Patient5 had partial HP and patients6 had complete HP).			**Cochlear microphonics** averaged thresholds were unchanged after **opening of the cochlea**. "Opening of the cochlea does not seem to affect hearing thresholds".
11	(Arnoldner et al., 2010)		The mean follow-up time was 7.85 months. - All cases had HP. - complete HP= 5/11 - partial HP =6/11 - **The 3 CY** cases had partial HP. - **5/8 patients with RW** approach had complete HP. - **3/8 patients with RW** approach had partial HP.		This study proves that both refined surgical techniques and atraumatic electrodes (FlexEAS) are mandatory to preserve residual hearing after cochlear implantation. - Monosyllabic test scores improved from 9% with HA alone to 48% with the CI and 65% in the EAS mode. - Mean HSM sentences in quite improved from 30% in the HA alone to 75% with the CI and 79% with the EAS mode. - Mean HSM sentence in the condition of noise (10 dB SNR) improved from 10% in Ha alone to 42% with the CI and 50% in the EAS condition.

Table 2-3 Primary outcomes (HP success) and secondary outcomes.

NO	Author	Short-term (1-6m)	Mid-term HP (6-12m)	Long-term HP (>12m)	Other outcome measures
12	(Guimaraes et al., 2015)	All patients had higher threshold after the surgery.	Mean time of testing 23.6months: HP was achieved in 89.4% of cases. - Complete HP = 5/19, 63% (5RW) - Partial HP= 12/19, 27% (1CY, 11RW) - No hearing preservation= 2, 10% (2CY), RW was not accessible in these cases.		- Statistical analysis show no significant effect of surgical approach on HP. - No significant difference in speech scores between both approaches.
13	(Bruce et al., 2014)	HP was achieved in 14/ 16 ears.	- The HP of the 13 patients **changes over time.** However, the reduction of the group overall **was not significant**.	- 7/10 patients with more than 2years follow up had complete HP, in fact 5 of them had improved hearing threshold.	- Speech perception score is better with the additional natural hearing than CI alone. - HP was possible with all electrode types.
14	(Erixon et al, 2015)	One month after surgery: the mean loss of residual hearing at low frequency range (125-500Hz) was 17dB.	**12 months after surgery:** the mean loss of residual hearing at low frequency range (125-500Hz) was 19dB.	**24 months after surgery:** the mean loss of residual hearing at low frequency range (125-500Hz) was 24dB.	- No significant correlation between the level of HP, **speech perception or patient satisfaction**. - All patients show **satisfaction** with their CI regardless of the level of HP.
15	(Fischer et al, 2015)	- The mean hearing threshold elevated in both groups (with and without electrode dislocation). - The mean hearing threshold changed over time (6,12, 24 weeks after the surgery).			- 7.9% of cases had electrode dislocation from ST to SV. - No hearing difference were noted between patients with and without dislocation. - "The dislocation rate did not significantly correlate with the **insertion depth**".
16	(Hassepass et al., 2015)	At initial activation: - there was a significant increase in the PTA threshold at low frequency range compared to pre-operative PTA.	- Slight change over time (1,3,8months), but not significant.		- No significant difference in the level of HP between the **CY group and the RW group.** - 82.9% ST insertions, 14.6% dislocations from the ST to the SV. - Dislocation happens in 4/14 patients from the CY group and 2/27 from the RW. - Gradual improvement of speech perception scores across time.
17	(Helbig et al., 2011)	intermediate testing (1-10months) -14 subjects preserve residual hearing, - Complete hearing loss = 5/ 22 (22.7%) - PTA shift within 10dB = 4/22 (18.2%). - PTA shift between 11-30dB = 9/22 (40.9%). - PTA shift >31dB = 4/22 (18.2%).	Most recent testing (6-36months) 11/14 (79%) had stable HP (within 10dB) at the most recent test. - PTA shift within 20dB = 2/14 (14%). - PTA shift >20dB = 1/14 (7%).		- **Monosyllable testing i**n quiet shows significant improvement over time. - 2/6 cases with CY insertion and 3/16 with RW insertion lost all RH. - **S**table HP was noticed **over time.** - No statistically significant relation between **insertion depth and PTA shift.**

Table 2-3 Primary outcomes (HP success) and secondary outcomes.

NO	Author	Short-term (1-6m)	Mid-term HP (6-12m)	Long-term HP (>12m)	Other outcome measures
18	(Santa Maria et al., 2013)	The hearing preservation rate was 100% - Complete (42.9%) - Partial (50%) - Minimal HP (7.1%)	At 12months: - Complete (22.2%) - Partial (66.7%) - Minimal HP (11.1%)	12-24 months: - Complete (33.3%) - Partial (22.2%) - Minimal HP (44.5%)	**- Speech discrimination** in noise improved between pre- and post-operative. **- The APHAB and GHABP** scores showed an improvement - Hearing preservation can be achieved in the short term but deteriorates with time over the medium term.
19	(Skarzynski et al., 2014)	At 1month: Overall thresholds at 500 Hz deteriorated slightly across the whole population. - Complete HP (within 10 dB) = 43% of cases. - Partial HP (Within 30 dB) = 86% of cases.	At 12 months: - Complete HP (within 10 dB) = 38% of cases. - Partial HP (Within 30 dB) = 79% of cases.		**- The average words score** in quiet, and noise improved between pre-op and post-operative. - The groups with higher preoperative threshold had better HP and speech perception scores in quiet and noise.
20	(Skarzynski et al., 2016)	At activation: Mean S value 73% - Complete HP = 12/19 (63%). - Partial HP = 3/19 (16%). - Minimal HP = 4/19 (21%)	At 12 months: Mean S value 75% - Complete HP = 10/19 (53%). - Partial HP = 5/19 (26%). - Minimal HP = 4/19 (21%)	Mean S value 67% Mean S value 67% - Complete HP = 10/19 (53%). - Partial HP = 5/19 (26%). - Minimal HP = 4/19 (21%)	- Shallower angular insertion correlate with better HP. - Contralateral ear showed stable hearing.
21	(Suhling, et al., 2016)	At initial fitting the median HL of - 17.5 dB (FLEX20), - 20 dB (FLEX24), - 24 dB (FLEX28). At initial fitting a HL of =<15 dB was achieved in 45.6% TFEA20 subjects. 29.4% TFEA24 subjects. 15.0% TFEA28 subjects.	At 12months: - medial HL of: - 15 dB (FLEX20), - 19.4 dB (FLEX24), - 32.5 dB (FLEX28). stable	-	* Shorter arrays provide better HP - Significant differences were found between the TFEA28 and TFEA20 at 3,6 AND 12 months. - Significant differences were found between the TFEA28 and TFEA24 at 12 months. - The percentage of total HL (> 30 dB) at 12 months was significantly higher with the TFEA28 (57.9%) group than in the TFEA24 (33.3%) or TFEA20 (23.1%) group.

Table 2-3 Primary outcomes (HP success) and secondary outcomes.

NO	Author	Short-term (1-6m)	Mid-term HP (6-12m)	Long-term HP (>12m)	Other outcome measures
22	(Sun et al., 2015)	Hearing preservation rate (average PTA deterioration of 10 dB at 250, 500, and 1,000 Hz) for each surgical approach was: 65% of cases in the CY group 80% of cases in the RW group.			- The level of hearing deterioration in the RW group was lower at all frequencies compared with the cochleostomy group. However, **no statistically** significant difference in the preservation of residual hearing was found in the two surgical **approach groups (RW and CY).** - Significant difference in the level of HP between the Standard (55.6%) and FLEX SOFT (86.4%) groups. **"**The result may be due to the CY group having a higher percentage of Standard electrode users (55%) than the RW approach group (35%)**"**.
23	(Bruce et al., 2011)	- "This study also demonstrates that hearing preservation can be achieved using a ''cochleostomy'' approach rather than the more commonly advocated ''round window'' approach".			- "this study demonstrates that residual hearing may be preserved with a deep insertion of a cochlear implant electrode array".
24	(Moteki et al., 2016)		At 1year post-operative: - Complete HP=5/19 (26%), - Partial HP= 11/19(58%), - Minimal HP= 2/19 (11%) - Total loss of RH= 1/19 (5%)	At 2 years post-operative: - Complete HP=5/19 (26%), - Partial HP= 11/19(58%), - Minimal HP= 2/19 (11%) - Total loss of RH= 1/19 (5%)	- "EAS showed better results than electric stimulation alone, in spite of an absence of speech perception with acoustic stimulation".
25	(Adunka et al., 2014)	- One patient from the CY group (1 of 8, 12.5%) completely lost hearing as a result of surgery. - All subjects in the round window group retained at least some ipsilateral hearing after surgery.		At 14 months: - "There was no significant difference (p= 0.327) between the 2 cohort's residual hearing obtained preoperatively and at the 12-month post-operative"	

2.4.1 Article appraisal

The Downs and Black (1998) checklist was used to assess the quality of the studies. This checklist is designed to assess the level of evidence in both randomised and non-randomised trials, and only RCTs can have a complete score. The assessment outcome showed that seven studies had ‘good’ quality, two studies had ‘poor' quality, and most articles (16/25) had ‘fair’ quality. Of the 25 articles, one was prospective (Skarzynski et al., 2014), while the majority were retrospective. Appendix 3 shows the results of all articles.

2.4.2 Duration of follow-up

The timing of postoperative hearing assessment varied between studies. The follow-up period of each study was reported as a mean, and few studies reported follow-up as a range (Table 2-1). Of the 25 studies, 4 had a mean follow-up less than 6 months, 1 of which reported threshold only one week after surgery (Radeloff et al., 2012), 11 studies had a mean follow-up between 6 and 12 months, 7 studies had a mean follow-up between 12 and 24 months, and only 3 studies had more than 24 months of follow-up (Moteki et al., 2016, Helbig et al., 2011a, Bruce et al., 2014).

The mean follow-up did not represent the timing of the final outcomes in all studies, as some reported HP outcomes at multiple intervals. 19/25 articles reported short-term HP (1–6 months after surgery). All studies reported significant differences between the preoperative and postoperative audiograms at activation; 12 of these 19 studies reassessed HP at the 12-month follow-up, and 10 of the studies reported stable HP compared to the initial review. Five studies reported HP at mid-term (6–12 months) and long-term (>12 months) HP outcomes (Bruce et al., 2014, Erixon and Rask-Andersen, 2015, Mick et al., 2014, Santa Maria et al., 2013, Skarzynski et al., 2016, Moteki et al., 2016); of these 5 studies, 3 showed stable RH compared with their previous follow-up (Bruce et al., 2014, Skarzynski et al., 2016, Moteki et al., 2016). Table 2-3 presents the HP outcomes of the studies at each of the follow-up periods.

2.4.3 Inclusion criteria for HP

The definition of RH varies between studies. Although the primary objective of all studies is HP, the inclusion criteria varied widely among them. The general focus of the described inclusion criteria was RH at low frequencies; however, there was no agreement on the included frequencies, which ranged between 125 Hz and 2000 Hz. Moreover, there was no agreement on the amount of RH. Various PTA thresholds were used as cut-off points (<60 dB, <65 dB, 75 dB, and 80 dB) (Table 2-1). Some of the studies used descriptive definitions, like ‘measurable hearing at low-frequency range’, ‘severe high frequency and relatively residual low frequency’, ‘mild-to-moderate low-frequency HL and severe-to-profound sensorineural high-frequency HL, ‘normal to moderate HL in the low- to mid-frequencies, and sloping severe to profound HL in the mid-to-high frequencies bilaterally’, ‘profound sensorineural HL for frequencies over 750 Hz’, ‘recordable hearing at 125, 250 and 500 Hz’, and ‘patients with profound high-frequency HL and acoustically aidable low-frequency hearing’ (Table 2-1).

2.4.4 Method of calculating HP

The method of calculating HP varied widely across the literature, and consequently, the definition and classification of HP varied as well. The inclusion criteria and the frequencies used to quantify the degree of HP differed between studies. However, most studies considered the change in PTA at low frequencies; most used frequencies ranged between 125 Hz and 2000 Hz, and few studies used 125–8000 Hz.

The 25 studies included in this review used nine different methods for quantifying the success of HP (Table 2-1). These nine methods could be divided into three main themes. The first theme was used in 8/25 studies, and it involved the use of statistical methods to compare the preoperative and postoperative mean/median of the pure tone threshold for a specific range of frequencies. The second theme, used in 14/25 studies, used categorical scales to describe the success of HP. There were many categorical scales used in the included studies. For example, some studies considered HP successful if the postoperative hearing threshold was within 10 dB of the preoperative threshold (Bruce et al., 2014). Other studies considered more than one category. For example, they defined complete HP as a <10-dB shift in PTA and partial

HP as >10-dB shift in PTA (Helbig et al., 2011a). Several other categorical scales are shown in Table 2-1.

The third theme used the relative change in hearing threshold, as described by the HEARRING Group. This method was first proposed in 2013 as a universal definition and classification system for HP (Skarzynski et al., 2013). Skarzynski et al. (2013) described a formula to calculate relative changes in the preoperative dynamic range (Figure 2-1). The result of this formula is reported as a percentage, known as the 'S value'. According to the S value, the degree of HP can be classified into four categories. Table 2-4 shows the four degrees of HP. In our systematic review, only 3/25 studies used this method (Santa Maria et al., 2013, Skarzynski et al., 2016, Moteki et al., 2016). The outcomes of these studies were reported as complete HP, partial HP, minimal HP, or loss of all RH. All three studies used the RW approach in all cases, and their findings are summarised in Table 2-3.

Figure 2-2 The HEARRING Group's formular for Hearing preservation.

$$S = \left[1 - \left(\frac{(PTApost - PTApre)}{(PTAmax - PTApre)} \right) * 100 \right] [\%]$$

The HEARRING Group formula of HP classification system. PTAmax is the limit of the audiometer (see Table 1.1). PTApost is PTA measured postoperatively, while PTApre is PTA measured before the operation.

Table 2-4 The scale of the HEARRING Group's HP classification system.

Percentage of HP	**Classification**
>75%	Complete HP
26–75%	Partial HP
0–25%	Minimal HP
No measurable hearing	Loss of hearing/No hearing

2.4.5 Surgical approach

The method of electrode insertion into the cochlea was reported in most studies. Of the 25 studies, 1 study used a CY approach for all patients, 11 studies used a RW or extended RW approach for all patients, and 13 studies used a mixture of both approaches (Table 2-2).

Many of the studies mentioned the reason for using the CY approach in some cases. Of the 13 studies that used a mixture of both approaches, 8/13 used the CY approach in cases of limited accessibility or visibility of the RW, 1/13 used the CY approach based on surgeon preference (Bruce et al., 2014), and 4/13 did not mention any reason for using the CY approach (Table 2-2).

Studies that compared both surgical approaches

Of the 13 studies that used a mixture of both approaches, 3 aimed to investigate the effect of the surgical approach on HP (Hassepass et al., 2015, Sun et al., 2015, Adunka et al., 2014). All studies reported no significant effect of surgical approach on HP. The first study was conducted by Hassepass et al. (2015) and had a retrospective design. They reported that the CY approach was used if the RW was not accessible. The study used CI422 and had a mean follow-up of 8 months. They reported a stable hearing threshold at activation and a slight insignificant change overtime at 1, 3, and 8 months. In addition, Hassepass et al. (2015) investigated intra-cochlear trauma and reported electrode dislocation from the ST to the SV in 4/14 cases implanted via the CY approach and 2/27 cases implanted via the RW approach.

The second study used FlexSoft and Med-El standard electrode arrays and had a mean follow-up time of 3 months (Sun et al., 2015). This study considered RH as preserved when the change in PTA was <10 dB. The findings of this study highlighted a higher rate of HP in patients implanted with the FlexSoft electrode than the standard electrode ($p = 0.032$). In addition, the CY group had a higher percentage of standard electrodes (55%, 11/20) than the RW group (35%, 6/20), despite there being no significant difference in the level of HP between both approaches.

The third study had a retrospective design and used the CY if the RW was not accessible (Adunka et al., 2014). The study used Flex24 electrodes and had a mean follow-up time of 14 months. They reported that 1/8 cases with the CY approach lost all RH, while all cases with the RW approach retained some RH after surgery. The difference between both approaches did not show any statistical significance ($p = 0.327$).

Studies that used both approaches and did not aim to measure the effect of the surgical approach

Most studies (10/13) that used a mixture of both approaches did not aim to measure the effect of the surgical approach; 5/10 of these studies reported the level of HP regardless of the surgical approach (Fischer et al., 2015, Bruce et al., 2014, Radeloff et al., 2012, Lee et al., 2010a, Gstoettner et al., 2009), and the remaining 5 studies commented on the outcomes of each approach separately (Arnoldner et al., 2010, de Carvalho et al., 2013, Adunka et al., 2013, Helbig et al., 2011a, Guimaraes et al., 2015). The CY approach was used when the RW was not accessible in all studies. Two of the five studies reported that patients with the CY approach had partial HP (Arnoldner et al., 2010, de Carvalho et al., 2013).

Three out of the five studies had some cases with total loss of RH (Adunka et al., 2013, Helbig et al., 2011a, Guimaraes et al., 2015). The first study reported that HP was achieved in 7/8 CY cases and in 10/10 RW cases (Adunka et al., 2013). The second study was conducted by Helbing et al. (2011) and included 16 cases implanted via the RW approach and 6 cases implanted via the CY approach. The FlexSoft electrode was used for all subjects. The study reported a total loss of RH in 3/15 subjects with RW insertion and in 2/6 subjects with CY insertion.

The third study included 16 cases implanted via the RW approach and 3 cases implanted via the CY approach (Guimaraes et al., 2015). The authors reported a tendency of better HP following the RW approach; however, it was not significant ($p = 0.87$). Patients implanted via the RW approach had partial or complete HP. In contrast one out of three patients in the CY group had successful HP. The author believed that the results might have been biased due to the small sample size of the CY group ($n = 3$). The CY approach was used in this study in case of inaccessible RW. According to the author, unfavourable anatomy in CY conditions could be the main reason for asymmetric HP outcomes between both groups.

Studies that used the CY approach only

Bruce et al. (2011) was the only study that used the CY approach exclusively. This study explored deep insertion of the FlexSoft electrode array while using the CY approach. The depth of insertion in this study was limited to the resistance point. As a

result, full insertion was achieved in 10 cases, and 4 cases had one extra-cochlear electrode. The study did not have specific criteria to classify the degree of HP; however, they considered stability and changes in hearing level measured in decibels in the range of 125 Hz to 2000 Hz. The study reported that HP was observed in all 14 cases. HP was considered successful in 12/14 cases, as the remaining 2 patients experienced deterioration in the level RH at later follow-ups.

Studies that used the RW approach only

The RW approach was used alone in 11 out of 25 studies. The method of reporting HP varied between studies which made the comparison difficult. The HEARRING Group classification system was used in 3/11 articles (Santa Maria et al., 2013, Skarzynski et al., 2016, Moteki et al., 2016). Santa Maria et al. (2013) and Moteki et al. (2016) reported that partial HP was achieved 1 year after activation in the majority of cases (66% and 58%, respectively), followed by complete HP (22.2% and 26%, respectively), and minimal HP (11.1% and 11%, respectively). After 2 years post-surgery, Moteki et al. (2016) reported stability of RH when assessed 12 to 24 months after surgery. In contrast, Santa Maria et al. (2013) reported that most patients had minimal HP (44.5%), followed by complete HP (33.3%), and partial HP (22.2%).

The findings of Skarzynski et al. (2016) were different in that they reported that most patients had complete HP at activation (63%), followed by minimal HP (21%), and partial HP (16%). RH was reassessed 24 months after surgery, which showed that most cases had complete HP (53%), followed by partial HP (26%), and minimal HP (21%). All three articles that used the HEARRING Group method reported that most patients had either partial or complete HP. None of these studies showed total loss of RH.

Some studies used a certain shift in the postoperative PTA, measured in decibels, as a cut-off point for HP; however, these cut-off points differed between studies. A <10-dB PTA shift was used by two studies as a mark of successful HP (Brown et al., 2015, Skarzynski et al., 2014). Brown et al. (2015) used CI422 and reported complete HP in all patients at low frequencies (125–1000 Hz). Skarzynski et al. (2014) used the same electrodes and reported that 43% of their subjects had complete HP at activation and

43% of cases had partial HP (PTA shift 10–30 dB). At 1 year follow-up, subjects showed stable RH; 38% had complete HP, and 41% had partial HP.

Another study used a 20-dB PTA shift as a mark of significant change in RH (Mahmoud et al., 2014). They reported that all patients showed preserved hearing and that none of the patients met the criteria for significant change in RH (greater than 20 dB reduction in threshold across low-frequencies [250- 3000Hz]). Minimal changes were observed at the 12-month follow-up; no details were provided about these changes. Suhling et al. (2016) categorised the PTA shift into three categories: <15 dB, 16–30 dB, and >30 dB. This study used Flex20, Flex24, and Flex28 electrodes and reported better HP using shorter electrodes. The first assessment at initial fitting showed that 30/120 (25%) of subjects had a <15-dB PTA shift, 27/120 (22.5%) had a 15–30-dB PTA shift, and 22/120 (18.3%) had a >30-dB PTA shift. At 12 months post-surgery, 33/79 (41.7%) subjects showed a <15-dB PTA shift, 20/79 (25.31%) had a 15–30-dB PTA shift, and 26/79 (32.29%) had a >30-dB PTA shift. Other studies reported the mean change at different frequency ranges and reported successful HP. However, it is difficult to compare these results with other studies and draw meaningful conclusions (Erixon et al., 2012, Usami et al., 2011, Usami et al., 2014a, Erixon and Rask-Andersen, 2015).

2.4.6 Electrode type and insertion depth

This systematic review includes studies that used modern LW electrode arrays that were longer than 20 mm. Seven different electrodes were used in the 25 studies included in this systematic review (CI422, Flex20, Flex24, Flex28, FlexSoft, Standard, and Combi40+). The main focus of all studies was HP, and they thus used atraumatic electrodes. However, some of the studies included cases that used Combi40+ (Lee et al., 2010a, Usami et al., 2011) or Med-El Standard electrodes (Fischer et al., 2015, Sun et al., 2015). Erixon and Rask-Andersen (2015) used custom-made electrodes in 1/18 cases in their study. Of the 25 studies, 15 used electrode arrays that were under 25 mm in length, 3 used electrode arrays over 25 mm in length (Hassepass et al., 2015, Adunka et al., 2014, Sun et al., 2015), and 7 used electrodes of different lengths (Bruce et al., 2014, Usami et al., 2014a, Erixon et al., 2012, Usami et al., 2011, Radeloff et al., 2012, Suhling et al., 2016) (Table 2-2).

Electrode length and surgical approach

The three studies that compared both surgical approaches used CI422 (Hassepass et al., 2015), Flex24 electrodes (Adunka et al., 2014), and FlexSoft, Standard (Sun et al., 2015). The two studies that used <25-mm electrodes reported no significant difference between the surgical approaches. The mean follow-up time of the first study was 8 months (Hassepass et al., 2015), while the mean follow-up time of the second study was 12 months (Adunka et al., 2014). The last study used conventional-length (>25 mm) electrodes and reported no significant difference between approaches at the 3-month follow-up (Sun et al., 2015). Finally, Bruce et al. (2011) used FlexSoft electrodes and was the only study to use the CY approach for all cases. The study reported successful HP with deep insertion via the CY approach at 1-month follow-up.

Studies that used electrodes of different lengths

In our systematic review, seven studies used electrodes of different lengths. One of the studies reported HP irrespective of the electrode type (Fischer et al., 2015). Furthermore, they reported that the rate of electrode dislocation did not significantly correlate with the insertion depth. The remaining six studies investigated the effect of electrode length on the degree of HP; four of the studies showed no significant correlation between electrode depth and HP and reported that RH was preserved in all cases (Bruce et al., 2014, Usami et al., 2014a, Erixon et al., 2012, Usami et al., 2011).

Two out of the six studies reported some relationship between insertion depth and HP, suggesting better HP with shallower insertion (Radeloff et al., 2012, Suhling et al., 2016). The first study reported that all cases implanted with the longer electrode (FlexSoft) lost all RH 1 week after surgery. In contrast, all cases implanted with the shorter array (Flex20) had successful HP (Radeloff et al., 2012). The second study used Flex20, 24, and 28 electrodes. The study reported a significant difference in HP between the Flex20 and Flex28 electrodes at the 3-, 6-, and 12-month follow-up and a significant difference between the Flex24 and Flex28 electrodes at 12-month follow-up (Suhling et al., 2016).

2.4.7 Use of corticosteroids, antibiotics, and hyaluronic acid

Corticosteroid use during surgery was reported in 19 of the 25 studies we reviewed (Table 2-2), while the remaining 6 studies did not mention administration of corticosteroids. The regimen, dose, and type of corticosteroids used varied among the studies that confirmed corticosteroid usage. Some studies used intraoperative parenteral corticosteroids, while others used topical corticosteroids and/or postoperative corticosteroids. Successful HP was reported by four of the six studies that did not comment on the use of corticosteroids (Lee et al., 2010a, Helbig et al., 2011a, Skarzynski et al., 2014, Suhling et al., 2016). Of the 19 studies that confirmed administration of corticosteroids, all reported successful HP either at activation or 12 months after surgery (Table 2-3).

The administration of prophylactic antibiotics was mentioned in 13/25 studies (Table 2-2). Of these 13 studies, 10 showed successful HP in most patients. In contrast, the remaining three studies showed either a significant shift in HP or total loss of RH in some patients (Lee et al., 2010a, Hassepass et al., 2015, Helbig et al., 2011a). Six of the twenty-five studies used hyaluronic acid during electrode insertion (Adunka et al., 2013, Gstoettner et al., 2009, Mahmoud et al., 2014, Arnoldner et al., 2010, Sun et al., 2015, Bruce et al., 2011); all six of these studies reported successful HP.

2.4.8 Secondary outcomes

The primary outcome of all the included studies was HP. However, some studies had secondary objectives related to HP. For example, 15 studies investigated the outcome of speech perception; all reported significant improvement in speech perception scores compared with preoperative scores. Seven studies reported that the speech perception scores following EAS were better than electric stimulus alone (Adunka et al., 2013, Gstoettner et al., 2009, Mahmoud et al., 2014, Usami et al., 2014a, Arnoldner et al., 2010, Bruce et al., 2014, Moteki et al., 2016), two studies reported that speech perception improved over time (Hassepass et al., 2015, Helbig et al., 2011a), and two studies reported no significant difference in speech perception scores between both surgical approaches (Adunka et al., 2014, Guimaraes et al., 2015). Patient satisfaction surveys were used in two studies and showed improvement compared with preoperative responses (Santa Maria et al., 2013, Erixon and Rask-Andersen, 2015);

the Erixon and Rask-Andersen study showed no correlation between patient satisfaction and the level of HP or speech perception.

Two studies assessed electrode position, and both reported a low rate of dislocation (Fischer et al., 2015, Hassepass et al., 2015). Hassepass et al. (2015) found no significant relationship between electrode dislocation and surgical approach. Radeloff et al. (2012) used cochlear microphonics and found that the thresholds did not change after opening the cochlea. Usami et al. (2011) assessed the vestibular evoked myogenic potential (VEMP) and caloric response after the operation and found that both responses could be preserved.

2.4.9 Results of the pooled data

As seen earlier, comparing the two surgical methods is challenging. There are more than 9 methods for quantifying and reporting HP. Heterogeneity in outcome reporting hinders meaningful comparison between the studies. Furthermore, several studies reported total HP in all individuals, regardless of surgical approach. For that reason, it was not possible to conduct a meta-analysis. However, some of the included studies provide raw audiogram data. Therefore, it was possible to combine all the available raw data and compare HP outcomes between approaches.

2.4.9.1 Sample characteristics

Of the 25 studies, it was possible to extract data from 10 articles. We contacted 15 authors to provide additional data. Two authors provided us with their raw PTA data, which brings the total number of included studies to 12 (Adunka et al., 2013, de Carvalho et al., 2013, Erixon et al., 2012, Gstoettner et al., 2009, Lee et al., 2010a, Brown et al., 2015, Mahmoud et al., 2014, Usami et al., 2011, Usami et al., 2014a, Radeloff et al., 2012, Arnoldner et al., 2010, Guimaraes et al., 2015), and the total number of cases in all studies was 128. All included studies were non-randomised and retrospective. The largest sample size was 30 cases, and the smallest was 5 cases. The most commonly used electrodes in the included studies were Flex24 (86.7%), followed by CI422/CI522 (7.8%), and FlexSoft (5.5%). The levels of HP in patients who received Flex24 and CI422/522 were analysed because their properties were similar. Ages in the sample populations ranged from 3 to 87 years old, with only 3 paediatric patients. The most commonly reported frequencies were 250, 500, and

1000 Hz. The reported follow-up period varied between the studies; because 100 of the 128 cases had a 12-month follow-up time, it was chosen for the analysis.

The analysis of HP data included 100 patients who had 12 months of follow-up. Before analysing the data, variables and outcomes were tested for frequency and distribution. The data were analysed using SPSS 24. The relationship between HP and surgical approach was assessed by conducting a Welch t-test. The HEARRING Group formula and classification system were employed to handle the data, as described by Skarzynski et al. (2013) (Figure 2-2 and Table 2-4). The HEARRING Group formula calculates the S value (%), which represents the relative change in RH. The S value was translated into a categorical scale.

2.4.9.2 Difference in hearing preservation between the RW and CY approach

In this sample, there were 14 cases of CY and 86 cases of RW. The mean HP (S value) of the CY group was 44.6% (SD= 32.2), and the mean HP (S value) of the RW group was 59.3% (SD= 28.7). Figure 2-3 shows that most patients in our sample had partial HP (58%), followed by complete HP (28%), minimal HP (7%), and total loss of RH (7%). Figure 2-4 compares the degree of HP between both surgical approaches. Both groups had a similar percentage of patients in the partial and complete HP categories; in contrast, the CY group showed a higher percentage of total loss of RH (Figure 2-4).

This difference between both groups was investigated by conducting a Welch's t-test. The Welch test was chosen due to the unequal sample sizes of the groups. The results of the Welch test showed that there was no significant difference in the level of HP between both groups ($F[1, 30.17]= 2.58$, $p<0.127$) (Table 2-5 and Table 2-6).

Figure 2-3 The percentage of patients in each HP category, irrespective of the surgical approach.

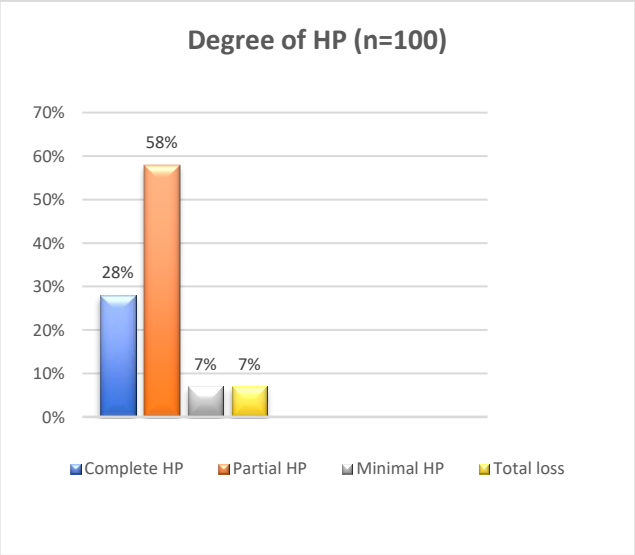


Figure 2-4 The percentage of patients in each HP category according to the surgical approach.

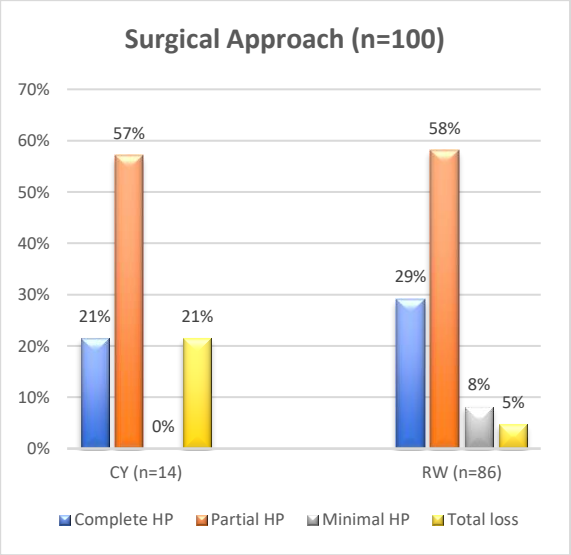


Table 2-5 The HP results of both groups and the number of patients in each HP category in the low-frequency range (250–1000 Hz) 12 months after surgery.

			Categories of HP at low-frequency range (250–1000 Hz) 12 months after surgery				
			Complete HP	Partial HP	Minimal HP	Total loss of RH	Total
Surgical approach	Cochleostomy	Count	3	8	0	3	14
		%	21.4%	57.1%	0.0%	21.4%	100.0 %
	Round window	Count	25	50	7	4	86
		%	29.1%	58.1%	8.1%	4.7%	100.0 %
Total		Count	28	58	7	7	100
		Expected Count	28.0	58.0	7.0	7.0	100.0

Table 2-6 Results of the Welch test.
There was no significant difference in the level of HP between both surgical groups.

		Statistic	df1	df2	Sig.
Percentage of HP at low-equency range (250–1000 Hz) 12months after surgery	Welch	2.579	1	16.515	.127
	Brown-Forsythe	2.579	1	16.515	.127

a. Asymptotically F distributed

2.5 Discussion

This systematic review aimed to compare HP among patients implanted with modern atraumatic LW electrodes employing either the RW or CY approach. We included 25 studies. The RW approach was more common in the literature. Most of the recently published articles reported on HP using the RW approach only. In contrast, only one study used CY as the main approach for all patients, based on the surgeon's preference. Three articles aimed to compare the effects of surgical approach on HP. Other studies demonstrated the possibility of HP and used the CY approach as an alternative approach if the RW approach was not possible. Comparing the results of different studies was difficult due to the heterogeneity of HP quantification methods.

2.5.1 Definition and classification systems for hearing preservation

A great discrepancy in reported results was due to two points that made the results difficult to compare: HP categorical classification and inconsistency in the definition of HP. The same observation was reported by Santa Maria et al. (2014). Our systematic review found nine different methods for quantifying the success of HP. Most of these methods used categorical scales, and few studies used relative change, as described by the HEARRING Group (Skarzynski et al., 2013). The categorical scales method could be misleading as it does not consider the level of preoperative RH. For example, a 10-dB, 30-dB, or 40-dB shift in patients with normal to mild HL at low frequencies cannot be compared to patients with severe preoperative HL. Moreover, these scales may be affected by the maximum audiometer levels in patients who have a high hearing threshold or minimal RH. For that reason, a specific change in decibels cannot be used to assess HP in all patients.

In contrast, a few studies (3/25) used the HEARRING Group method. The HEARRING Group method can calculate changes more accurately as it considers the relative change in PTA for each patient and reports the result as a percentage (S value) (Skarzynski et al., 2013). The values are then translated to a four-category scale. This classification system allows for more meaningful comparison between studies as it functions independently from the preoperative hearing threshold and can be used for patients with any measurable hearing threshold. Patients may not notice their preserved hearing, yet it affects their clinical outcomes. The concept of HP is no longer

limited to patients with a substantial amount of RH, and postoperative hearing assessment can be used as an indicator of cochlear health after surgery. We anticipate that future research will employ this strategy, allowing us to gain a deeper understanding of HP.

2.5.2 Surgical approach

In this systematic review, we found more studies that used the RW approach than the CY approach. Most studies used the RW approach for all cases, and most of them reported successful HP. Only one study used the CY approach for all patients and showed successful HP with deep insertion.

We found three studies that aimed to compare both surgical approaches (Hassepass et al., 2015, Sun et al., 2015, Adunka et al., 2014). The CY approach was utilised in all three studies in settings of low visibility or limited access to the RW, which may have skewed the results because of unfavourable cochlear orientation. However, none of the three studies reported a significant difference between the two procedures. Another bias was noted in one of the three studies. Sun et al. (2015) used two types of electrodes: Med EL Standard and FlexSoft. The second electrode is known to be less traumatic, which was reported in the study. The study highlighted that the CY approach group had a higher percentage of standard electrodes (55%, 11/20) than the RW group (35%, 6/20). Despite this limitation, they found no significant difference in the level of HP between both approaches. Therefore, the question remains unanswered in ideal conditions; it is possible that the CY approach is superior if used in perfect RW orientation and with identical atraumatic electrode array. In their meta-analysis in 2014, Santa Maria et al. concluded that the CY approach provided better HP than the RW approach.

To obtain a more accurate answer and overcome the limitation imposed by the heterogeneity of the methods, we attempted to pool raw audiogram data from patients implanted with moderate-length (20–25 mm) atraumatic LW electrodes and compare the HP level between both approaches. The statistical analysis of the pooled data did not show any significant difference in the level of HP between both approaches. This finding was in line with a previous systematic review (Havenith et al., 2013). The current evidence shows no superiority of either surgical approach, and it supports the possibility of preserving RH when using either approach.

2.5.3 Time of PTA assessment

The duration of follow-up after the operation was inconsistent across the literature. The audiological assessment results were reported at various periods, ranging from 1 month to 24 months after surgery. We noticed that the majority of studies reported short- to mid-term outcomes, within the first year. The same finding was reported in a previous systematic review (Santa Maria et al., 2014). The three studies that compared both surgical approaches had three different follow-up intervals: 3 months (Sun et al., 2015), 8 months (Hassepass et al., 2015), and 12 months (Adunka et al., 2014). All three studies showed no significant difference between the approaches, suggesting that both surgical approaches were equally effective in preserving RH in the short- to mid-term.

Some studies in this systematic review reassessed RH at 12 and 24 months, and stability of hearing was reported by 77% (10/13) and 57% (4/7) of the studies, respectively. Similar results were reported in previous studies (Mowry et al., 2012). Another study reported that 50% of patients had complete HL or minimal HP after 24 months of being implanted with FlexEAS via the ERW approach (Santa Maria et al., 2013). Gstoettner et al. (2006) studied the stability of RH post-implantation with the Med-El standard electrode. All patients had stable hearing 2 years before the operation. After following patients for 25 months, it was noted that 21.7% (5/23) of the patients had delayed loss of RH. A previous meta-analysis found that studies with more extended follow-up periods had a higher rate of partial HP and a lower rate of complete HP (Santa Maria et al., 2014). These studies suggest the need for long-term follow-up reporting because deterioration can occur after several months.

Loss of postoperative RH may occur at an early or late stage. RH is lost at an early stage because of physical damage to the intra-cochlear trauma, mainly due to electrode insertion. In contrast, delayed loss of RH may occur due to chronic inflammation in the cochlea, which leads to oxidative stress, cell apoptosis, ST neo-ossification, and fibrous tissue growth around the electrodes (Bas et al., 2012, Adunka and Kiefer, 2006, Nadol and Eddington, 2006, Li et al., 2007). It is possible that studies assessing the hearing threshold of their candidates early after implantation reported

better results than those which conducted their assessment 12 months or later. This highlights the necessity for long-term research evaluating hearing beyond 24 months.

2.5.4 Electrode array and insertion depth

The effect of the electrode array has been investigated in many studies. LW electrodes have been shown to be less traumatic than pre-curved electrodes (Boyer et al., 2015, James et al., 2006). This systematic review attempted to minimise the effect of electrode design by including studies that used modern atraumatic LW electrode arrays, and most of these studies showed successful HP. According to the examined studies, both short (<25 mm) and long (>25 mm) electrodes could be used to obtain HP with both surgical techniques (Hassepass et al., 2015, Sun et al., 2015, Adunka et al., 2014, Bruce et al., 2011).

Most studies that compared the HP outcomes using different electrode arrays reported no significant effect of electrode array type or insertion depth on HP (Erixon et al., 2012, Bruce et al., 2014, Fischer et al., 2015, Usami et al., 2011, Usami et al., 2014a). In contrast, two other studies suggested that shorter arrays provided better HP (Radeloff et al., 2012, Suhling et al., 2016). It appears that most studies do not support this relationship; variation between studies could be related to the methods of quantifying HP. In accordance with our findings, Santa Maria et al. (2014) reported a mixed trend depending to the definition of HP and suggested no correlation between HP and electrode type or insertion depth.

Many studies suggested that the benefits of deep insertion and full coverage overcame the limitations of shallow insertion, especially in cases of late loss of RH that necessitated re-implantation of a longer electrode array (Helbig et al., 2016). Patients are exposed to the dangers of cochlear trauma and the risks associated with general anaesthesia when they undergo a second surgery. Following the loss of RH, patients implanted with longer electrodes had better speech discrimination compared with those implanted with shorter electrodes (Friedmann et al., 2015). Therefore, it may be preferable to use longer electrodes and deeper insertions to be able to convert to total electrical stimulation in cases of late-onset HL (Eshraghi et al., 2016, Nguyen et al., 2016).

2.5.5 Use of systematic corticosteroids, antibiotics, and hyaluronic acid

The use of corticosteroids, hyaluronic acid, and antibiotics are factors that may affect the preservation of RH (Santa Maria et al., 2013). It is difficult to identify and assess the influence of each individual element due to the lack of reporting of these variables in the published research. Corticosteroids appear to have a positive impact on HP; most studies (18/19, 95%) that administered corticosteroids during surgery reported successful HP. In contrast, the rate of successful HP was lower (4/6, 67%) in studies that did not comment on corticosteroid administration. This finding is consistent with many previous publications (Cho et al., 2016, Kuthubutheen et al., 2015).

Antibiotic administration was underreported in the literature. Only 13 out of 25 studies reported their administration of antibiotics. Ten of the thirteen studies (77%) that utilised prophylactic antibiotics reported successful HP. In contrast, the remaining three studies demonstrated a significant shift in HP or a complete loss of RH in some patients. Evidence is still unclear regarding the indication of prophylactic antibiotics in CI patients. Earlier meta-analyses revealed a significant association between HP and corticosteroids, but not antibiotics (Verschuur et al., 2015). In another systematic review, Causon et al. (2015) reported the same finding. Most articles did not comment on the administration of hyaluronic acid; however, all the studies that used it reported successful HP.

2.5.6 Strengths and limitations

This review included the use of homogeneous modern atraumatic LW electrodes, making the comparison relevant to current surgical practice. This systematic review had three limitations. The main limitation of this review relates to the heterogeneity of the methods used to quantify the success of HP. Because of these differences, it was difficult to make meaningful comparisons between studies; therefore, conclusions must be made with caution. The second limitation was that a meta-analysis could not be performed due to a lack of similarity among outcome measures and a lack of reporting of some factors. Third, most of the included articles used the RW approach as the main procedure and used the CY as an alternative approach. Finally, most of the included studies were retrospective in design.

2.6 Conclusion

There is no significant relationship between HP and surgical approach when using modern LW electrodes. The level of HP changes over time. Published HP studies have several limitations: first, HP reporting is inconsistent across the literature due to the use of various quantifying methods; second, most publications are retrospective studies and report short-term results; third, there is inconsistent reporting of some possible factors; and fourth, all studies used the CY approach when the RW was not accessible, which is known to increase the risk of trauma and likely introduced bias to the comparison. There is a need for a higher level of evidence, such as that provided by RCTs, to investigate long-term HP, control all confounding factors, and make conclusions regarding this topic. In addition, it would be helpful to use radiological imaging to correlate long-term HP with intracochlear changes.

Chapter 3 : Predicting scalar position of the electrode array using CBCT and its correlation with surgical approach, cochlear size, and the level of hearing preservation: A retrospective cohort study

The systematic review in the previous chapter assessed the current body of evidence and determined that hearing preservation can be achieved with both surgical techniques (round window and cochleostomy). However, there are limitations to the available evidence. First, all studies employed the cochleostomy technique as an alternative when the RW was not visible or accessible, which skewed the comparison. Second, the number of CY cases is quite low. Thirdly, the inclusion criteria and quantification method of HP are heterogeneous, making comparisons extremely challenging. These limitations demonstrate the need for additional research to achieve more accurate results.

This chapter will conduct a retrospective study that assesses intra-cochlear electrode trauma and HP. The study will employ CBCT scans to determine electrode placement. The focus of this thesis is to examine the association between electrode position, insertion depth, hearing sensitivity, surgical technique, and cochlear size.

Abstract

Introduction

The aim of cochlear implantation (CI) surgery is to place the whole electrode array inside the scala tympani (ST). Electrode dislocation from the ST is associated with poor speech outcomes and loss of residual hearing (RH) (Skinner et al., 2007). Several factors might lead to electrode displacement from the ST. This study aims to establish whether there is a relationship between electrode dislocation and 1. surgical approach, 2. cochlear size, as identified by the diameter of the basal turn using the Escude et al. (2006) method, 3. Angular insertion depth, and 4. Hearing preservation (HP).

Method

The study includes a cohort of adult patients who had CI between May 2015 and May 2018 at the Royal National Throat, Nose and Ear Hospital (RNTNEH). All included patients were post-lingually deaf with normal ear anatomy and received atraumatic lateral-wall electrode arrays. Cone-beam computer tomography (CBCT) was used to assess the scalar position of the electrode array and measure the diameter of the basal turn of the cochlea and the depth of insertion. Unaided hearing was assessed within 6 months post-operatively.

Results

The cohort comprised 226 patients. After reviewing the surgical and audiology notes, 36 patients (39 ears) had post-operative CBCT and met our inclusion criteria: 12 males, 24 females, 24 right ears, and 15 left ears. The mean age of the subjects was 51.78 years (SD= 17.90), ranging from 24–87 years; 6 subjects had sudden hearing loss and 31 had progressive hearing loss. The mean duration of deafness was 25.74 years (SD= 17.35). In 35 ears, the electrode arrays were inserted through the round window, and in 4 ears they were inserted through a cochleostomy.

Most patients (32%) had complete HP, followed by partial HP (26%), minor HP (21%), and complete loss of RH (21%). There was a significant association between electrode displacement and HP level (p= 0.008). There was a significant association between angular insertion depth and cochlear size (p= 0.006). There was no correlation between electrode displacement, cochlear size, and angular insertion depth (p= 0.63 and p= 0.36, respectively).

Conclusion

It was possible to assess the electrode array scalar position with the CBCT. Most arrays in this study did not show any dislocation. Several patients had some electrodes on the array that were classified as possible scala tympani (PST); the proportion of these dislocated electrodes correlated with the level of HP. The influence of trauma on RH is not limited to severe trauma. Minor trauma, such as basilar membrane bulging or rupture, can also impact RH. Cochlear size was correlated with angular depth of insertion, but not with electrode placement.

3.1 Introduction

3.1.1 Imaging and cochlear implantation surgery

Cochlear implantation (CI) is a standard treatment for patients with severe to profound hearing loss. The indications for CI are expanding to involve patients with residual hearing (RH) and single-sided deafness (Campbell et al., 2013). On this basis, this procedure must be assessed and improved to be safer for newer candidates. Smooth electrode insertion into the scala tympani (ST) is critical for hearing preservation (HP) and optimal outcomes. In contrast, electrode trauma during insertion of the electrode array can damage intra-cochlear structures and affect RH. The impact of this damage might be related to the severity of the trauma and the affected parts of the cochlea. The incidence of trauma is multifactorial; for example, it can be influenced by the type of electrode array (LW or PM), insertion depth, and the surgical approach of the electrode insertion (RW or CY).

Lateral-wall (LW) arrays are less traumatic than perimodiolar (PM) electrode arrays (Turner et al., 2008, Skarzynski et al., 2014, Boyer et al., 2015, James et al., 2006). Modern atraumatic arrays have been shown to be less traumatic and improve the outcomes of HP (Hassepass et al., 2015). The influence of surgical approach has been a point of debate for many years. Currently, the level of evidence in the literature is weak; most available evidence is retrospective, not well controlled for the type of electrode array (Sun et al., 2015) and uses the CY approach as an alternative as discussed in the previous chapter. These limitations indicate the need for further assessment of this topic.

Insertion depth is another factor that might be associated with electrode trauma and loss of RH. This topic has been debated in previous articles and was discussed in section 1.4.2.2. The debate continues about the effect of electrode length on electrode trauma. Escude et al. (2006) studied the correlation between the diameters of the basal turn, cochlear size, and insertion depth. Escude et al.'s (2006) study indicated a negative relationship between cochlear size and insertion depth. These findings suggest a possible indirect relationship between cochlear size and electrode trauma, which will be investigated in this chapter.

3.1.2 Imaging and cochlear implant surgery

Post-operative imaging can be used to assess electrode position and insertion depth. Moreover, it helps to identify complications, such as electrode buckling, displacement, or electrode migration. Understanding what occurs precisely after implantation is essential to improve practice and inform device development and manufacturing. HP is considered a key factor in improving the patient's ability to discriminate sound in noise and music perception (Cullington and Zeng, 2011). These important outcomes have driven the need for high-resolution imaging and have motivated researchers to study the condition of the cochlea after implantation and the incidence of intra-cochlear trauma (Guldner et al., 2012a). Plain x-ray and conventional computed tomography (CT) techniques are limited when studying intra-cochlear changes as they have low spatial resolution and significant electrode artefacts.

Cone-beam CT (CBCT) scanning is considered one of the best modalities to mitigate the issues associated with conventional x-ray and CT techniques. CBCT has a high spatial resolution and minimal electrode artefacts; it is less expensive and does not expose patients to the higher dose of radiation associated with conventional CT (Ruivo et al., 2009, Saeed et al., 2014). The accuracy of CBCT has been compared to other imaging techniques. Faccioli et al. (2009) compared CBCT to multi-slice CT (MSCT) and reported that CBCT produced sufficient quality images and a low radiation dose for assessing patients with CI. Perenyi et al. (2016) and Ruivo et al. (2009) reported that CBCT was a reliable diagnostic tool and could be an alternative to MSCT.

Furthermore, the reliability of CBCT has been studied in fresh temporal bone studies, where electrode arrays were assessed via CBCT imaging and verified by histology. It was found that there was no significant difference between the results of CBCT and histology in predicting electrode array location (Iso-Mustajarvi et al., 2017, Dietz et al., 2016, Marx et al., 2014, Saeed et al., 2014), array kinking, and the number of intra-cochlear contacts (Cushing et al., 2012).

Despite CBCT having been validated to have excellent reliability in cochlear electrode placement, few studies have used it as an outcome measure to assess factors that

affect HP in patients (Boyer et al., 2015, Fischer et al., 2015). Most published works used older imaging modalities to identify electrode placement. This study will use CBCT as the primary outcome to assess surgical trauma and electrode position. Using such a modern tool might help to obtain more accurate results.

3.2 Aim and objectives:

Intra-cochlear trauma is one of the main causes of RH loss. Factors influencing intra-cochlear trauma are not fully characterised. This study aims to investigate some of these factors based on modern, atraumatic LW arrays. This study utilises CBCT scanning to assess electrode array position and investigates the relationship between electrode position, surgical approach, HP, insertion depth, and cochlear size.

The objectives of the study are:

1. To compare the incidence of electrode trauma among adult CI patients who were implanted through RW and CY approaches.
2. To investigate the relationship between the proportion of electrode contact in the ST (DST) and the level of HP.
3. To identify cochlear size based on the diameter of the basal turn, as described by Escude et al. (2006).
4. To investigate the relationship between angular insertion depth and cochlear size.
5. To examine the relationship between electrode position, angular insertion depth and cochlear size.

3.3 Methods

3.3.1 Subjects

This study comprised a cohort of 226 adult patients who had received cochlear implants between May 2015 and May 2018 at the Royal National Throat, Nose and Ear Hospital (RNTNEH). This study included post-lingually deaf patients with normal inner ear anatomy, implanted with an atraumatic LW electrode and had post-operative CBCT. The study included three types of cochlear devices (Cochlea CI422/522, , and Med-ELFlex28); all other types of arrays were excluded. Patients who had a history of meningitis were excluded from the study. Table 3-1 shows the inclusion and exclusion criteria of the study.

Table 3-1. Inclusion and exclusion criteria of the retrospective study.

Inclusion criteria	Exclusion criteria
1. Adult patients (>18 years). 2. Patients who were implanted between May 2015 and May 2018. 3. Patients who were implanted with a moderate-length atraumatic LW array (Cochlea CI422/522, and Med-ELFlex28). 4. Patients who had post-operative CBCT scans. 5. Normal cochlea and no history of meningitis.	1. Paediatric patients. 2. Patients who were implanted before May 2015. 3. Patients who were implanted with an old, rigid array. 4. Patients who were implanted with a pre-curved array or mid-scala array. 5. Patients who had no post-operative CBCT. 6. History of trauma, deformity, or meningitis.

3.3.2 Surgery

The standard soft surgical technique was used in all surgeries. The surgery started with a mini post-auricular incision followed by mastoidectomy, posterior tympanotomy, and the creation of a subperiosteal pocket for the device. The bed for the receiver package was drilled in some cases. Electrode arrays were inserted into the cochlea

through the RW or a CY. The CY was drilled anteroinferior to the RW. The round window niche (RWN) bony overhang was drilled in most subjects with the RW approach. Systematic intra-operative corticosteroids, antibiotics, and fascia were used for most subjects. The posterior tympanotomy was sealed with soft tissue or muscle. All patients in our cohort were operated on by four experienced CI surgeons.

3.3.3 Outcome measures

3.3.3.1 Pure-tone audiometry

The level of HP was determined for patients who had post-operative pure-tone audiometry (PTA). The hearing assessment was conducted in a double-walled sound-proof booth. The sound stimulus was delivered using a calibrated audiometer (Grayson Stadler 61) and through an over-ear headphone set (TDH-39P).

Unaided PTA was conducted during the first 6 months after operation. Long-term HP was outside the scope of this study. Changes in the hearing threshold of each frequency were determined using the HEARRING Group formula and classification system (Skarzynski et al., 2013), which was explained in detail in Section 2.4.4 in the systematic review chapter. The formula is:

$$S\ (\%) = 1 - ((PTA_{Post} - PTA_{Pre}) / (PTA_{max} - PTA_{Pre})) \times 100.$$

The formula aims to calculate the value of 'S%', which determines the level of HP. The level of HP is divided into four categories: complete HP (100–75%), partial HP (49–26%), minimal HP (1–25%), and total loss of RH (0%).

3.3.3.2 Assessment of intra-cochlear electrode placement

CBCT had been used at the RNTNE hospital as a standard procedure for patients with CI for 3 years at the time of this study. CBCT was used to measure the diameter of the basal turn of the cochlea, angular and linear insertion depths, and scalar placement of the electrode array. All patients were assessed via CBCT scan within the first month after the operation.

The device used in this study was a 3D Accuitomo (J. Morita MFG. Corp., Kyoto, Japan). All scans were performed using a tube voltage of 90 kV and a tube current of 5 mA with 360-degree rotation. Image projection was obtained from a small cylindrical

volume, 6 cm in diameter and height, with 3D isotropic 0.125 × 0.125 × 0.125 mm voxels. The scanned images were evaluated using bespoke software (idixel One Volume Viewer, V 1.6.0.2.0, J. Morita MFG Corp., Kyoto, Japan). This software enables visualisation of images in the X, Y, and Z planes, facilitating radiological assessment of the scalar position of each electrode. Multiplanar reconstructed images with a slice thickness of 0.25 mm were produced.

Electrode array scalar placements were assessed and approved by experienced radiology and otology consultants. Figure 3-1 shows the method that was used to obtain an optimum angle for assessment of the position of each electrode. The electrode insertion aimed for the ST. In some conditions, the electrode array might be displaced to the scala vestibuli (SV) or scala media (SM). For more accurate results, electrode location in the cochlea was identified using the following scoring system: (-2) definitely in the SV, (-1) possibly in the SV, (0) uncertain scalar position, (1) possible ST, (2) definite ST, and (-3) if the electrode was located outside the cochlea (Table 3-2). This scaling system was validated and used in a previous PhD thesis (Saleh, 2013).

Table 3-2. The scoring system used to identify the electrode location inside the cochlea.
This scaling system was validated and used in a previous unpublished PhD thesis (Saleh, 2013).

Number	Scalar location	Definition
2	**Definite ST**	*The electrode array can be seen clearly in the inferior part of the cross-sectional image of the cochlear duct.*
1	**Possible ST**	*The electrode array is probably located in the inferior part of the cross-sectional image of the cochlear duct, just under the basilar membrane (touching/pushing the membrane).*
0	**Uncertain**	*The location of the electrode could not be determined.*
-1	**Possible SV**	*The electrode array is probably in the superior part of the cross-sectional image of the cochlear duct*
-2	**Definite SV**	*The electrode array can be clearly seen in the superior part of the cross-sectional image of the cochlear duct.*
-3	**Extra-cochlear**	*The electrode is seen outside the cochlea.*

3.3.3.3 The diameter of the basal turn

The diameter of the basal turn was measured using the method described and used by similar studies (Erixon and Rask-Andersen, 2013, Escude et al., 2006, Dietz et al., 2016); Figure 3-2 demonstrates this method. Diameter A was measured from the midpoint of the RW passing through the midpoint of the cochlea (modiolus) to the opposite LW, and diameter B was drawn as a perpendicular line on diameter A. The cochlear size was then identified based on the length of diameter A, as described by Escude et al. (2006). Table 3-3 demonstrates the three sizes of the cochlea in relation to diameter A.

3.3.3.4 The depth of insertion

The depth of insertion was measured as linear depth (mm) and angular depth (degrees). The linear depth of insertion was measured by tracing the array from the RW to the tip of the array. The angular depth of insertion was assessed using the method used by (Xu et al., 2000). This method involves drawing a line from the superior semi-circular canal through the vestibule and RW, and then drawing a perpendicular line between the modiolus and RW (Figure 3-3 A, B and C).

Table 3-3. The three sizes of the cochlea in relation to diameter A based on the method of Escude et al. (2006).

Size	Diameter A (mm)
Small	8.25–9.24
Medium	9.25–10.24
Large	≥10.25

3.3.4 **Data analysis**

Data were collected from patients' files and surgery notes. Microsoft Excel was used to collect the data. Statistical analysis was performed using IBM SPSS, version 27 (IBM Corp., USA).

Data were assessed for normality using the *Shapiro–Wilk* test. The test revealed normal distribution for all variables except the level of HP and the proportion of dislocated electrodes.

Pearson's correlation test was used to assess the relationship between parametric variables. It was used to assess the relationship between (1) diameter A and B, (2) linear and angular insertion depth, and (3) diameters and depth of insertion.

Spearman's test was used to assess the relationship between non-parametric variables (1) electrode position and the level of HP, (2) the linear insertion depth and cochlear size, (3) the angular depth of insertion and electrode position, and (4) cochlear size and electrode placement.

3.3.5 Ethical considerations

This study was approved locally by the RNTNE hospital and registered with the audit lead as a service evaluation.

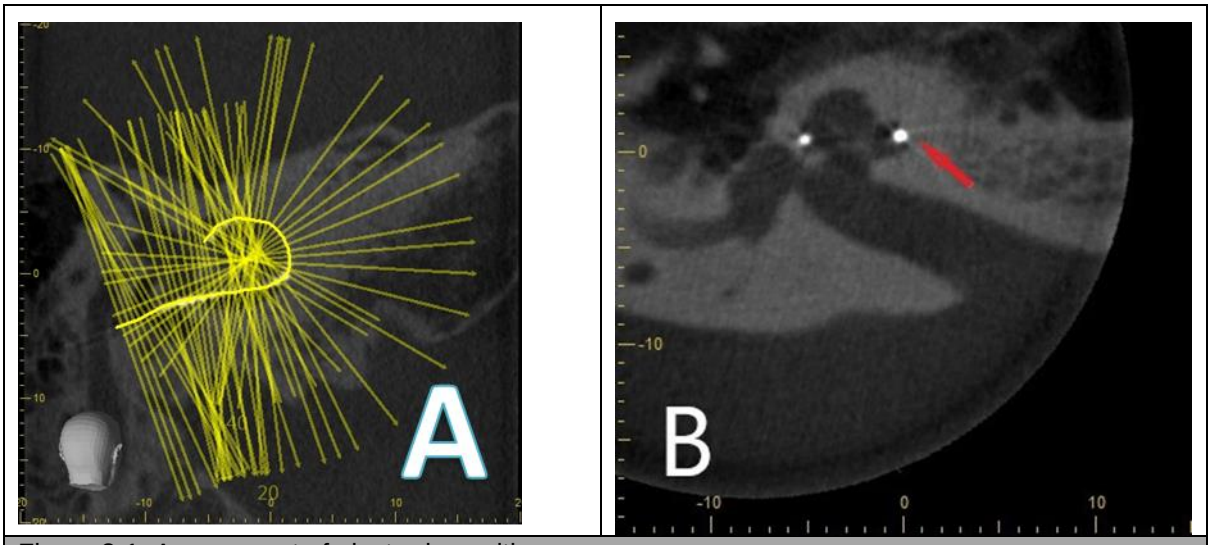


Figure 3-1. Assessment of electrode position.
Image A: the electrode array was traced to help adjust the cross-sectional angle of view to produce an optimum view of each electrode, like in Image B.

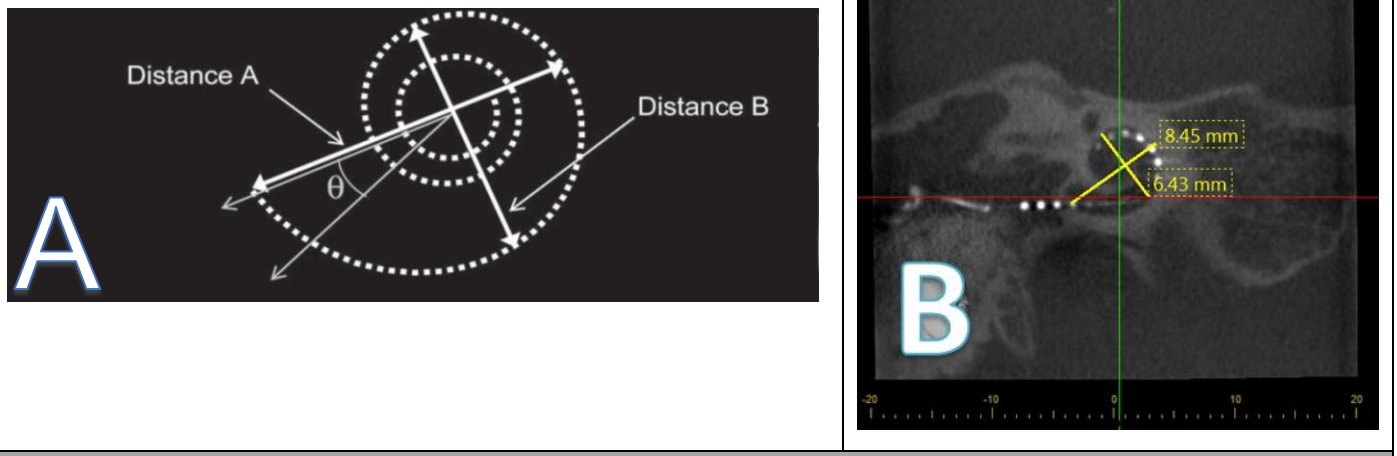
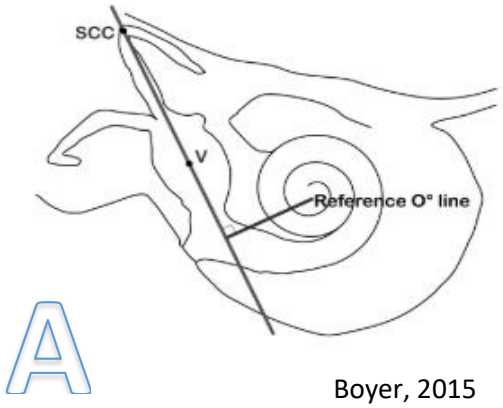
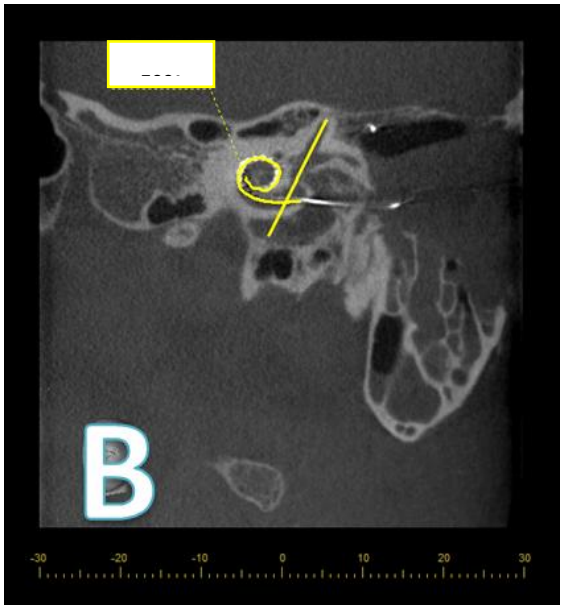


Figure 3-2. The diameter of the cochlea.
Image A demonstrates the two diameters of the basal turn of the cochlea (A and B), as described by Escude et al. (2006). The measurement of diameter A starts from the midpoint of the round window, through the modiolus, to the opposite lateral wall. Diameter B is a perpendicular line to diameter A. Image B shows an example of measurement of both diameters.



Boyer, 2015



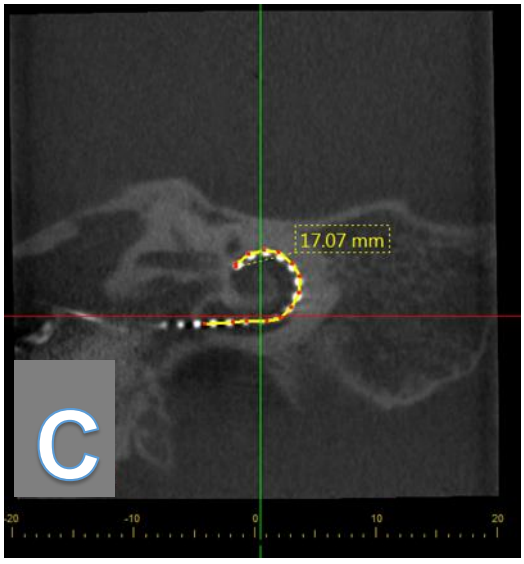


Figure 3-3. Measurement of the depth of insertion.
Measurement of the angular depth of insertion was performed as described by Xu et al. (2000) and illustrated by Boyer et al. (2015) in image A. Image A shows a reference line drawn from the apex of the semi-circular canal, passing through the vestibule, and another perpendicular line passing through the middle of the cochlea spiral. Image B shows an estimate of the angular depth of insertion. Image C shows traking for electrode array to measure the linear depth of insertion.

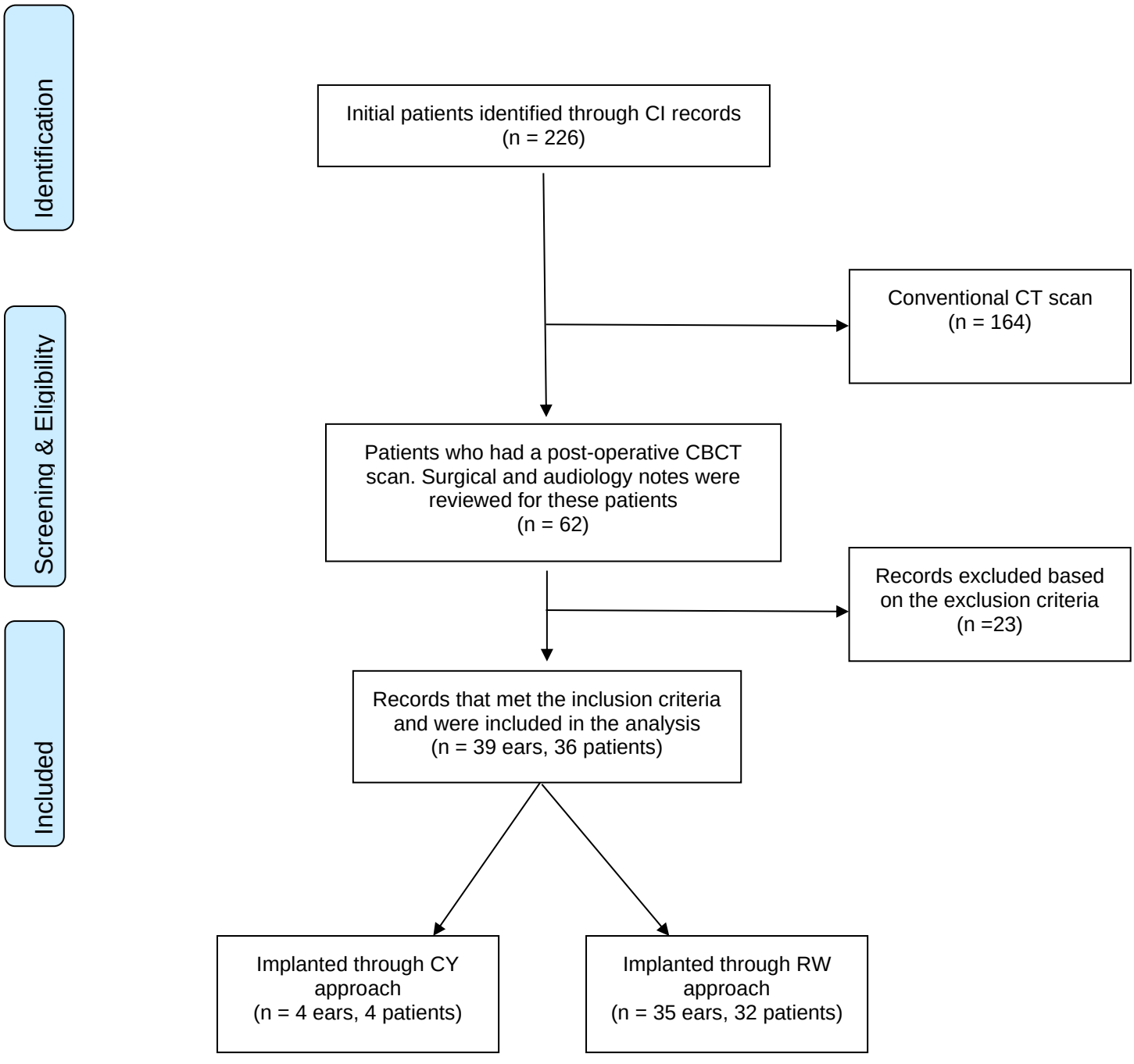
3.4 Results

3.4.1 Demographics

The cohort comprised 226 patients, and 62 patients were identified to have undergone post-operative CBCT, which was the primary outcome of our study. Surgical and audiology notes were reviewed for the 62 files. Thirty-six patients (39 ears) met our inclusion criteria (Figure 3-4). The cohort included 24 right ears and 15 left ears, 12 males and 24 females; the mean age of the subjects was 51.78 years (SD= 17.90). Five of the subjects had sudden hearing loss, while thirty-one had progressive hearing loss. The mean duration of deafness was 27.40 years (SD= 17.43). Intra-operative corticosteroids and antibiotics and post-operative antibiotics were used in 37, 37, and 21 ears, respectively.

The aetiology of hearing loss was unknown for most of the cases (17 ears); 7 subjects had genetic causes: 4 subjects (7 ears) had Usher's syndrome, 1 subject (2 ears) had connexin 26-relating hearing loss, 1 subject had Waardenburg syndrome, and 1 subject had Perrault syndrome. Moreover, 5 subjects (5 ears) had congenital causes, 2 subjects (3 ears) had trauma, 1 had Meniere's disease, 3 had infections, and 1 had auditory neuropathy.

Figure 3-4. Flow chart of the retrospective study design.



Abbreviations and acronyms; CI= cochlear implant, CT= computed tomography, CBCT= cone beam computed tomography, CY= cochleostomy, RW= round window)

3.4.2 Electrode displacement and surgical approach

The sample population in this study included 39 ears. The results showed that most patients were implanted through the RW approach; the RW approach was used in 35 ears (90%), while the CY approach was used in only 4 ears (10%). In two cases, the CY approach was used because the RW was not accessible.

Electrode scalar position was assessed in all ears and revealed six possible traumas. Electrode assessment showed that six patients had some electrodes classified as possible ST; all these patients had undergone the RW approach (Table 3-4 and Figure 3-5). Moreover, nine patients had extra-cochlear electrodes, eight of which were implanted through the RW, and one via CY insertion (Table 3-5). Table 3-15 shows the raw data and clinical findings for the whole sample.

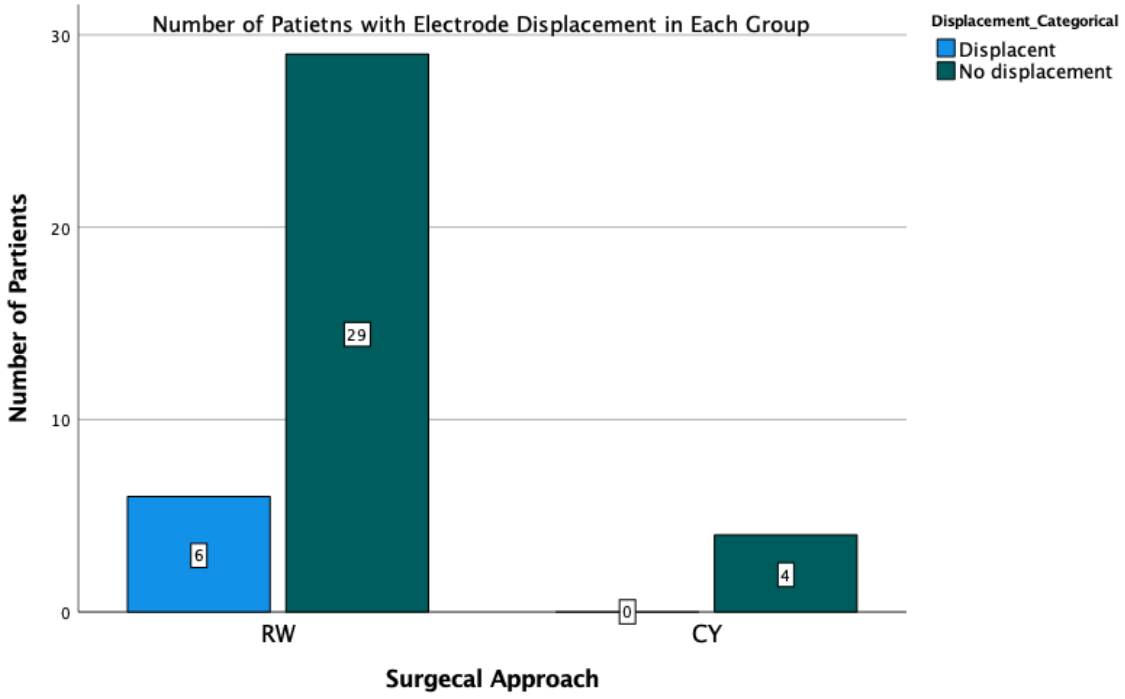


Figure 3-5. The number of patients with electrode displacement in each surgical group; RW= round window, CY= cochleostomy

Table 3-4. The number of patients with electrode displacement for each surgical approach.

		Electrode position		
		Displaced	No displacement	Total
Surgical Approach	RW	6	29	35
	CY	0	4	4
Total		6	32	39

RW= round window, CY= cochleostomy

Table 3-5. The number of patients with extra-cochlear electrodes for each surgical approach.

		Extra-cochlear electrode position		
		Yes	No	Total
Surgical Approach	RW	8	27	35
	CY	1	3	4
Total		9	30	39

RW= round window, CY= cochleostomy

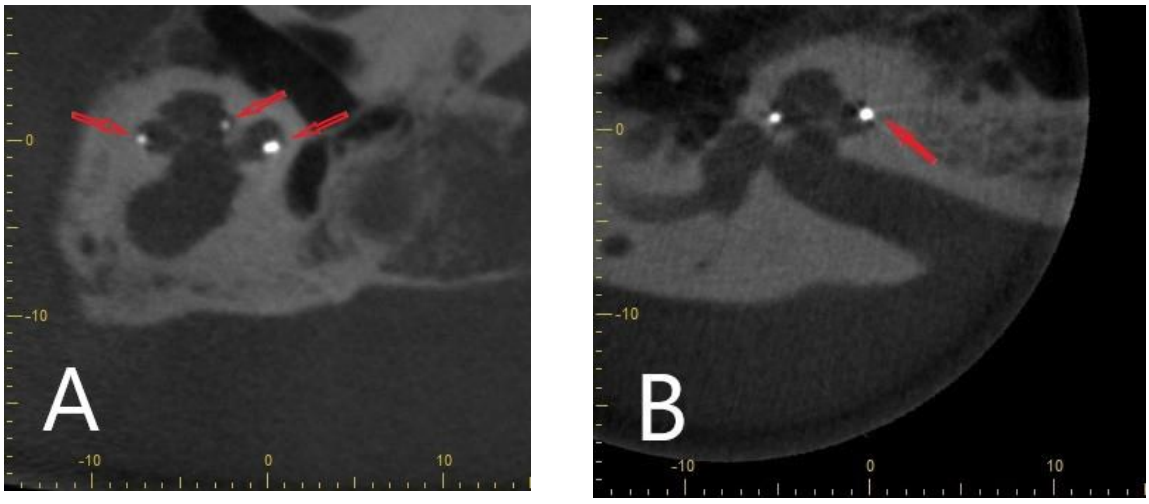


Figure 3-6. An example of electrode scalar position.
Image A shows electrodes located in the scala tympani in the base and mid-turn of the cochlea.
Image B shows electrode location in the scala tympani, just under the basilar membrane.

3.4.3 Electrode displacement and hearing preservation

The results showed that most patients did not undergo post-operative unaided PTA. Only 19 ears underwent pre-operative and post-operative unaided PTA. Complete HP was achieved in 32% (6), partial HP in 26% (5), minimal HP in 21% (4), and total loss of RH in 21% (4) of the ears, (Figure 3-7).

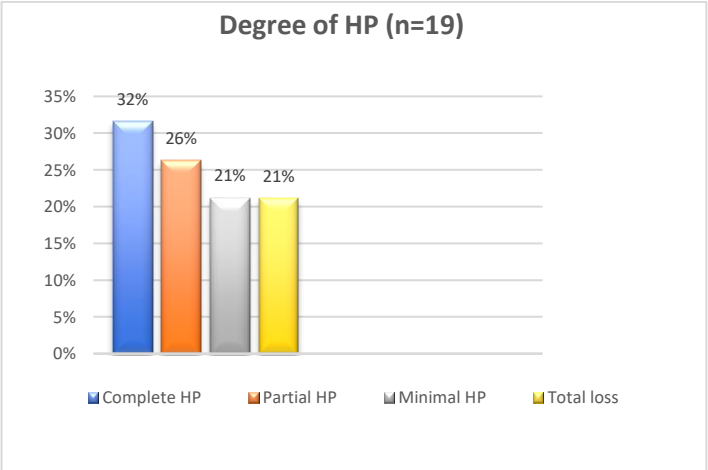


Figure 3-7. Hearing preservation levels of the 19 ears with pre-operative and post-operative unaided PTA.

The relationship between HP and electrode position was examined using the Spearman's rank correlation coefficient test because electrode position is nonparametric. The results of Spearman's test showed a significant strong positive correlation between the proportion of electrodes definitely placed in the ST and the level of HP based on the scoring system described by Skarzynski (2013) (rho = 0.587, df = 17, p = 0.008) (Table 3-6). In contrast, there was no significant relationship between HP and the percentage of extra-cochlear electrodes (rho = 0.58, df = 17, p = 0.74).

Table 3-6. Spearman's correlation results between the accuracy of insertion and the level of HP.

			Percentage of electrodes definitely at the ST	Percentage of extra-cochlear electrodes
Spearman's rho	HP (%)	Correlation coefficient	.587**	-.08
		Sig. (2-tailed)	.008	.74
		N	19	19

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

3.4.4 Identifying the cochlear size

Cochlear diameter and depth of insertion were assessed in 32 ears. It was not possible to measure these parameters in 7 ears due to technical issues with the radiology software. The mean diameter of the basal turn was 9.91 mm (SD= 0.55) for diameter A and 6.60 mm (SD= 0.46) for diameter B, with ranges of 8.14–10.30 mm and 5.43–7.38 mm, respectively. According to the illustration of diameter A (Table 4.3), the cohort included 59.4% (19 subjects) small cochlea, 34.4% (11 subjects) medium cochlea, and 6.3% (2 subjects) large cochlea.

Table 3-7. The number of patients in each cochlear size category according to diameter A.

Size	Diameter A (mm)	Number of ears	Percentage (%)
Small	8.25–9.24	19	59.4
Medium	9.25–10.24	11	34
Large	≥10.25	2	6.3
Total	-	32	100

A Pearson correlation coefficient test was performed to assess the linear relationship between diameter A and B. The test showed a significant strong positive relationship between diameter A and B (r [30] = 0.74, p<0.001) (Table 3-8 and Figure 3-8).

Table 3-8. The results of Pearson's correlation coefficient test between diameter A and B for 32 ears.

Correlations

		Diameter B
Diameter A	Pearson's correlation coefficient	.697**
	Sig. (2-tailed)	<.001
	N	32

**. Correlation is significant at the 0.01 level (2-tailed).

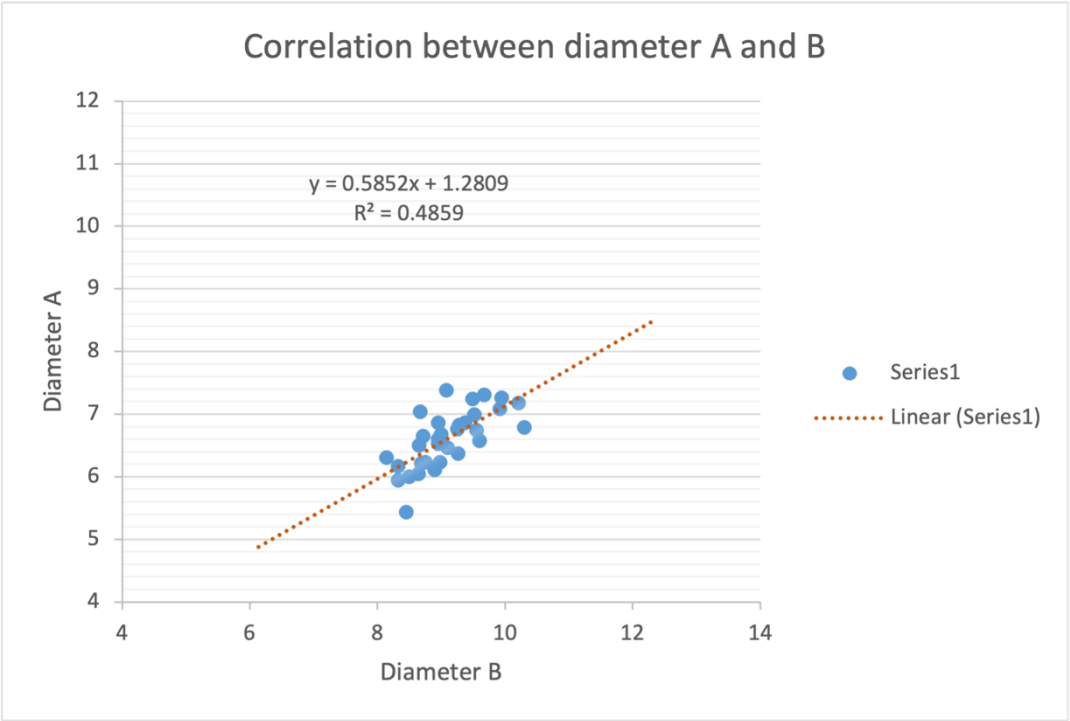


Figure 3-8. The positive correlation between diameter A and B in 32 ears.

3.4.5 The relationship between insertion depth and cochlear size

Angular depth of insertion and linear depth of insertion were assessed in all patients. The mean angular depth was 421.9 degrees (SD= 75.40) and the mean linear depth was 21.52 mm (SD= 2.50), with ranges of 8.14–10.30 degrees and 5.43–7.38 mm, respectively. The relationship between the linear and angular depth was tested using the Pearson's correlation coefficient test. The test showed a strong significant positive relationship between the linear and angular depth of insertion ($r [37] = 0.79$, $p<0.001$) (Table 3-9 and Figure 3-9).

Spearman's test was used to assess the relationship between the insertion depth and cochlear size because the cochlear size is nonparametric. The statistical analysis did not show any significant correlation between cochlear size and linear insertion depth (rho=0.122, df=30, p=0.507) or angular insertion depth (rho=0.146, df=30, p<0.426) (Table 3-10). The relationship was reassessed after excluding patients with incomplete insertion to rule out the effect of incomplete insertion. The Spearman correlation test

showed a significant negative correlation between cochlear size and angular insertion depth (rho= -0.538, df=23, p=0.006) (Table 3-12 and Figure 3-11). Similarly, the correlation between angular insertion depth and each of diameter A and B were tested with Pearson's correlation coefficient test, which revealed significant negative correlations (r [23] = -0.521, p<0.008 and r [23] = -.637, p<0.008, respectively) (Table 3-11 and Figure 3-10).

Table 3-9. The results of Pearson's correlation coefficient test between the angular and linear insertion depths and diameter A and B.

Correlations

		Linear depth (All cases)	Angular depth (All cases)	Diameter A (All cases)	Diameter B (All cases)
Linear depth	Pearson correlation	1	.790**	.166	.228
	Sig. (2-tailed)		<.001	.364	.210
	N	39	39	32	32
Angular depth	Pearson correlation	.790**	1	-.224	-.226
	Sig. (2-tailed)	<.001		.219	.214
	N	39	39	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

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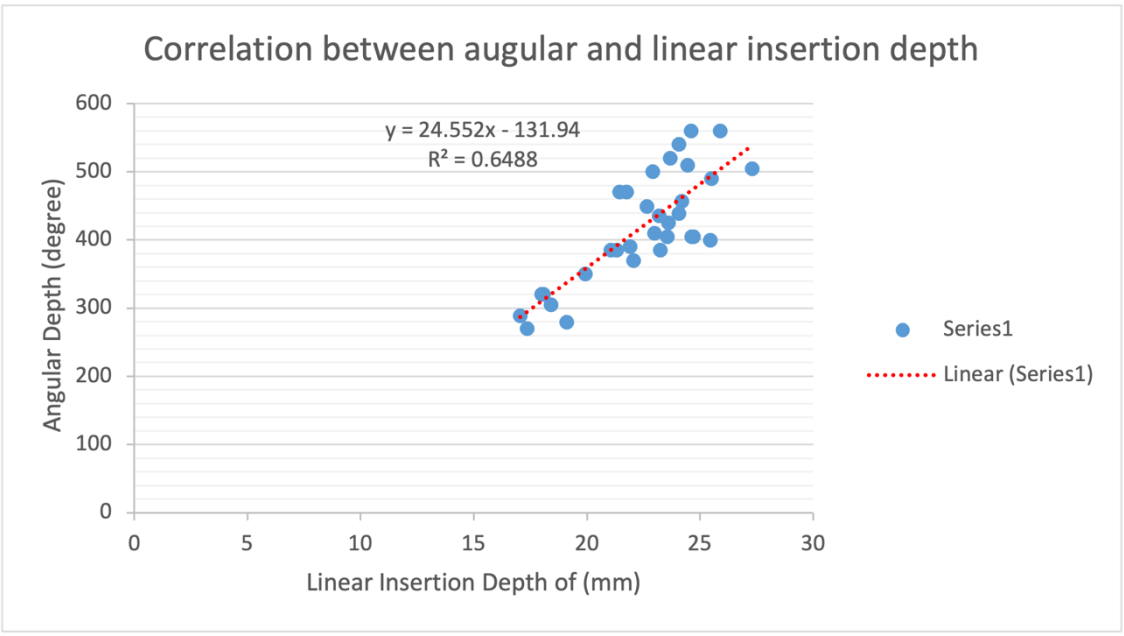

Figure 3-9. The positive correlation between the angular and linear depths of insertion for all subjects (n=32 ears).

Table 3-10. The results of Spearman's correlation test between cochlear size and the angular and linear depths of insertion for all subjects (n=32 ears).

			Linear depth (All cases)	Angular depth (All cases)
Spearman's rho	Cochlear size	Correlation coefficient	.122	-.146
		Sig. (2-tailed)	.507	.426
		N	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

Table 3-11. The results of Pearson's correlation coefficient test between the angular and linear depths of insertion and diameter A and B after excluding patients with incomplete insertion (n = 25 ears).

		Diameter A	Diameter B
Linear depth (Full insertion only)	Pearson's correlation coefficient	-.144	-.066
	Sig. (2-tailed)	.587	.754
	N	25	25
Angular depth (Full insertion only)	Pearson correlation coefficient	-.521**	-.637**
	Sig. (2-tailed)	.008	<.001
	N	25	25

**. Correlation is significant at the 0.01 level (2-tailed).

Table 3-12. The results of Spearman's correlation test between cochlear size and the angular and linear depths of insertion after excluding patients with incomplete insertion (n = 25 ears).

			Linear depth (Full insertion only)	Angular depth (Full insertion only)
Spearman's rho	Cochlear size	Correlation coefficient	- .228	-.538**
		Sig. (2-tailed)	.272	.006
		N	25	25

**. Correlation is significant at the 0.01 level (2-tailed).

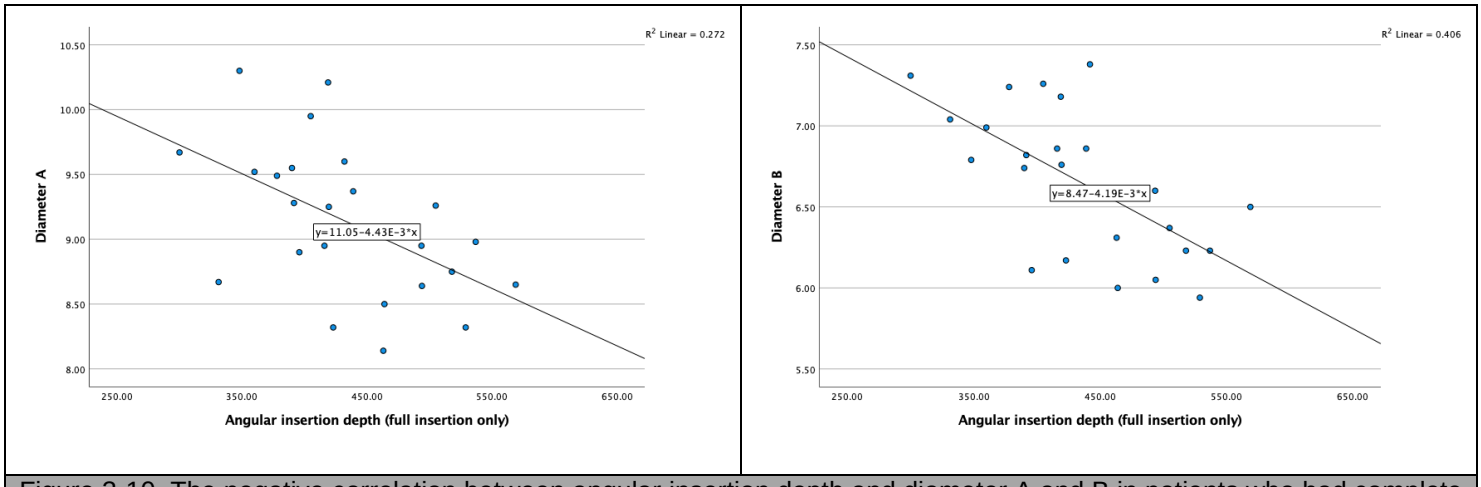

Figure 3-10. The negative correlation between angular insertion depth and diameter A and B in patients who had complete insertion (n= 25 ears).

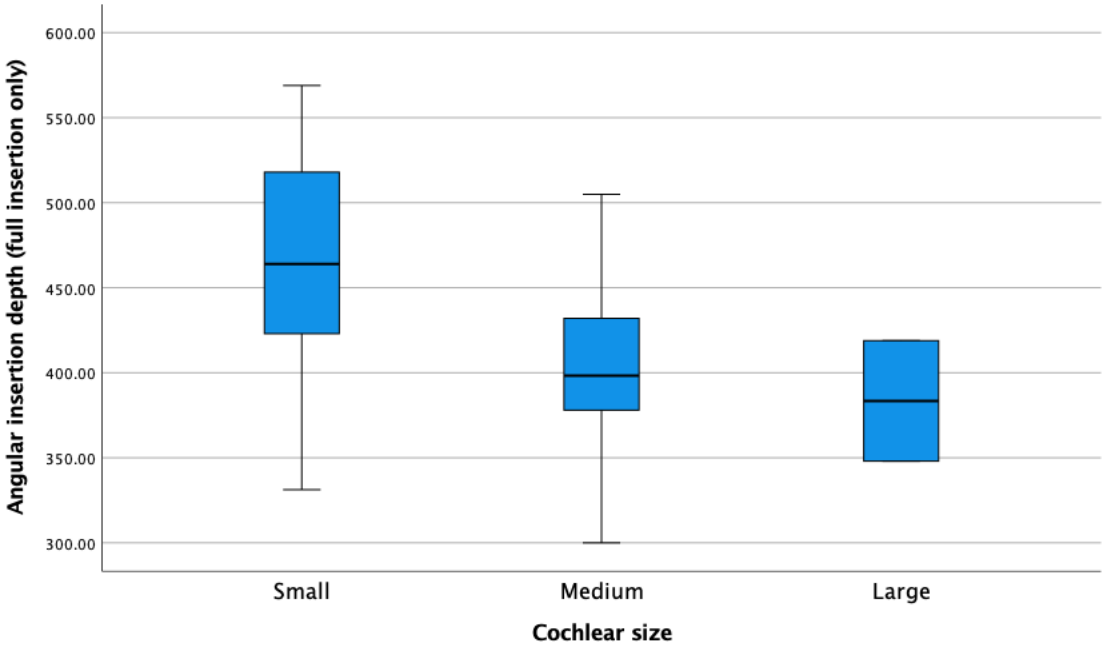

Figure 3-11. Box plot of the confidence interval of the mean angular insertion depth for each cochlear size (n = 25 ears).

3.4.6 The relationship between electrode position, insertion depth, and cochlear size

The relationship between electrode position, cochlear size, and depth of insertion was assessed. The Spearman's test was used as both cochlear size and electrode position are nonparametric. Spearman's test did not reveal any significant relationship between electrode placement and cochlear size (rho= 0.09, df=30, p=.63), linear depth of insertion (rho= 0.008, df=37, p=0.96), angular depth of insertion (rho= 0.15, df=37, p=.36), or device manufacturer (rho= -0.023, df=37, p=0.89) (Table 3-13). Finally, the proportion of extra-cochlear electrodes did not show a significant correlation with the cochlear size (Table 3-14).

Table 3-13. The results of Spearman's correlation between the proportion of electrode displacement and cochlear size, linear and angular insertion depth, and device manufacturer.

			Percentage of electrodes definitely at ST
Spearman's rho	Size of the cochlea	Correlation coefficient	.089
		Sig. (2-tailed)	.628
		N	32
	Linear depth	Correlation coefficient	.008
		Sig. (2-tailed)	.960
		N	39
	Angular depth	Correlation coefficient	.150
		Sig. (2-tailed)	.363
		N	39

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).
- ST= scala tympani

Table 3-14 The results of Spearman's correlation test between cochlear size and the proportion of extra-cochlear electrodes (n=32 ears).

			Percentage of extra-cochlear electrodes
Spearman's rho	Cochlear size	Correlation coefficient	-0.303
		Sig. (2-tailed)	.092
		N	32

**. Correlation is significant at the 0.01 level (2-tailed).

In this study, only a small number of people got implants through the CY approach. This made it difficult to compare the two surgical methods. Diameter A and B were significantly correlated with each other. The size of the patient's cochlea was determined based on diameter A using the method described by Escude et al. (2006). Correlation analysis was performed between the accuracy of insertion, cochlear size, HP, and depth of insertion. The results suggested significant correlation between electrode position and the level of HP. Moreover, there was a significant correlation between cochlear size and the angular insertion depth. Other correlations did not reach the level of significance.

Table 3-15. Sample population demographics and clinical findings
The table shows descriptive data of the surgical approach, device, level of hearing preservation (as described in Skarzynski's [2013] method), depth of insertion, cochlear size based on diameter A (as described by Escude et al. [2006]), and the scalar position of the electrodes inside the cochlea (as described in Table 3-2).

Ear	Age	Gender	Surgical approach	Device	Total no. of electrodes	Intra-cochlear electrode placement (No. of electrodes in each category of the scoring system)[2]						Percentage of electrodes definitely at ST (DST)[3]	Insertion depth		Diameter		Cochlear size	Level of HP [1]	
	(years)	M= Male F= Female	RW = 1 CY = 2	SlimJ = 1 CI522 = 2 Flex28 = 3 CI422 = 4		DST	PST	Uncertain	PSV	DSV	Extra-cochlear		Linear	Angular	A	B	S= small M=medium L= large	percentage (S =%) [1]	HP Categorical [1]
1	31	F	1	1	16	12	1	0	0	0	3	92.3	16.5	298	8.45	5.43	S	0%	TL
2	57	F	1	1	16	15	0	0	0	0	1	100.0	19.4	389.6	8.95	6.53	S	-	-
3	49	F	1	2	22	17	2	0	0	0	3	89.5	16.5	287	8.69	6.21	S	-	-
4	87	M	1	3	12	12	0	0	0	0	0	100.0	27.3	505	9.26	6.37	M	-	-
5	31	F	1	2	22	19	3	0	0	0	0	86.4	22.8	537	8.98	6.23	S	14%	M
6	31	F	1	2	22	21	1	0	0	0	0	95.5	20.9	464	8.5	6	S	6%	M
7	71	F	1	1	16	16	0	0	0	0	0	100.0	20.5	423	8.32	6.17	S		-
8	56	F	1	1	16	16	0	0	0	0	0	100.0	23.6	529	8.32	5.94	S	86%	C
9	33	F	1	2	22	22	0	0	0	0	0	100.0	22.2	494	8.64	6.05	S	64%	P
10	48	F	1	2	22	22	0	0	0	0	0	100.0	22.8	439	9.37	6.86	M	100%	C
11	55	M	1	3	12	12	0	0	0	0	0	100.0	24.5	569	8.65	6.5	S	100%	C
12	37	F	1	2	22	22	0	0	0	0	0	100.0	20.5	470	**	**	**	-	-
13	37	F	1	2	22	22	0	0	0	0	0	100.0	20.0	426	**	**	**	-	-
14	73	F	1	3	12	8	0	0	0	0	4	100.0	16.0	323	8.72	6.65	S	-	-
15	62	M	1	2	22	20	0	0	0	0	2	100.0	17.2	303	9	6.68	S	-	-
16	49	M	1	2	22	22	0	0	0	0	0	100.0	19.9	348	10.3	6.79	L	95%	C
17	42	F	2	2	22	22	0	0	0	0	0	100.0	20.9	415.9	**	**	**		-
18	66	F	1	2	22	22	0	0	0	0	0	100.0	20.2	395.9	8.9	6.11	S	0%	TL
19	53	F	1	3	12	12	0	0	0	0	0	100.0	25.3	518	8.75	6.23	S		-
20	24	M	2	4	22	22	0	0	0	0	0	100.0	23.4	512	**	**	**	33%	P
21	77	F	1	2	22	22	0	0	0	0	0	100.0	22.9	405	9.95	7.26	M	-	-
22	32	F	2	2	22	22	0	0	0	0	0	100.0	22.7	419.5	9.25	6.76	M	14%	M
23	82	M	1	1	16	16	0	0	0	0	0	100.0	20.8	378	9.49	7.24	M	-	-

Table 3-15. Sample population demographics and clinical findings

The table shows descriptive data of the surgical approach, device, level of hearing preservation (as described in Skarzynski's [2013] method), depth of insertion, cochlear size based on diameter A (as described by Escude et al. [2006]), and the scalar position of the electrodes inside the cochlea (as described in Table 3-2).

Ear	Age	Gender	Surgical approach	Device	Total no. of electrodes	Intra-cochlear electrode placement (No. of electrodes in each category of the scoring system)[2]						Percentage of electrodes definitely at ST (DST)[3]	Insertion depth		Diameter		Cochlear size	Level of HP [1]	
	(years)	M= Male F= Female	RW = 1 CY = 2	SlimJ = 1 CI522 = 2 Flex28 = 3 CI422 = 4		DST	PST	Uncertain	PSV	DSV	Extra-cochlear		Linear	Angular	A	B	S= small M=medium L= large	percentage (S =%) [1]	HP Categorical [1]
24	63	F	1	1	16	16	0	0	0	0	0	100.0	24.1	493.6	8.95	6.6	S	-	-
25	76	F	1	3	12	11	0	0	0	0	1	100.0	23.2	419	9.92	7.08	M	19%	M
26	51	F	1	2	22	22	0	0	0	0	0	100.0	20.4	360	9.52	6.99	M	51%	P
27	37	M	1	3	12	6	6	0	0	0	0	50.0	24.7	418.9	10.21	7.18	L	-	-
28	37	M	1	2	22	20	0	0	0	0	2	100.0	17.5	322.0	9.1	6.5	S	100%	C
29	38	F	1	1	16	16	0	0	0	0	0	100.0	23.3	442	9.08	7.38	S	-	-
30	49	M	1	2	22	19	3	0	0	0	0	86.4	23.3	416	8.95	6.86	S	0%	TL
31	66	F	1	2	22	22	0	0	0	0	0	100.0	21.7	391.6	9.28	6.82	M	-	-
32	80	M	1	2	22	22	0	0	0	0	0	100.0	19.5	300	9.67	7.31	M	6%	M
33	31	M	1	2	22	22	0	0	0	0	0	100.0	22.7	331.3	8.67	7.04	S	-	-
34	45	F	1	2	22	22	0	0	0	0	0	100.0	20.7	463.1	8.14	6.31	S	59%	P
35	81	M	1	1	16	16	0	0	0	0	0	100.0	20.1	390	9.55	6.74	M	100%	C
36	32	F	1	1	16	16	0	0	0	0	0	100.0	21.9	432	9.6	6.57	M	64%	P
37	26	F	2	3	12	11	0	0	0	0	1	100.0	23.3	434	**	**	**	-	-
38	45	F	1	3	12	11	0	0	0	0	1	100.0	22.5	419	**	**	**	-	-
39	45	F	1	3	12	12	0	0	0	0	0	100.0	25.5	572	**	**	**	-	-
Total / Mean			RW = 35 CY = 4	SlimJ = 9 CI522 = 20 Flex28 = 9 CI422 = 1	-	39	6	0	0	0	9	39	Mean = 21.51 ± 2.5 mm	Mean = 421.88 ± 75.40°	Mean = 9.91 ± 0.55 mm	Mean = 6.60 ± 0.46 mm	S=19 M=11 L=2 Total = 32	Mean = 48 ± 40%	C = 6 P = 5 M = 4 TL = 4 Total = 19

1. The level of hearing preservation (HP) was classified into four categories based on Skarzynski's classification (described in Table 1.2). C = complete HP, P = partial HP, M = minimal HP, TL = total loss of residual hearing.
2. Intra-cochlear electrode placement: DST = definite scala tympani, PST = possible scala tympani, uncertain, PSV = possible scala vestibuli, DSV = definite scala vestibuli, and extra-cochlear.
3. The proportion of electrodes that were definitely in the scala tympani was calculated after subtracting extra-cochlear electrodes.
4. **: it was impossible to assess due to a technical issue in the radiology software.

3.5 Discussion

Achieving HP in CI is multifactorial. Electrode trauma is one of the main reasons for loss of RH. This study aimed to assess the incidence of intra-cochlear trauma and investigate its relationship with surgical approach, HP, insertion depth, and cochlear size. The study was controlled to the type of electrode array, as we included exclusively atraumatic moderate-length LW arrays (Cochlea CI422/522, Advanced-bionic SlimJ, and Med-ELFlex28). LW arrays are known to be less traumatic than perimodiolar and mid-scala electrodes (Turner et al., 2008, Skarzynski et al., 2014).

Electrode placement was assessed in all subjects. The results showed nine cases of incomplete insertion and six cases that were classified as possible ST (PST). The position of the electrode array in these cases was marginal to the basilar membrane (BM). The results did not show any confirmed electrode dislocation from the ST to the SV. The use of atraumatic LW electrode arrays could explain the absence of electrode dislocation between scalae in our sample.

3.5.1 Comparing electrode placement and hearing preservation between both surgical approaches

The results showed a significant difference in the number of patients between the two surgical approach groups. The number of patients in the CY group was very small (4/39), while the number of patients in the RW group was 35. On this basis, it was impossible to compare electrode positions between the two approaches using statistical methods. Electrode placement was assessed in all patients. The results showed that none of the CY patients had electrode dislocation, while six of the patients in the RW group had some degree of dislocation and were classified as PST. Extra-cochlear electrodes were noted in the eight cases in the RW group and one case in the CY group. In addition, the number of patients who underwent pre-operative and post-operative unaided PTA was very small. It was possible to calculate the level of HP in 2 patients in the CY group and in 17 patients in the RW group. Therefore, it was impossible to compare electrode placement or level of HP between surgical approaches using statistical methods.

These findings highlight two points. First, the audiological practices in our centre regarding post-operative follow-up lack consistency in the assessment of RH. It is known that RH reflects the health and condition of intra-cochlear structures, which influence patient outcomes (Carlson et al., 2011, Eshraghi, 2006). Therefore, unaided PTA should be a routine assessment for all patients. Second, available data for the CY approach was generally very limited when conducting the retrospective study; a similar trend was noted in the literature. Recent HP studies showed a significant difference between the sizes of their RW and CY groups. For example, the sample population of Guimaraes et al. (2015) consisted of 16 cases with a RW approach and 3 cases with a CY approach. In another study conducted by Lee et al. (2010a), the number of patients implanted through the RW was eight versus two via CY; the two studies conducted by Gstoettner et al. (2009) and de Carvalho et al. (2013) had the same issue.

Surgeon preference is the main reason for the small numbers of CY cases. Most surgeons tend to use the CY approach only if the RW is not accessible, which was reported in the surgical notes of 2/4 cases in the CY group in our study. It is possible that the recent shift in practice is the main reason behind the difference between the number of cases in both approaches. Moreover, this change has led to biased comparisons of both approaches. Santa Maria et al. (2014) suggested that this shift in practice occurred rapidly and without sufficient evidence. With the current limited numbers of CY cases, it is difficult to reach clear conclusions about the effect of surgical approach, which is reflected in the conflicting results of published systematic reviews (Havenith et al., 2013, Santa Maria et al., 2014, Causon et al., 2015). This highlights the need for prospective research to address this topic. A randomised controlled trial to address this issue will be presented in Chapters 5 and 6.

3.5.2 The relationship between electrode position and the level of hearing preservation

This study aimed to investigate factors related to scalar dislocation and their influence on HP. We attempted to accurately determine electrode array position using the previously described scoring system (Table 3-2). The results showed that most

electrodes were definitely in the ST (DST), while few of them were determined as possibly in the ST (PST) as they were located just under the surface of the BM (touching/pushing). None of the patients in this study had electrode dislocation from the ST to the SV.

Despite CBCT being a reliable and sensitive tool for estimating electrode location inside the cochlea, it is difficult to estimate changes at the histological level. Most clinical studies that use CT scans are limited to identifying severe intra-cochlear trauma (i.e., electrode dislocation to SV) that is known to decrease RH (Adunka et al., 2005, Boyer et al., 2015). This study aimed to evaluate various degrees of trauma.

None of the patients in our sample had severe trauma (i.e., electrode dislocation into the SV); however, some patients had some electrodes classified as possible ST, which could have resulted in minimal trauma to the BM. Electrode position (PST) and the level of HP showed a significant correlation. This correlation suggests that minimal trauma to the BM negatively influences the level of HP. This finding highlights that successful ST insertion does not guarantee atraumatic surgery, which could explain the loss of RH in some patients. Identifying the nature of minimal trauma in vivo remains challenging (O'Connell et al., 2016d).

Previous histological studies have described several mechanisms of intra-cochlea trauma that might occur during electrode insertion (Roland and Wright, 2006, Wardrop et al., 2005). Electrode insertion into the cochlea might cause trauma to the BM, LW, osseous spiral lamina, or modiolus. Loss of RH could occur immediately after surgery due to trauma to these structures (Roland and Wright, 2006), or it could occur after some time due to other factors, such as fibrosis and osteogenesis (Nadol, 1997, Bas et al., 2012, Gstoettner et al., 2000). The severity of electrode trauma depends on the damaged structures. Eshraghi et al. (2003) developed a severity scale for cochlear trauma. The scale identifies the electrode location and the damage it caused to the inner structures of the cochlea. The scale has five degrees: 0 indicates no trauma, 1 refers to an elevation in the BM, 2 refers to rupture of the BM, 3 refers to electrode crossing from the ST to the SV, and 4 refers to severe trauma. Severe trauma includes ‘fracture of the osseous spiral lamina or modiolus or tear of stria vascularis’.

Trauma to the BM may be minimal, such as bulging or tearing of the BM or Reissner's membrane, which can lead to the disturbance of structures and the mixing of endolymph and perilymph (Shaddock et al., 1985). Moreover, the damage might affect BM vibration and occlude the blood circulation of the spiral vessel lying underneath the BM (Roland and Wright, 2006). Electrode dislocation to the SM or SV results in more severe trauma. This degree of dislocation would affect the peripheral process of the auditory nerve and lead to degeneration of the spiral ganglion (Spoendlin, 1984, Sugawara et al., 2005).

Histological studies remain the gold standard in assessing electrode trauma of the cochlea (O'Connell et al., 2016d); however, expecting the exact audiological outcome of each trauma mechanism remains challenging as it is difficult to differentiate between them in vivo. Further research is needed to determine the exact correlation between the type of cochlear trauma and its effect on HP in vivo. Post-mortem histological studies may contribute to the understanding and investigation of this relationship (O'Connell et al., 2016d).

3.5.3 The correlation between cochlear size and the insertion depth

The morphology of the human cochlea varies between individuals (Wurfel et al., 2014b). Even though studies show a variety in the insertion depths between patients (Finley et al., 2008 and Adunka et al., 2005), a single electrode length is commonly used for most cases (Kuthubutheen et al., 2019). Therefore, the characteristics of a patient's cochlea might affect their HP outcomes.

One of the objectives of this study is to test the correlation between the insertion depth and cochlear size when using a soft surgical approach and moderate-length atraumatic array. Diameter A was utilised to determine the size of the cochlea. The diameter A range in this study (8.14–10.30 mm) was comparable to that of Escude et al. (2006) (7.9–10.8 mm, n=42) and Franke-Trieger and Murbe (2015) (8.1–10.4 mm, n=37). This study showed a significant correlation between diameter A and B, which is similar to the results reported by Escude et al. (2006). Moreover, our results showed a significant positive correlation between angular and linear depth of insertion, which

aligns with the results reported in previous studies (Manrique et al., 2014, Franke-Trieger and Murbe, 2015, Escude et al., 2006).

The relationship between the cochlear size and angular insertion depth was assessed for the whole sample and no significant correlation was found. The correlation test was repeated after excluding the nine cases of incomplete insertion. As a result, the correlation test revealed a significant negative correlation between angular depth and cochlear size. These findings aligned with previous findings reported by Escude et al. (2006) who used the Nucleus 24 Contour Advance electrode array and two depths of insertion (19 mm and 17 mm). They reported a significant correlation in the group with an insertion depth of 17 mm.

Similarly, Kuthubutheen et al. (2019) used two electrodes (Flex31 and Flex28) and reported a significant correlation between the cochlear size and angular insertion depth among the group implanted with the shorter electrode array (Flex28). Franke-Trieger and Murbe (2015) studied this relationship and found it to be significant in patients implanted with CI422. Full insertion was not possible in all cases, and the linear insertion depth of those patients ranged between 18.6 mm and 26.2 mm. The reason for shallow insertion in the study was electrode resistance, which was similar to the conditions in our study. They found a strong correlation in patients who had full insertion (25-mm group) and those who had an insertion depth of 23 mm. In contrast, no correlation was found with shallow insertion (<20 mm).

Identifying cochlear size is a helpful tool in predicting the insertion depth, which helps to limit insertion trauma, specifically in smaller cochleae. However, it seems that this correlation can be affected by the resistance encountered during electrode insertion and may result in incomplete insertion. The impact of resistance can be seen clearly in our results and the results of Franke-Trieger and Murbe (2015). Therefore, this correlation should be interpreted cautiously as it is possible to encounter resistance at any point during the insertion process. When reaching the point of resistance, the insertion process should be terminated, as further insertion could result in trauma (Adunka and Kiefer, 2006).

3.5.4 The correlation between electrode position, insertion depth, and cochlear size

Intra-cochlear trauma is multifactorial, and the depth of insertion is thought to be one of its causative factors, as angular insertion depth is correlated with cochlear size (Escude et al. (2006). This study investigated the relationship between electrode position and insertion depth from two angles: directly, with the insertion depth, and indirectly, with the cochlear size. We did not find a significant correlation between electrode position and either insertion depth or cochlear size.

Previous studies have examined the relationship between insertion depth and electrode trauma. The findings of these studies are inconsistent; some studies reported a significant correlation between deeper insertion and electrode trauma (Finley et al., 2008, Adunka and Kiefer, 2006), while others reported no significant correlation (Wanna et al., 2015, O'Connell et al., 2016a, O'Connell et al., 2016b, Kisser et al., 2016). These conflicting findings could be related to the differences in surgical protocols and electrode arrays that were used in these studies.

Surgeons at our centre controlled the insertion depth based on insertion resistance. This method appears to be safe for patients. In our sample, some cases had incomplete insertion, and none of the cases had definite electrode dislocation to the SV. Moreover, the results described in the previous section (3.5.3) indicated a negative correlation between angular insertion depth and cochlear size among patients with full insertion, but not among patients with partial insertion. Resistance can be encountered at any stage during insertion and can affect the correlation between these two variables.

Because a small-sized cochlea has a deeper angular insertion depth than a large-sized cochlea, it was interesting to evaluate whether a small-sized cochlea might lead to a higher frequency of trauma. The results of this study concluded that there was no significant relationship between electrode position and either insertion depth or cochlear size when using atraumatic LW arrays and controlling for insertion resistance.

3.5.5 Strength and limitation

The current study assessed electrode conditions using one of the most accurate radiological modalities. This study is one of few that used CBCT in vivo. Moreover, our study controlled the effect of the electrode type; all electrodes included in this study were moderate-length atraumatic LW electrodes.

This study has some limitations. Due to the nature of retrospective studies, it was impossible to include enough patients that fit our inclusion criteria. For that same reason, the sample population varied significantly regarding the number of patients who underwent each surgical approach (RW and CY). This limitation indicates the need for a prospective study to overcome the effect of a variable that depends on the surgeon's preference or patient's condition, such as surgical approach. Even though CBCT is standard practice, it was not performed for all subjects in our centre. Moreover, we noted that CBCT was conducted for many patients with post-operative complaints or complications, which might have introduced selection bias and affected the accuracy of the results. Therefore, the findings of this study should be interpreted with caution. These limitations are expected in retrospective studies and highlight the need for a well-controlled prospective study to provide more definitive answers. Chapter 5 and 6 present a double blinded randomised controlled trial, that aim to investigate the outcomes of CI patients after being randomised between both approaches.

3.6 Conclusion

This study aimed to investigate the relationship between scalar placement of electrode array, HP, surgical approach, cochlear size, and insertion depth. CBCT evaluation indicated that some patients had possible dislocation in some electrodes (classified as PST). The proportion of these electrodes compressing and causing bulging of the BM appeared to influence HP. Therefore, electrode trauma is not limited to electrode dislocation but might include compression and bulging of the under-surface of the BM. The results showed no significant correlation between the accuracy of electrode placement and cochlear size or depth of insertion. There was a significant correlation between the cochlear size and angular depth among patients with full insertion but not among those with partial insertion. Cochlear size is a valuable tool to predict the depth of insertion. However, this correlation can be affected by insertion resistance that could be encountered at any stage during insertion.

Chapter 4 : A contemporary survey of cochlear implant surgical practice for hearing preservation in the United Kingdom

The findings of the systematic study presented in chapter 2 revealed a small number of surgical cochleostomies (CY). In addition, the CY method was utilised as an alternative in the majority of studies. Some aspects of HP surgery were not well reported and medical regiment. The same results were observed in the retrospective study (chapter 3).

In light of the limited evidence and lack of guidelines, it is necessary to evaluate the current practise of HP CI and to comprehend the perspective of CI surgeons. This chapter will perform a survey to evaluate the current HP practise with respect to inclusion criteria, electrode selection, surgical method, drug regimen, and audiological evaluation.

Abstract

Background

Over the last 4 decades, cochlear implantation (CI) has become an established intervention for the management of individuals with severe-to-profound deafness. During this period, there has been considerable evolution of implant devices, electrode arrays, surgical techniques, speech processing strategies, and eligibility criteria. The most recent National Institute for Health and Care Excellence (NICE) guidelines for CI candidacy included subjects with more residual hearing (RH) than earlier guidelines. This survey aims to assess the current surgical practices of hearing preservation (HP) in CI patients in the United Kingdom, including device choice, type of the electrode, surgical approach, peri-operative medication, and audiology follow-up.

Method

A national web-based survey was developed to collect responses from all the UK-based consultant CI surgeons within the National Health Service (NHS).

Results

The response rate of this survey was 68%, where 39 of the 57 consultant CI surgeons responded to the survey. This response rate represents 80% of all the UK CI centres. Eighty-seven percent of surgeons preferred to use conventional-length electrode arrays for all cases. All surgeons preferred to use lateral-wall array for HP cases, while 79% of surgeons preferred the same array for standard cases. Electrode insertion though the round window (RW) was the most common technique in all cases. Most surgeons (97%) used the extended round window (ERW) or cochleostomy (CY) approach only if the RW was not accessible. Most surgeons preferred to seal the electrode array insertion point in both CY (85%) and RW (77%) approaches. Most surgeons agreed on the usage of intra-operative intravenous corticosteroids for all cases. Local application of corticosteroids was preferred by 69% and 41% of surgeons in HP and standard cases, respectively. Antibiotics were used similarly in both standard and HP cases.

Conclusion

The field of CI has undergone many stages of improvement and innovation, including changes in surgical practice over the years. Most surgeons agree on the usage conventional-length lateral-wall electrode arrays, the RW approach, and the use of intra-operative corticosteroids and antibiotics. However, practices differ regarding pre- and post-operative corticosteroid and antibiotic regimens. Further research is needed to produce a standardised protocol for HP to allow more robust reporting and comparison of outcomes across CI centres at a national and international level.

4.1 Introduction

Patients undergoing cochlear implantation (CI) derive limited benefit from their residual hearing (RH). However, it is increasingly evident that patients with more post-implantation RH have better speech recognition and music appreciation (Gantz et al., 2005). This and the need to maintain cochlear well-being for future interventions and technology are the motivations behind a 'soft' surgical approach to protect this RH and intra-cochlear structures.

Device manufacturers continue to improve their electrode array designs with more flexibility and less trauma, leading to a positive effect on surgical outcomes, especially hearing preservation (HP). The candidacy criteria for CI have become less stringent (Gibbin et al., 2003, Vickers et al., 2016), and this is reflected in the most recent National Institute for Health and Care Excellence (NICE) guidelines (NICE, 2019).

Surgical technique has also changed over the last few decades due to consistent improvements and innovation of CI electrodes and their devices. Since the introduction of CI in the UK in the 1980s, only two surveys have evaluated the surgical practices of CI. The results of both surveys were published in a single article in 2003 by Gibbin et al. Both surveys reflected the views of 24 of surgeons in the UK and Republic of Ireland. These surveys investigated surgical techniques among CI surgeons. The objectives of these surveys were to consider the main principles of CI, including incision, soft-tissue flaps, the bed for the receiver package, securing the device, facial nerve monitoring, cochleostomy (CY), sealing the CY, wound closer, and antibiotic (AB) coverage. A similar survey was recently published by Carlson et al. (2018) that included the views of the CI surgeons in North America. With the rapid technological advancements and consistent improvement in CI procedures, the current focus of CI surgeons is to improve the quality of the CI procedure. This survey aims to bridge the temporal gap in the UK interval and review the current surgical practices of HP in CI patients.

4.2 Objective

The objective of this survey is to assess the current surgical practices for HP in CI among the consultant surgeons in the UK, including device choice, surgical techniques, electrode insertion, medications, and audiological follow-up.

This survey will help surgeons compare their practices to the majority viewpoints of UK-based CI surgeons and to help direct future research and innovations. The results of this research will contribute the experiences of practitioners to the current evidence in the literature.

4.3 Methods

4.3.1 Questionnaire design

A review of the literature revealed that there were no recent studies that described the surgical practice of HP in the UK. The most recent survey that addressed this topic was conducted in 2003 and investigated the main aspects of the surgery (Gibbin et al., 2003). Another recent survey was conducted in the United States of America (Carlson et al., 2018). The scope of the most recent survey was widened to include other aspects of the surgery and covered several aspects of HP (Carlson et al., 2018). Therefore, the questions in this questionnaire were adapted from Carlson et al. (2018) and some questions were customised to fit our objectives (Appendix 4). The questionnaire was distributed to surgeons (Mr. Azhar Shaida, Mr. Sherif Khalil, Mr. Robert Nash, and Prof. Shakeel Saeed) for their feedback to verify that it contained relevant information and details that addressed all elements of this topic.

The survey was divided into four sections: device selection, surgical approach, electrode insertion, and audiological follow-up. All four sections inquired about the perspectives and surgical practices of the individual surgeons rather than the team or centre. The questionnaire followed a multiple-choice format.

The survey consisted of questions that compared the surgical practises for standard CI and HP cases. The terms ‘hearing preservation case’ (HPC) and ‘standard case’ (SC) were defined at the beginning of the questionnaire for clarity and accuracy. Our definition of ‘standard case’ was any patient undergoing CI with any definable or measurable air-conduction hearing threshold on pure-tone audiometry. We defined an ‘HP case’ as any patient with a substantial amount of RH and planned electro-acoustic stimulation (EAS) CI.

4.3.2 Questionnaire distribution and subject recruitment

A search was conducted on the website of the British Cochlear Implant Group (BCIG) (www.bcig.org) for the names of all CI centres in the UK. By contacting the centres, the names and email addresses of all consultant CI surgeons in the UK were acquired.

A SurveyMonkey® account was created. A survey webpage with 22 questions was created, and individual URLs to the webpage were emailed to all CI surgeons in the UK on the 10th of December 2019. The survey was left open for 3 months, and four reminder emails were sent to maximise the response rate.

4.3.3 Data analysis

All questionnaires were fully answered and were included in the analysis. The data were exported to a Microsoft Excel spreadsheet. To highlight the results of the multiple-choice questions, descriptive analysis and graphical illustration of the questionnaire data were provided in a comprehensible style. The results were presented in the form of numbers and relative frequencies (percentages) of the total number of responses.

4.3.4 Ethical approval

Research ethics approval was granted for this study through the Research Ethical Committee at the Health Research Authority (HRA). REC reference number: 18/LO/1405.

4.4 Results

4.4.1 Population demographic

We identified 57 consultant CI surgeons from the 20 CI centres that were listed on the BCIG website. All the identified centres were part of the NHS. A link to the survey webpage was sent to all 57 consultant surgeons via their individual email addresses. Of the 57 emails, 4 (7%) emails were returned or opted out, 13 (22.8%) did not have any response, 40 (70.2%) were opened, and 39 (68.4%) were completed. The 39 respondents worked in 16 of the 20 CI centres in the UK.

The respondents were asked about their clinical experience in the CI field as a consultant, and they were divided into five categories based on their years of experience (Table 4-1). Responses reflected individual practices, not centre protocols.

Table 4-1. The duration of clinical practice of the participants in the CI field as a consultant surgeon.

	Number of years	Percentage (%)	No.
	a. 1–5	23	9
	b. 6–10	23	9
	c. 11–15	23	9
	d. 16–20	10	4
	e. >20	21	8
Total		100	39

The questionnaire started with a key question inquiring about the indication of using an HP protocol, which included device selection, surgical technique, and the usage of a specific medication regimen. Nearly half (n= 19, 49%) of the respondents used an HP protocol whenever they had a patient with any measurable hearing, followed by 16 (41%) surgeons who used an HP protocol for patients with hearing threshold better than 60 dB at any low frequency (125–1000 Hz). Four (10%) of the surgeons restricted HP protocol to patients with normal-to-mild hearing loss at low frequencies (125–1000 Hz).

4.4.2 Device choice

The first section of the survey focused on device selection for HP cases, focusing on the length of the electrode array, laterality (pre-curved or lateral-wall [LW] array), and manufacturer. Surgeons were asked about the length of the electrode arrays used for HP cases. The results showed that 34 (87%) of the surgeons preferred a conventional-length electrode array for all cases, while 2 (5%) surgeons decided on the length of electrode array based on radiological evidence, 2 (5%) surgeons decided the length of electrode array based on the pre-operative hearing threshold, and only 1 (3%) surgeon preferred to use a hybrid electrode array for HP (Figure 4-1).

The following question asked if there was any preference in manufacturer for HP cases. Participants were able to choose more than one option. The responses to this question showed that 7 (18%) surgeons had no manufacturer preference, while most surgeons (62%, n=24) preferred to use Cochlear Corp. devices, followed by 16 (41%) who preferred Advanced Bionics devices, and 10 (26%) who preferred MED-EL GmbH devices.

The last question in the device section inquired about the type of electrode array (pre-curved or LW) that the surgeons preferred to use for both standard and HP cases. All surgeons (100%) preferred to use a LW electrode array for HP cases; however, 79% (30) preferred LW for standard cases, and 21% (8) preferred pre-curved arrays for standard cases (Figure 4-2).

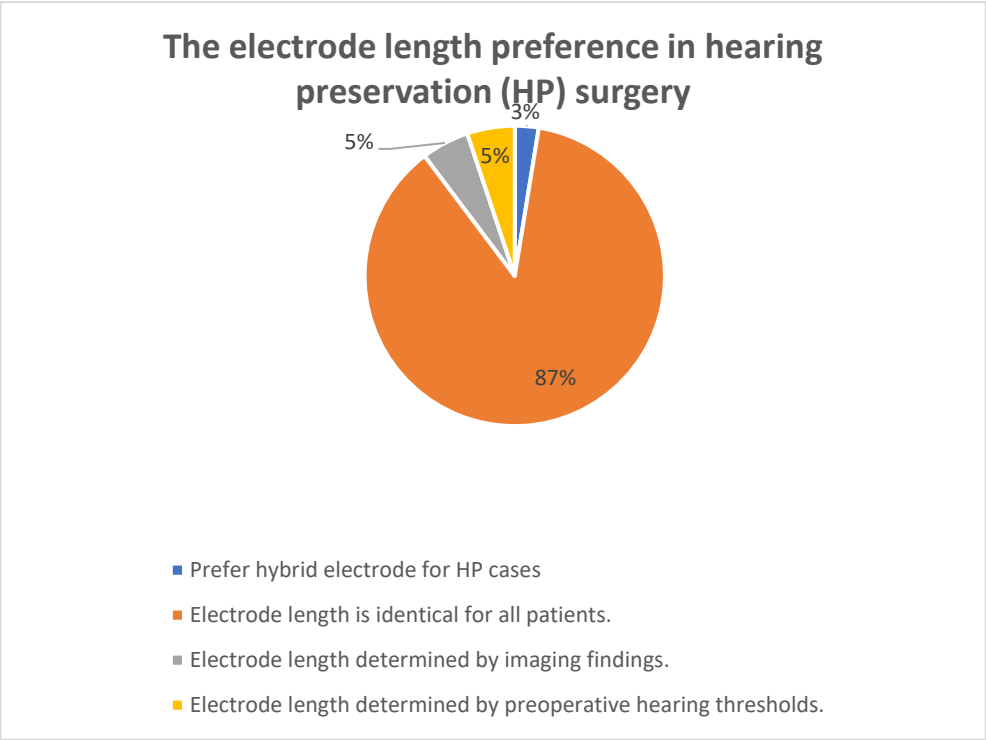

Figure 4-1. The preferences of surgeons when choosing the length of electrode arrays for patients with residual hearing.

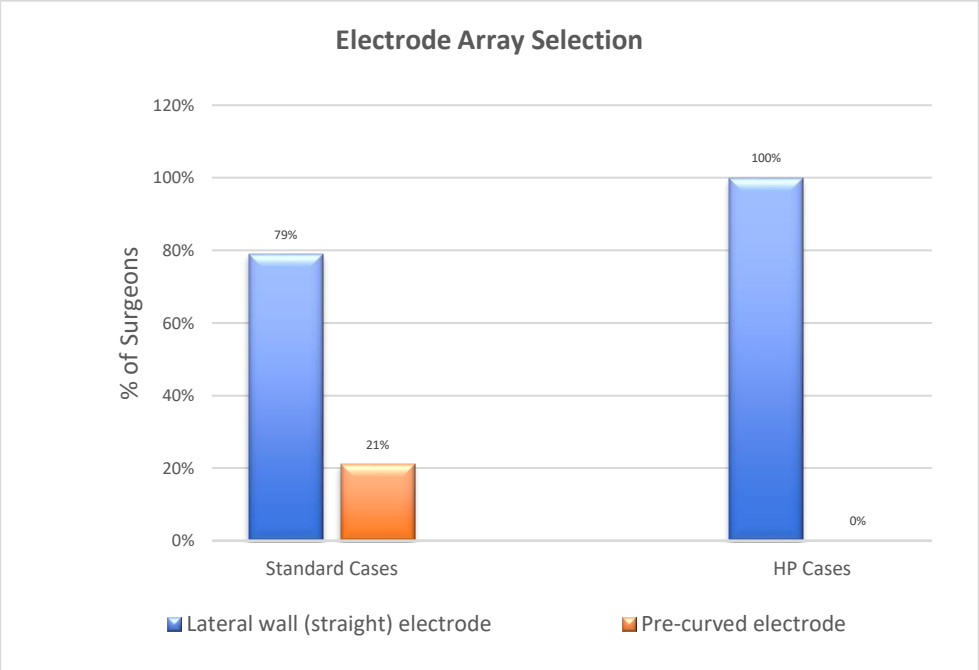

Figure 4-2. Comparison of surgeons' preferred electrode array for standard and HP cases.

4.4.3 Surgical procedure

4.4.3.1 Electrode insertion

This section of the survey explored the surgeons' electrode insertion preferences, including the insertion technique into the scala tympani (ST) (round window [RW], cochleostomy [CY], or extended round window [ERW]), speed of insertion, and sealing of the cochlear opening. Surgeons were able to choose more than one option to reflect their insertion technique preferences.

In HP cases, 37 (95%) respondents preferred electrode insertion through the RW, 1 (3%) preferred an ERW approach, and 1 (3%) preferred a CY approach. Regarding the speed of insertion, 28 (72%) respondents took more than 1 minute to insert the array, 8 (21%) inserted the array within 30–60 seconds, and 3 (8%) inserted the array in less than 30 seconds.

In standard cases, 34 (87%) of the respondents preferred electrode insertion through the RW, 10 (26%) preferred an ERW approach, and 3 (8%) preferred a CY approach. Regarding the speed of insertion, 14 (36%) respondents took more than 1 minute to insert the array, 17 (44%) inserted the array within 30–60 seconds, and 8 (20%) inserted the array in less than 30 seconds.

After RW insertion, 30 (77%) of the surgeons preferred to use soft tissue, 1 (3%) used both soft tissue and fibrin glue, and 8 (20%) did not use any sealing. After CY insertion, 33 (85%) surgeons preferred to use soft tissue (muscle or fascia) for sealing, 1 (3%) used soft tissue and fibrin glue, and 5 (13%) preferred not to seal the CY site.

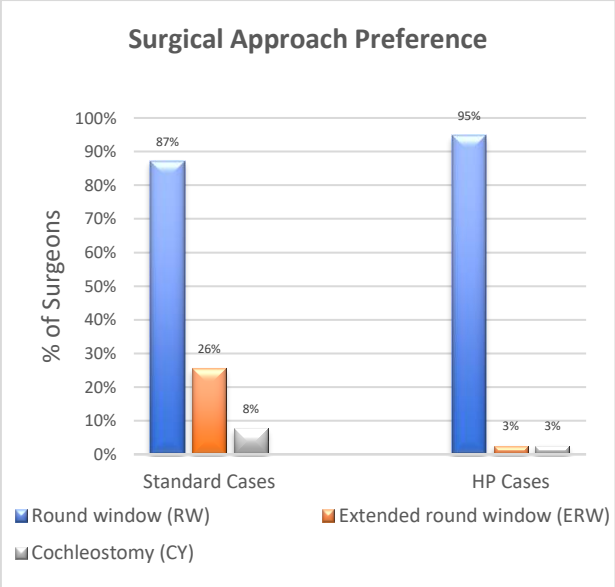

Figure 4-3. The preferred method of electrode array insertion in both standard and HP cases. For this question, surgeons were able to choose more than one option.

Surgeons were asked about the technique of CY drilling. Thirty-three (85%) surgeons drilled the bone then used a fine hook or needle to open the membranous labyrinth, while 6 (15%) surgeons preferred to drill all the way to the cochlear duct. The majority of surgeons 38 (97%) used an ERW or CY approach if the RW was not accessible.

4.4.3.2 The usage of antibiotics, corticosteroids, and hyaluronic acid

Participants were asked to choose one or more option to describe their regimen of corticosteroids and ABs. Table 1.2. details the surgeons' protocols when using corticosteroids and ABs. The results indicated that oral corticosteroids were used by 10% of surgeons for HP cases. Most surgeons used corticosteroids during surgery for standard and HP cases. Local application of corticosteroids was used by 69% (n=27) of surgeons for HP cases, while 41% (n=16) of surgeons used it as a standard.

In HP surgery, 37 (95%) of the surgeons used intra-operative intravenous (IV) ABs, 15 (38%) used post-operative oral ABs, and 7 (18%) used post-operative IV ABs. For routine cases, 38 (97%) of the surgeons used intra-operative IV ABs, 13 (33%) used post-operative oral ABs, and 7 (18%) used post-operative IV ABs (Table 4-2). Regarding the usage of hyaluronic acid (HA), the majority (34, 87%) of surgeons did not use it in any case, 3 (8%) used it in all cases, and 2 (5%) used it only for standard cases.

Table 4-2. Responses to questions that compared surgeons' practices when operating on hearing preservation and standard cases.

Which electrode array do you routinely use for standard cases and HP?

	Standard cases		HP cases	
	Percentage	Number	Percentage	Number
a. Lateral-wall (straight) electrode	79	31	100	39
b. Pre-curved electrode	21	8	0	0

Corticosteroid regimen for standard cases and HP cases? (Select one or more)

	Standard cases		HP cases	
	Percentage	Number	Percentage	Number
a. Pre-operative oral	0	0	10	4
b. Pre-operative IV	23	9	21	8
c. Intra-operative IV	72	28	77	30
d. Intra-operative local	41	16	69	27
e. Post-operative oral	3	1	31	12
f. Post-operative IV	8	3	13	5
g. None	8	3	10	4

Antibiotic regimen for standard cases and HP cases? (Select one or more)

	Standard cases		HP cases	
	Percentage	Number	Percentage	Number
a. Intra-operative IV	97	38	95	37
b. Post-operative oral	33	13	38	15
c. Post-operative IV	18	7	18	7
d. None	0	0	0	0
e. Depends on the case	0	0	0	0

The speed of electrode insertion for standard cases and HP?

	Standard cases		HP cases	
	Percentage	Number	Percentage	Number
a. Less than 30 sec	21	8	8	3
b. Between 30 and 60 sec	44	17	21	8
c. More than 1 min	36	14	72	28

Which surgical approach do you routinely use for electrode insertion? (Select one or more)

	Standard cases		HP cases	
	Percentage	Number	Percentage	Number
a. Round window (RW)	87	34	95	37
b. Extended round window (ERW)	26	10	3	1
c. Cochleostomy (CY)	8	3	3	1

Abbreviations in this table; IV= intravenous, sec= second, min= minutes.

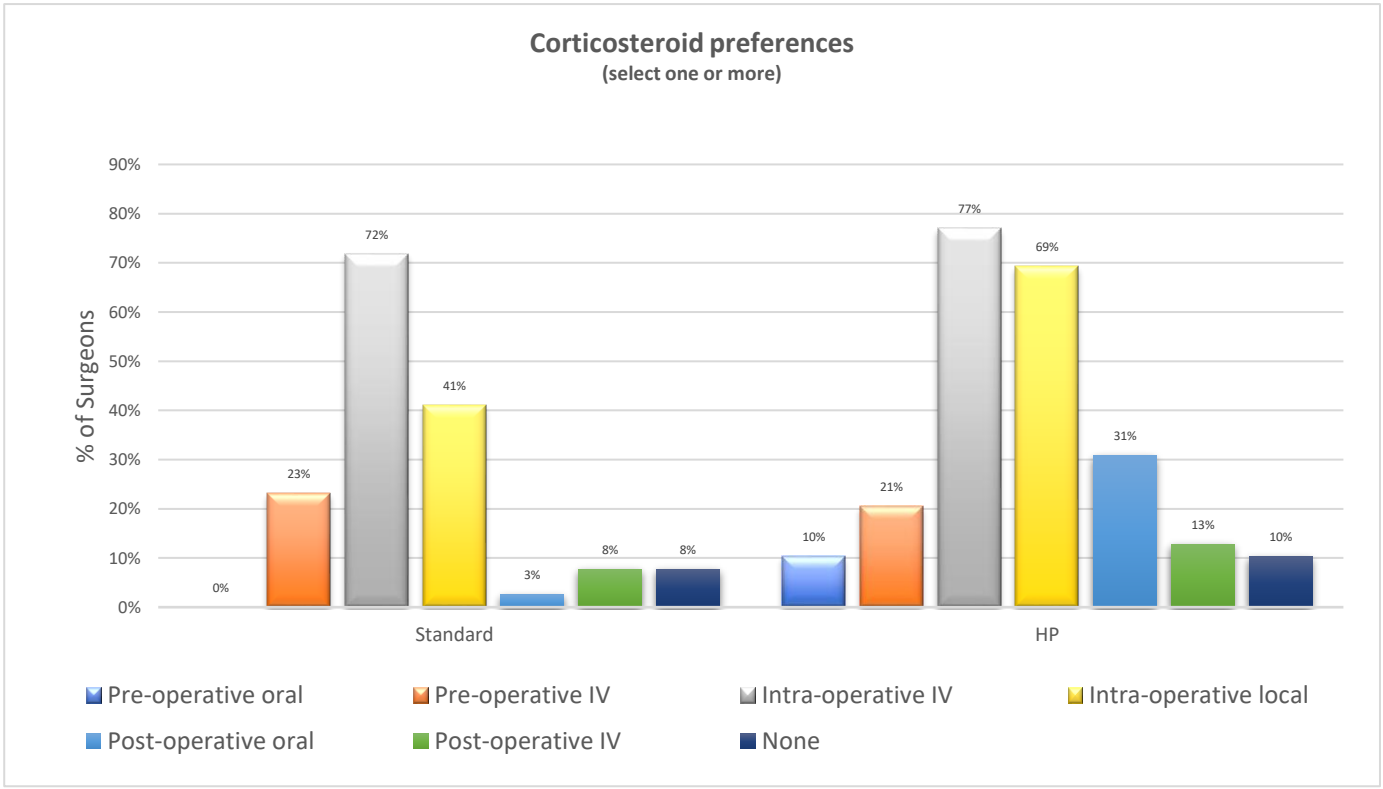

Figure 4-4. A comparison between surgeons' preferences regarding the use of corticosteroids when operating on standard cases versus hearing preservation cases.
For this question, surgeons were able to choose more than one option.

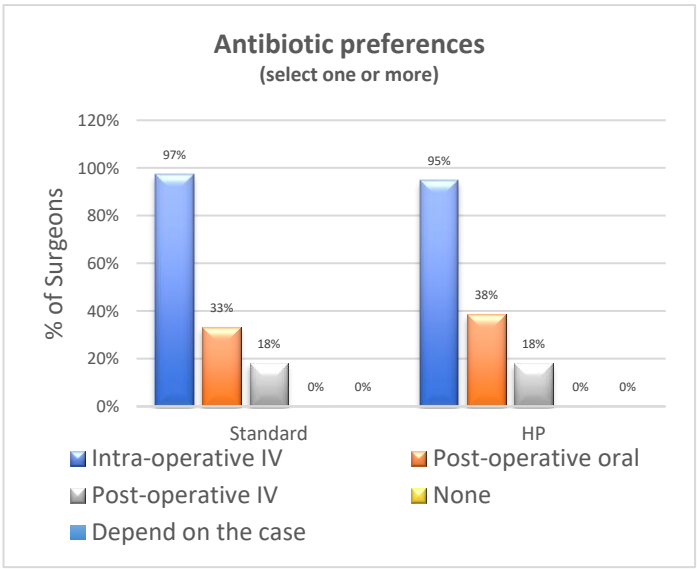

Figure 4-5. A comparison between surgeons' preferences regarding the use of antibiotics when operating on standard cases versus hearing preservation cases.
For this question, surgeons were able to choose more than one option.

4.4.4 Audiology monitoring

In this section, surgeons were questioned about audiological monitoring during operation and follow-up appointments. Most surgeons (n=28; 72%) did not use intra-operative monitoring; 11 (28%) of the surgeons used intra-operative monitoring (ECohG). Some of the surgeons who used intra-operative monitoring reported that they had started to use it recently for research purposes.

Regarding post-operative hearing assessment, most surgeons (n=24; 62%) routinely request a post-operative, unaided PTA test for any patient with RH; 12 (31%) requested it for all patients, while 3 (8%) requested assessment only for EAS patients.

Regarding the frequency of unaided PTA assessment, 33% (n=13) of surgeons assessed patients' RH only once after surgery, while most of the surgeons (67%) preferred to assess RH more frequently, varying between every 3, 6, and 12 months (Figure 4-6).

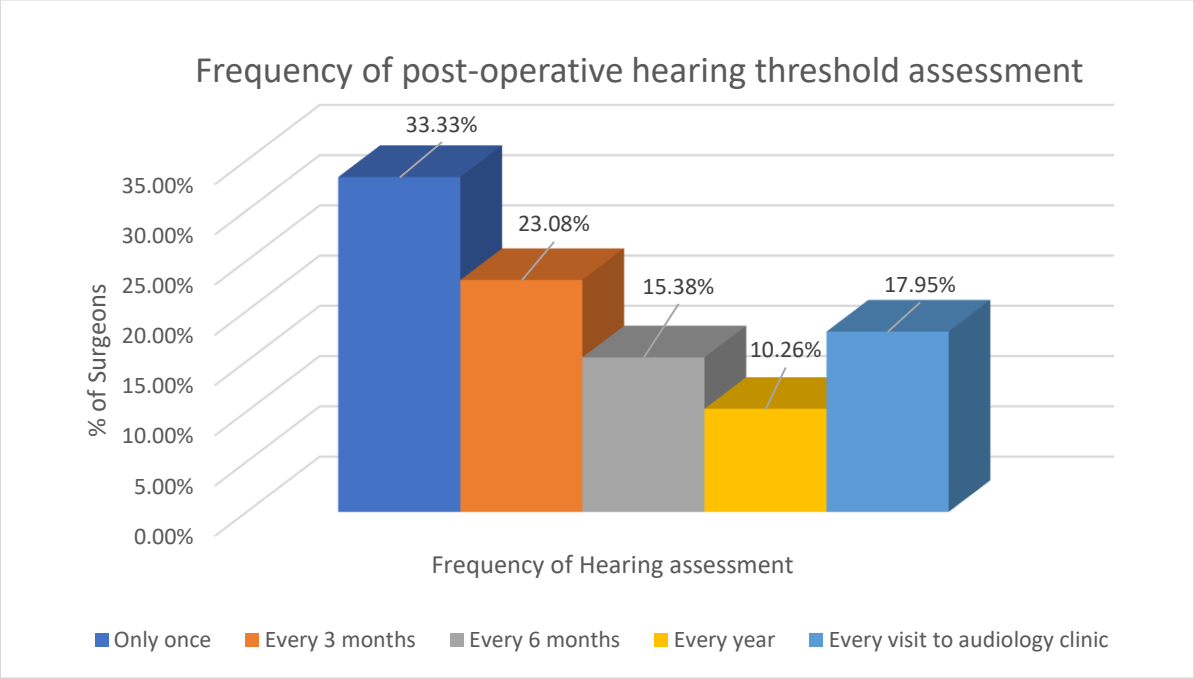

Figure 4-6. The frequency of unaided pure-tone audiometry (PTA) assessment after surgery to assess the stability of residual hearing.

4.5 Discussion

4.5.1 General

At its inception, CI was indicated for individuals with profound or total bilateral sensorineural hearing loss; over the years, as technology and surgical techniques have evolved, candidacy is no longer limited to such cases. The most recent UK candidacy criteria serve to highlight this change (NICE, 2019), as do the criteria in many countries. The number of patients with RH and those who might benefit from EAS is increasing. There is no standard protocol for preserving such RH from a surgical perspective. The lack of robust evidence is one of the reasons behind this lack of protocol. This UK-wide survey of surgeons' perspectives and experiences will help us identify the common surgical practises for HP surgery, as well as emphasise the need for prospective studies and standardisation.

To date, few published surveys have assessed the surgical practices of CI. The only survey that investigated this topic in the UK was published by Gibbin et al. (2003). The study included 24 participants and evaluated the general practice of CI surgery. A more recent survey was published exploring the surgical practices within the United State of America (USA), as it targeted members of the American Neurotology Society. The latter study included 81 surgeons' responses and investigated patterns in surgical and device-related practices (Carlson et al., 2018). The focus of early publications was basic skills; as the field has matured, the focus of the research has shifted to increasing the quality and outcomes of surgery. The focus of this survey is the preservation of RH and the inner structures of the cochlea.

4.5.2 Population demographics

This survey targeted consultant CI surgeons working in the NHS in the UK; 39 surgeons responded to the survey, which represents a substantial proportion (68%) of the 57 CI consultant surgeons in the UK. The 39 respondents worked in 16 of the 20 CI centres in the UK. Previous publications by Gibbin et al. (2003) and Carlson et al. (2018) represented the opinions of 24 and 81 surgeons, respectively.

The responses to this survey reflected the personal practices of each surgeon. This survey reflected a deep level of experience, as it was targeted exclusively to consultant surgeons and was similar to Gibbin et al. (2003); in contrast, Carlson et al. (2018) included both consultants and trainees.

4.5.3 The concept of hearing preservation and intra-cochlear structural preservation

The questionnaire started with a key point inquiring about the concept of HP and the indications of its protocols. The protocol might include the use of any specific electrode arrays, surgical approach, or medical regimen. It seems that very few surgeons (10%) restricted HP protocols to patients with a mild-to-normal low-frequency hearing threshold. In contrast, 41% of surgeons used a HP protocol for patients with a hearing threshold better than 60 dB at low frequency, while almost half (49%) of the surgeons used some protocols to protect RH for all patients regardless of the level of RH. Moreover, the responses to this question showed no consensus on the indication for HP protocol, which highlighted the need for standardisation in this area. Most surgeons tried to decrease trauma and preserve hearing in most patients; however, there is clearly a need for more robust evidence and protocols.

Until recently, there was no consensus on a specific definition of HP, which led to controversy in early publications. In (2013), Skarzynski et al. published a definition and grading system that was widely accepted. Most recent publications use this definition and grading system to describe the level of HP after the surgery despite the lack of a clear indication for HP surgery.

HP is beneficial to patients' post-operative outcomes. Previous research has shown that patients with RH perform better in background noise and music appreciation (Gantz et al., 2005, Gfeller et al., 2006). These benefits are not just limited to patients with a substantial amount of RH or those using EAS (Usami et al., 2014b). The benefit of HP surgery is the maintenance of the health of intra-cochlear structures (Bas et al., 2012). Post-operative unaided PTA is one of the preferred measures to assess the presence of intra-cochlear trauma. Even though it is not possible to measure the effect of trauma in patients with low hearing thresholds, research has shown that it is crucial to have smooth, atraumatic surgery and preserve intra-cochlear structures in all patients (Usami et al., 2014b). Therefore, HP at any level is a useful surrogate marker of 'cochlear well-being' (Saeed S R, personal communication, March 14, 2022)

4.5.4 Device choice

4.5.4.1 Electrode length

The majority of surgeons (87%) preferred to use conventional-length electrode arrays for all patients, while some surgeons decided on the length based on radiological evidence (5%) or the degree of RH (5%). Only one surgeon preferred to use hybrid electrodes for HP. These results are similar to the preferences of surgeons in the USA (Carlson et al., 2018). Most American surgeons (71%) prefer to use conventional-length electrode arrays for HP, while 29% prefer short arrays.

The responses in both surveys were in line with the literature. Evidence has shown that very deep insertion decreases the likelihood of HP; however, it is possible to preserve RH with conventional electrode length (Kisser et al. (2016). Even though short electrode arrays might provide better HP (Rader et al., 2013), conventional-length arrays provide better coverage of the cochlea (Gantz et al., 2009, Skarzynski et al., 2012), which becomes useful as RH deteriorates over time (Helbig et al., 2016). In contrast, short arrays may require a second surgery and re-implantation with a longer array. Initial implantation with a moderate-length electrode appears to prevent the need for a second surgery that would increase the risk of losing RH in addition to the risks associated with additional surgery and anaesthesia (Eshraghi et al., 2016).

4.5.4.2 Manufacturer

All device manufacturers produce atraumatic LW electrode arrays. For HP cases, our survey indicated that most surgeons (62%) preferred to use electrode arrays manufactured by Cochlear Corp., followed by Advanced Bionics (41%) and MED-EL GmbH (26%). This finding is similar to that of Gibbin et al. (2003). As of 1997, Cochlear Nucleus devices were the most used in adults (74%) and children (91%) in the UK, among other manufacturers, followed by MED-EL in the adult population (14%). At the end of 2001, the number of Cochlear Corp. devices used was the highest (78%) in the UK. Results from a survey in North America showed that Cochlear Corp. devices were used by 99% of centres, while Advanced Bionics and MED-EL devices were offered by 91% and 86% of centres, respectively (Carlson et al., 2018). The evidence has shown no significant difference in the level of HP among manufacturers (Santa Maria et al., 2014). Surgeons in the UK maintain their preferences over time. Further

investigation is needed to elucidate the reasoning behind these preferences and whether there are differences in HP outcomes.

4.5.4.3 The design of electrode array (lateral vs. pre-modiolar)

The LW array appears to be the most used by surgeons for both HP and standard cases. All surgeons (100%) preferred to use LW arrays for HP cases, and 79% of surgeons preferred to use them with standard cases. When comparing our results with the North American survey results, we noticed that a relatively equal number of surgeons used both arrays for standard cases. In contrast, most surgeons (86%) preferred to use LW arrays for HP (Carlson et al., 2018). This observation is in line with literature supporting the use of LW arrays for HP surgeries. Pre-curved arrays are potentially more traumatic and have a higher risk of dislocation from the ST (Boyer et al., 2015, James et al., 2006), which leads to loss of RH (Causon et al., 2015). In contrast, LW arrays are thinner and flexible, making them less traumatic and preferred for HP conditions (Wanna et al., 2014, O'Connell et al., 2016a, Boyer et al., 2015).

4.5.5 **Surgical procedure**

4.5.5.1 Electrode insertion

This survey indicated that surgeons more commonly used an RW insertion for both standard (87%) and HP cases (95%). However, 26% of surgeons preferred an ERW approach for standard cases and 3% preferred it for HP cases. CY was preferred by 8% of surgeons for standard cases and 3% preferred it for HP cases.

The practices of surgeons in this survey were similar to the practices of surgeons in the USA (Carlson et al. (2018). For standard cases, 64% of surgeons in the USA preferred RW insertion, 26% preferred an ERW approach, and 10% preferred CY. For HP cases, 86% of surgeons in the USA preferred RW insertion, 9% preferred an ERW approach, and only 5% preferred CY insertion.

Older surveys showed that most surgeons preferred a CY approach at that time. In 2003, the results of (Gibbin et al.)'s study indicated that 90% of UK-based surgeons used a CY, and 54% of them described using soft surgery. Two other surveys conducted by Adunka and Buchman (2007) and Iseli et al. (2014) reported that RW insertion was preferred by 19% and 69% of respondents, respectively. The results of these surveys showed that the practice has changed significantly over time.

In the early days of CI, many publications suggested that the CY approach was less traumatic (Clark et al., 1984), especially with older, more rigid electrodes. Despite the RW being considered a more natural access to the ST, it might lead to electrode trauma and dislocation into the scala vestibuli (SV) due to the configuration of the basal ST. In this respect, the CY approach allows for a more straight and direct access to the ST when inserting the electrode arrays (Addams-Williams et al., 2011).

The current trend in practice is to use the RW approach, especially in HP cases. This could be explained in part by the development of new atraumatic electrodes, which have improved the outcomes of the RW approach and led to a shift in practice (Hassepass et al., 2015). Despite this improvement, the level of evidence comparing both approaches is low and inconclusive. Several systematic reviews compared both approaches and reported conflicting results (Causon et al., 2015, Santa Maria et al., 2014, Havenith et al., 2013, Snels et al., 2019). There is a need for strong evidence and prospective studies comparing both approaches to help draw definitive conclusions and support the current practice with robust evidence.

4.5.5.2 Opening the membranous labyrinth

It is important to consider noise trauma during surgery. During CY, the intensity of drill noise might reach 110 dB when the bony labyrinth is very thin, and it might reach around 130 dB when exposing the membranous labyrinth. Therefore, it is advised not to drill all the way into the cochlea, but to stop drilling and open the membranous labyrinth using a fine hook or needle (Pau et al., 2007, Cipolla et al., 2012). Responses to our survey were in line with the literature and indicated that most surgeons (85%) intended to use a hook or needle, which is less traumatic and helps to better preserve hearing.

4.5.5.3 The usage of antibiotics, steroids, and hyaluronic acid

The results of this survey showed variability in the practice of HP among surgeons in the UK regarding the use of corticosteroids and ABs.

4.5.5.3.1 Antibiotics

CI surgery is considered a clean surgery and has a low rate of infection; however, any infective complications that might occur can be serious, such as wound infection,

device exposure, device rejection, and meningitis (Farinetti et al., 2014). Management of some of these infections might require explanation and re-implantation or delaying the activation of the device, which is costly and challenging for patients (Francis et al., 2008, Cohen and Hoffman, 1991). According to the results of a systematic review published by Anne et al. (2016) regarding the effect of perioperative ABs on CI surgery, the rate of CI infection is low (3–4.5%) and there is no strong evidence supporting the positive effect of ABs on patient outcomes. However, it was reported that ABs might help prevent serious complications (Anne et al., 2016).

The results of our survey did not show a significant difference in the use of ABs between standard and HP cases. More than 90% of surgeons used some form of prophylactic AB during surgery; 38% used post-operative oral ABs in HP cases only, and one-third used post-operative oral ABs routinely. Few surgeons (18%) used post-operative IV ABs equally in both standard and HP surgeries.

These results align with previous research (Gibbin et al., 2003, Barker and Pringle, 2008). Barker and Pringle (2008) conducted a specific survey investigating the use of prophylactic ABs by CI surgeons in the UK. They reported that all surgeons in the UK used some form of prophylactic AB during CI surgery, despite significant variation in protocols. There is a need for more evidence to guide the process of developing a standardised protocol for prophylactic AB use in CI surgeries (Anne et al., 2016, Barker and Pringle, 2008).

4.5.5.3.2 Corticosteroids

The results showed that most surgeons tended to use IV corticosteroids during the surgery (pre- or intra-operatively). The results of the North American survey were similar and showed that 92% of surgeons used intra-operative corticosteroids (Carlson et al., 2018). Our survey showed that local corticosteroids were used by 69% of CI surgeons in the UK for HP cases and by 41% (n= 16) for standard cases. In contrast, 44% of surgeons in North America used local corticosteroids generally (Carlson et al., 2018).

Pre-operative and post-operative oral corticosteroids seem to be used more often by surgeons in the USA: 30% and 55% of surgeons, respectively (Carlson et al., 2018). A smaller number of surgeons in the UK prefer to prescribe post-operative oral steroids

for both standard (3%) and HP cases (31%), while very few surgeons (10%) prescribe pre-operative oral steroids for HP cases only.

The results of both surveys showed that steroids were widely used among surgeons, and most of them agreed on using IV steroids during surgery. Corticosteroids are known to help with general inflammation and in sudden hearing loss (Rauch et al., 2011, Battaglia et al., 2014). Evidence in the literature has reported the positive effect of corticosteroids on HP when used systemically or locally during the operation (Rajan et al., 2012, Quesnel et al., 2011, Eastwood et al., 2010, Sweeney et al., 2015); therefore, it should be considered in all CI surgeries. Despite the growing evidence of the benefits of corticosteroids, there is no optimal protocol or regimen for their use. In the meantime, most surgeons agree on the usage of IV corticosteroids during surgery.

4.5.5.3.3 Hyaluronic acid

HA use in CI surgeries is thought to have many advantages. It reduces friction and prevents trauma during electrode insertion and prevents perilymph contamination by blood and bone dust. Moreover, it provides some magnification effect during CY insertion (Laszig et al., 2002, Abi Zeid Daou and Bassim, 2020).

The results of the controlled clinical trial published by Ramos et al. (2015) showed that HP outcomes were better when combining local corticosteroids and HA than when corticosteroids were used alone. It is believed that the role of HA is not limited to reducing insertion trauma, but that it increases the duration of exposure to corticosteroids at the RW membrane. Despite these benefits, the results of this survey showed that most surgeons (87%) did not prefer to use HA

4.5.6 **Audiology monitoring**

4.5.6.1 Intra-operative hearing monitoring

Electrocochleography (ECochG) is one of the methods used to detect electrode trauma and guide the process of electrode insertion. ECochG response can be recorded in 95% of patients with RH (Dalbert et al., 2018, Choudhury et al., 2012). The main advantage of this tool is that it facilitates real-time monitoring during the surgery, which helps smooth the insertion of the array and decrease intra-cochlear trauma, thereby preserving RH (Dalbert et al., 2018, Giardina et al., 2019). According to a

systematic review conducted by Dalbert et al. (2019), the evidence in this field is still growing, and there is a need for more studies to support this correlation. Almost one-third (28%) of respondents to our survey utilized this tool, and some of them said that they had begun to use it for research purposes. This observation is a strong indicator for surgical care and the potential improvement of HP surgery outcomes.

4.5.6.2 Post-operative hearing monitoring

Most surgeons (62%) in our survey tended to assess the level of post-operative RH for any patient with RH; 31% preferred to have a hearing assessment for all patients after operation, while only 8% restricted hearing assessment to patients who intended to use EAS devices. Post-operative PTA is important in all subjects with any measurable hearing as it not only measures the level of RH, but also reflects the health and condition of intracochlear structures (Eshraghi and Van de Water, 2006).

While 33% of surgeons chose to assess the level of RH once after the surgery, most surgeons (67%) preferred assessing the level of hearing threshold more frequently. This observation is in line with the results published in previous histological and clinical studies. Changes in hearing threshold can occur immediately after surgery due to noise trauma and insertion trauma (Eshraghi and Van de Water, 2006), or they can occur over time due to inflammation, fibrosis, and new bone formation (Seyyedi and Nadol Jr, 2013, Bas et al., 2012, Gstoettner et al., 2000). As a result, the level of RH might not stabilise until 24 months after surgery (Gstoettner et al., 2006). The responses of most surgeons in our survey indicated their concerns about various factors affecting the health of the cochlea.

4.5.7 **Strengths and limitations**

The main strength of this survey is that it was directed exclusively at consultant surgeons, which reflects a certain depth of experience in the study population. This survey had an adequate response rate from 16 of 20 programmes (80%), and as such represented the practice in the UK. This survey was limited to surgeons' opinions about surgical and audiological aspects of HP surgery. Another survey is needed to address the post-operative part of the management from the audiological viewpoint. Audiologists would help to complete the picture and provide a clear perspective on the conditions and needs of the patients.

4.6 Conclusion

The surgical practice of CI has changed over time when compared with previous surveys. Most surgeons consider a CY approach as an alternative when an RW approach is not possible. The surgical practice in the UK is similar to that in the USA regarding the route of insertion, electrode selection for HP, approach of electrode insertion, and usage of intra-operative corticosteroids.

This survey showed that there is no clear consensus on the indications for attempted HP, yet most surgeons agree on the use of LW conventional-length arrays and on the use of intra-operative corticosteroids and ABs for HP cases. However, the practice is inconsistent when it comes to the use of a pre- and post-operative regimens of corticosteroids and ABs. Further studies are needed to evaluate the most appropriate protocols for this group of patients, and the results of this survey could form the basis for a UK-wide, BCIG co-ordinated consensus document process.

Chapter 5 : A randomised controlled trial evaluating the effect of the surgical approach to the cochlea on hearing preservation and speech perception: RCT part 1

The survey results presented in chapter 4 revealed that the majority of surgeons utilise the round window (RW) as their primary approach to the cochlea and a cochleostomy (CY) as an alternate, despite the lack of evidence supporting the superiority of the RW technique. The outcome of our systematic review study in chapter 2 showed the potential to preserve residual hearing (HP) when inserting the electrode array through either approach, which is comparable to the findings of prior systematic reviews. Prior research has identified a number of known biases related to surgeons' preferences and the bias of using the CY approach in difficult conditions, where the RW is not visible or accessible.

This chapter describes a randomised controlled trial with double-blinding (RCT). The purpose of this study is to compare the outcomes of patients randomly assigned to the round window or cochleostomy approach. To overcome the limitations of earlier studies, this study applies a standardised surgical technique to all subjects.

The findings of this randomised controlled trial are described in chapters 5 and 6. Chapter 5 compares the audiological (hearing preservation and speech perception) and radiological (accuracy of scalar position and insertion depth) outcomes between the two surgical techniques. Chapter 6 examines the relationship between the audiological and radiological outcomes.

Abstract

Objectives

During cochlear implantation, the ideal electrode array insertion is atraumatic, is within the scala tympani, preserves residual hearing and is positioned to optimise its interface with the spiral ganglion cells. This can be undertaken via a round window or cochleostomy approach. The optimal approach to achieving these goals has not been definitively established. This paper describes the outcomes of both surgical approaches with regards to hearing preservation (HP) and speech perception. In addition, the scalar position of the electrode array using cone-beam computed tomography (CBCT) is assessed in the study groups.

Method

This was a two-arm double-blinded randomised controlled trial. The trial included adult post-lingual cochlear implant candidates, randomised to have the electrode insertion by round window insertion or cochleostomy. HP was assessed at 1, 3, 6 and 12 months after the surgery. Speech perception was assessed by Bamford–Kowal–Bench (BKB) sentences at 6- and 12-month follow-up. CBCT was used to assess the intra-scalar electrode position in all participants.

Results

Twenty-two participants were successfully recruited to the study: 12 in the round window (RW) group and 10 in the cochleostomy (CY) group. The CY group had significantly better level of HP overall. HP showed a significant difference between approaches at 1-month (P=0.02) and 3-month follow-up (P=0.01) but no significant difference at 6-month (P=0.21) or 12-month follow-up (P=0.065). The statistical analysis showed no significant difference between the two groups when examining BKB scores and the accuracy of electrode scalar placement.

Conclusion

The results from this novel randomised study show that the CY approach had a higher chance of initially preserving hearing, but this was not maintained at the 6-month review and later. Both approaches provided a similar accuracy and depth of electrode array insertion. The results of longer-term follow-up of this study group will be required to further characterise these findings.

5.1 Introduction

Cochlear implantation is an established intervention for the management of selected patients with severe to profound sensorineural hearing loss. Over the past decade, hearing preservation (HP) has been one of the key focal points for cochlear implant surgeons. This has gained more importance with the expansion of candidacy criteria to include patients with more residual hearing. Many factors affect HP during the surgery, including the type and length of the electrode array (Suhling et al., 2016, Adunka et al., 2004b), depth and speed of insertion, use of corticosteroids (Chang et al., 2009, Rajan et al., 2012) and antibiotics (Anne et al., 2016), and accuracy of electrode insertion into the scala tympani through the round window (RW) or a cochleostomy (CY) and its placement within the cochlea (Aschendorff et al., 2007, Adunka and Kiefer, 2006).

For optimal audiological outcomes, the electrode array's position needs to be in the scala tympani (ST) (Adunka and Kiefer, 2006, Kiefer et al., 2004, Aschendorff et al., 2007, Finley et al., 2008). Electrode placement or displacement into the scala vestibuli (SV) is considered intra-cochlear trauma and correlates with loss of residual hearing and poorer speech perception (Aschendorff et al., 2007, Skinner et al., 2007, Holden et al., 2013).

Broadly speaking, the insertion of the electrode array into the ST can be achieved through the RW or a CY. Lehnhardt (1993b) was the first to describe what is known as the soft-surgical approach, which evolved over time (Kiefer et al., 2004, Roland and Wright, 2006, Campbell et al., 2013). The superior efficacy of either surgical approach has been debated. Due to the nature of the electrode trajectory towards the modiolus during RW insertion, the CY approach showed better outcomes in early studies when using the older, more rigid arrays (Clark et al., 1984).

Modern flexible electrode arrays have shown a significant improvement because they are less traumatic than older arrays and can deform smoothly when impacting the modiolus, which directs it to pass inferiorly through the ST (Bae et al., 2019). This improvement has led to a shift in surgical practice, with limited evidence comparing both approaches with the same modern arrays (Santa Maria et al., 2014). In addition, intra-cochlear trauma varies in severity (Eshraghi et al., 2003), and electrode flexibility does not necessarily rule out the possibility of modiolus trauma, which can be

potentially avoided with the CY approach. This trauma may be more severe in conditions with difficult cochlear orientation, visibility or accessibility of the RW.

After the production of the new slim atraumatic arrays, many studies showed an improvement in HP outcomes of the RW approach. These positive outcomes led to a shift in surgical practice (Santa Maria et al., 2014). Since then, RW insertion has been regarded as the superior approach in most studies, whereas CY has been used in cases of difficult insertion or inaccessibility of the RW.

Due to the multifactorial nature of HP, previous retrospective clinical studies have limitations when comparing both approaches, such as using CY when RW is not accessible or comparing the outcomes of patients implanted with heterogeneous electrodes. Four recent systematic reviews have investigated this subject with conflicting results: the CY approach leads to the same (Havenith et al., 2013), better (Santa Maria et al., 2014) or worse HP outcomes than the RW approach (Causon et al., 2015). Most recently, Snels et al. (2019) conducted a meta-analysis and reported that RW showed superior HP levels only during the first 6 months after the surgery.

This reflects the need for a prospective study that controls all possible confounding factors and provides a better understanding of this topic. To our knowledge, this is the first prospective randomised controlled trial comparing both surgical approaches with control of other factors.

5.2 Aim and objectives

This study aimed to compare the outcomes of post-lingual adult cochlear implant candidates when randomised between the RW and CY approaches, using CBCT as an assessment tool to compare the electrode scalar position and depth of insertion, the level of HP and the scores of Bamford–Kowal–Bench (BKB) speech perception test.

The objectives of this study were:

- To determine whether a significant difference exists in the HP of residual hearing between both surgical approaches within the first 12 months after the surgery, at 1, 3, 6 and 12 months post-operatively.

- To compare the outcomes of Bench–Kowal–Bamford (BKB) tests for speech perception in quiet between the two surgical procedures.
- To compare the accuracy of electrode insertion into scala tympani (DST) between both surgical approaches.
- To compare the angular and linear insertion depth between both surgical approaches.

5.3 Methods

5.3.1 Study design and population

Participants were recruited from the Royal National Throat, Nose and Ear Hospital (RNTNEH), London, United Kingdom, from December 2018 to March 2020. The protocol of the trial was published in a public database, the ISRCTN register; the study number is 36337. The inclusion and exclusion criteria are shown in Table 5-1.

Table 5-1. Inclusion and exclusion criteria of recruited participants

Inclusion criteria	Exclusion criteria
- Adult patient (>18 years old). - Unilateral cochlear implant surgery. - Able and willing to give consent. - Meeting NICE criteria for cochlear implantation. - Working use of English for speech perception test. - Measurable hearing threshold at frequencies 250–1,000 Hz.	- Patients younger than 18 years. - Patients with cochlear obliteration or inner ear dysplasia. - Patients with any contraindication to cochlear implantation. - Patients with contraindications to the use of systemic steroids. - Patients with previous middle-ear surgery or planned bilateral implantation.

5.3.2 Patient recruitment

Patients were identified in the multi-disciplinary team (MDT) panel meeting. Patients who met the inclusion criteria were recruited to the trial in the otology clinic. Several weeks later, and during the device choice appointment, patients had the chance to discuss the trial before giving written informed consent. After giving consent, patients were randomised between the two surgeries. Both the patient and the researcher were blinded to the assigned surgical approach. The startified randomisation method was used in this study. Stratified randomization is a sampling technique in which the entire research population is separated into subgroups with similar characteristics or attributes. The stratified groups are then sampled using simple random sampling, in which each element within the same subgroup is selected unbiasedly and completely at random. Stratified randomization prevents imbalances between treatment groups with regards to known factors (Suresh, 2011). This method has the advantage of controlling and balancing the electrode type among groups. This method was employed by an independent researcher to randomly allocate patients to intervention groups using Microsoft Excel. On the day of surgery, surgeons were informed about the surgical approach of electrode insertion. This outcome will be stored in the patient notes, and also in a central trial database. The process of recruitment is illustrated in the flowchart in Figure 5-1.

5.3.3 Sample size

The calculation of the sample size of this trial was based on (Skarzynski et al., 2016), for which we had the test–retest reliability and standard deviation. The calculation was done using mixed-methods ANOVA to measure the effect of the surgical approach and devices. The sample size was calculated using G*Power software using mixed-methods ANOVA, a large effect size (d=0.4) and a high power of 0.95. This trial's required number was 36 patients divided between two homogeneous devices: 18 for each device and nine for each surgical approach. The COVID-19 pandemic interrupted recruitment, so interim results are presented for 22 patients.

5.3.4 Surgery

The cochlear implant surgery was performed using a postauricular incision and a facial recess approach to expose the RW area in all cases. An electrode array was inserted through either the RW or CY approach, which was drilled anteroinferior to the RW.

Aspiration of the perilymph was avoided in all cases. Topical corticosteroids were not applied. Electrode arrays were inserted slowly into the ST over no less than 30 seconds to the first point of resistance. The RW was sealed with connective tissue. The receiver part of the implant was secured in a periosteal pocket. The surgery was undertaken by five experienced cochlear implant consultants, using the same protocol, which included (1) slow-speed drilling and insertion, (2) intraoperative IV dexamethasone and systemic prophylactic antibiotics, (3) postoperative 30 mg of oral steroids for 5 days, (4) oral antibiotics (co-amoxiclav) for two days and (5) CBCT scan 1 week after the operation. In order to overcome the study's timeframe limits and recruit the whole sample, this study employed two types of homogeneous atraumatic lateral-wall electrode arrays commonly used at our hospital: the Slim J from Advanced Bionic and the CI622/CI522 from Cochlea Corp.

5.3.5 Outcome measures

5.3.5.1 CBCT imaging and reviewing of scans

CBCT was conducted for all patients within 1 week after the operation, using a 3D Accuitomo (J. Morita MFG. Corp., Kyoto, Japan). The parameters used in this are similar to those described in Chapter 3, Section 3.3.3.2.

All scans were assessed for angular and linear depth of insertion and electrode scalar position. The depth was measured using the same method explained in Chapter 3, Section 3.3.3.4. Electrode scalar placement was assessed for each electrode using a scale to establish the accuracy of placement, which was illustrated in Chapter 3, Table 3-2. Each electrode was assigned a value (2: definitely in ST, 1: possible ST, 0: query, -1: possible ST, -2: definitely in ST, 3: extra-cochlear). The scans were judged by two independent raters: an experienced consultant radiologist and an experienced cochlear implant surgeon.

5.3.5.2 Unaided hearing threshold and speech tests

The level of HP was assessed at four time points after the surgery: 1, 3, 6 and 12 months. Speech perception ability was evaluated using the BKB speech test 6 and 12 months after the surgery. The BKB speech test and unaided pure tone audiometry (PTA) took place in a double-walled sound-proof booth. Ear-level loudspeakers (Plus XS.2, Canton) were used to present the speech stimulus, and participants were seated 1 metre from the speaker. The results of the BKB in quite were scored out of 100 based on the number of correct key words. The unaided hearing assessment threshold was performed using a calibrated audiometer (Grayson Stadler 61), and an over-the-ear headphone set (TDH-39P) was used to present the stimulus.

The HEARRING group's formula and classification system (Skarzynski et al., 2013) were used to calculate the relative change in the level of HP across all 11 frequencies (125-8,000 Hz); see Figure 1-5 and Table 1-3 in Chapter 1.

5.3.6 **Statistics**

Data were collected during routine clinic visits at 1-, 3-, 6- and 12-month follow-up visits. Due to the COVID-19 pandemic, there were some missing data. There were no missing demographic or preoperative data. Postoperative PTA was missing data in three patients at 6-month follow-up, speech perception tests were missing data in one patient at 6 months and one patient at 12 months, and radiological data for one patient could not be obtained due to technical issues.

The nature of missing data was examined using the Little's Missing Completely at Random (MCAR) test, which was not significant (p= 0.361), and no pattern existed for the missing data. These findings suggest that our data was MCAR, which can be handled using multiple imputations (MI) (Moons et al., 2006). The MI function in SPSS was used to impute the missing data. Five datasets were created using ten iterations (Rubin, 1987). According to Rubin's rules, the five datasets were pooled to create a complete dataset (Groenwold et al., 2012, Moons et al., 2006, Rubin, 1987). All results from the pooled dataset are reported. As a sensitivity test, the original dataset with missing values was analysed and compared with the imputed dataset. The

comparison showed no difference in the level of significance between both datasets for all tests.

Statistical analysis was undertaken with SPSS 27 (IBM, USA). Data were assessed for normality using the Shapiro–Wilk test. The two-sample t-test was the test of choice for parametric data, and the Mann–Whitney U test was used for nonparametric data, to compare the outcomes between both surgical approaches. Mixed-methods ANOVA was used to investigate between and within-subject differences in the level of HP over time.

5.3.7 Ethical considerations

The trial was ethically approved by the Research Ethical Committee at the Health Research Authority (HRA). The registration number of this trial is IRAS: 63284; REC reference: 18/LO/1405.

5.4 Results

5.4.1 Demographics

The interim result of this trial represents 22/36 of the proposed sample, divided between both surgical approaches: 12 in the RW group and 10 in the CY group. The sample consisted of 10 males and 12 females. The mean age of participants was 57.91 years (SD= 16.35). The mean duration of deafness was 31.82 years (SD= 10.88). This sample included 12 patients implanted with the Slim J Advanced Bionic device and 10 implanted with a slim straight cochlear device (CI622/CI522). The RW group includes 6 patients that received Slim J device and 6 patients implanted with Slim stright device. Similarly, the CY group includes 6 patients that received the Slim J device and 4 patients that received the Slim stright device. Table 5-14 presents more details about the demographics of our sample. Figure 5-1 shows the number of patients at all stages of this trial, from identifying patients to analysis.

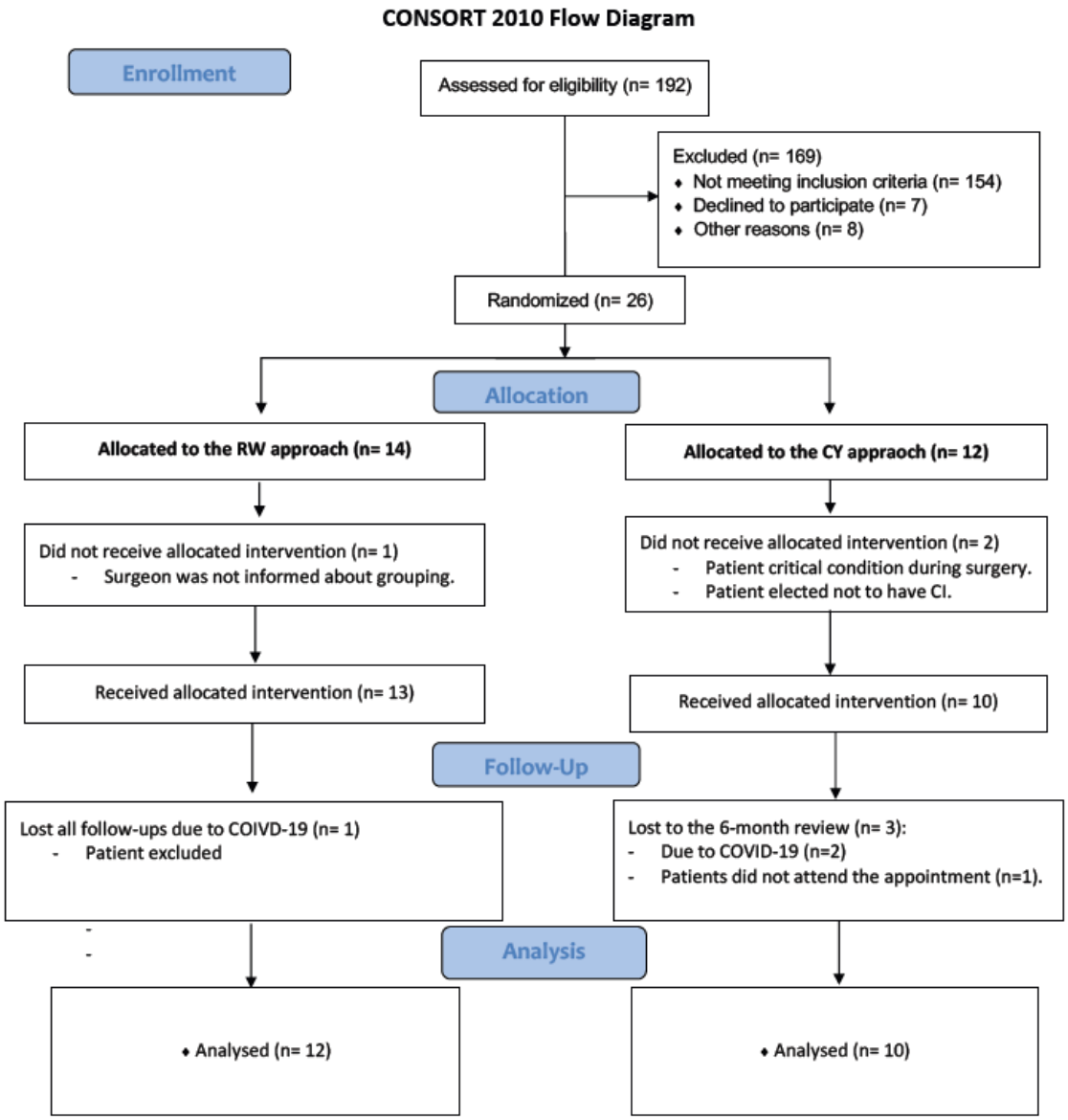

Figure 5-1 CONSORT flow diagram
The diagram shows the numbers of patients in all stages of the trial. Data were imputed for patients missing one follow-up but not imputed for the last patient, who missed all appointments.

5.4.2 Hearing preservation

The level of HP was assessed at four time points after the surgery (1, 3, 6 and 12 months). The majority of patients had partial HP at all follow-up. The results show changes in the level of HP over time. The mean HP was better in the 1-month follow-up than the 3-, 6- and 12-month follow-up [M=41.46 (SD=25.48), 34.90 (SD=22.44), 35.13 (SD=21.71) and 29.15 (SD=25.92), respectively]. Figure 5-2 shows the number of patients in each HP category at 1, 3, 6 and 12 months after surgery. The breakdown of these means into surgical approaches showed that CY participants got more HP than RW participants in all follow-ups, as shown in Table 5-2.

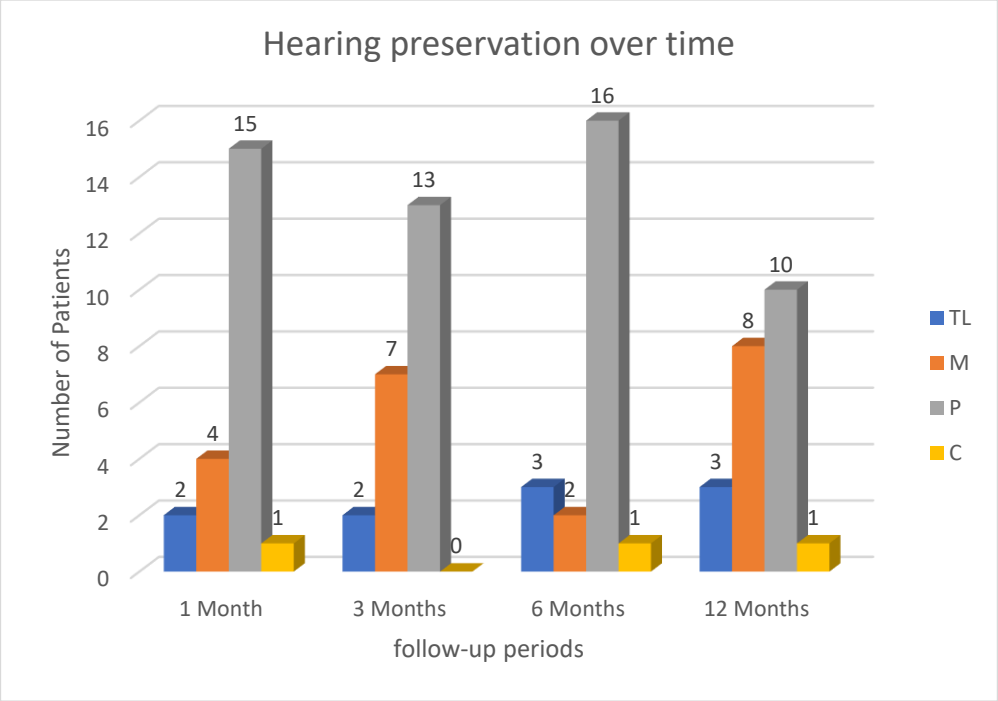

Figure 5-2 Results of HP over time
The classification method of Skarzynski (2013) was used to categorise the outcomes of hearing assessment into four levels: complete HP (C), partial HP (P), minimal HP (M) and total loss of hearing (TL).

Table 5-2 Descriptive statistics for level of HP (S value) for each surgical approach group

	Surgical Approach	Mean (S Value)	Std. Deviation	N
Percentage of HP 1 month postoperative	RW	30.37	21.69	12
	CY	54.77	24.06	10
	Total	41.46	25.48	22
Percentage of HP 3 months postoperative	RW	24.16	19.41	12
	CY	47.79	19.41	10
	Total	34.90	22.44	22
Percentage of HP 6 months postoperative	RW	29.60	20.17	12
	CY	41.77	22.64	10
	Total	35.13	21.71	22
Percentage of HP 12 months postoperative	RW	19.89	22.31	12
	CY	40.25	26.61	10
	Total	29.15	25.92	22

The results of the two-way mixed ANOVA showed that:

1. A significant effect existed of time of assessment on the level of HP ($F_{3,60}=3.66$, $P=0.017$, partial $\eta p2=0.155$).

2. No significant interaction existed between surgical approaches and the HP scores over time ($F_{3,60}=1.093$, $P=0.359$, partial $\eta p2=0.052$). Figure 5-3 shows the pattern of change in HP over time in both groups. The breakdown of conditions shows that at the 1-month follow-up, CY participants had greater HP (M=54.77, SD=24.05) than RW participants (M=30.37, SD=21.68); at the 3-month follow-up, CY participants had greater HP (M=47.79, SD=19.41) than RW participants (M=24.16, SD=19.41); at the 6-month follow-up, the level of HP of the RW group improved (M=29.60, SD=20.17) but was still not higher than the CY group (M=41.77, SD=22.64); and at the 12-month follow-up, the level of HP decreased in both groups, and CY participants still had greater HP (M=40.25, SD=26.61) than RW participants (M=19.89, SD=22.31).

3. In contrast, a significant main effect existed of the surgical approach on HP scores overall [$F (1, 20)=6.001$, $P=.0.024$, $\eta p2=.231$; Table 5-4].

Table 5-3 Results of mixed ANOVA, tests of within-subjects effects

Tests of Within-Subjects Effects

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HP Time	Sphericity Assumed	1711.27	3	570.42	3.66	.017	.155
	Greenhouse–Geisser	1711.27	2.39	716.29	3.66	.026	.155
	Huynh–Feldt	1711.27	2.87	596.07	3.66	.019	.155
	Lower-Bound	1711.27	1.00	1711.27	3.66	.070	.155
HP Time Surgical Approach	Sphericity Assumed	511.63	3	170.54	1.09	.359	.052
	Greenhouse–Geisser	511.63	2.39	214.16	1.09	.352	.052
	Huynh–Feldt	511.63	2.87	178.21	1.09	.358	.052
	Lower-Bound	511.63	1.00	511.63	1.09	.308	.052
Error (HP Time)	Sphericity Assumed	9358.41	60	155.97			
	Greenhouse–Geisser	9358.41	47.78	195.86			
	Huynh–Feldt	9358.41	57.42	162.99			
	Lower-Bound	9358.41	20.00	467.92			

Table 5-4 Results of mixed ANOVA, tests of between-subjects effects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	113586.55	1	113586.55	77.01	.000	.794
Surgical Approach	8850.66	1	8850.66	6.00	.024	.231
Error	29498.09	20	1474.90			

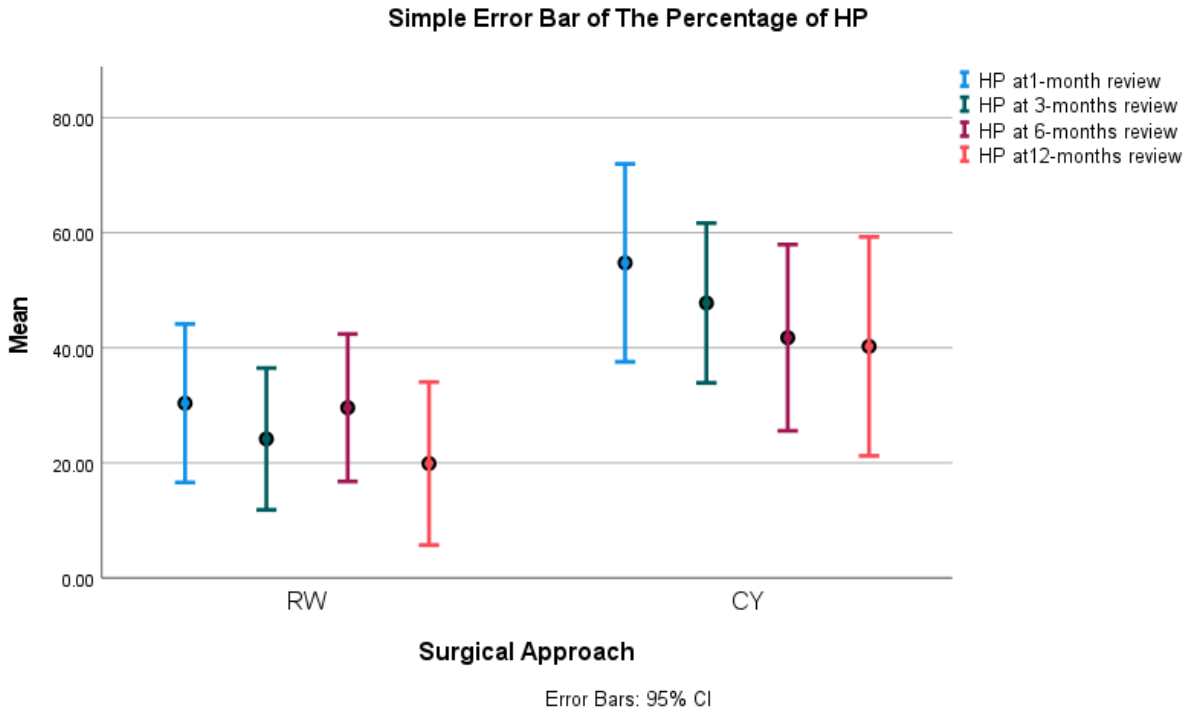

Figure 5-3 The means of HP over the time in both surgical groups.
The figures shows the error bars of the 95% confidence interval for the mean of unaided PTA in both groups at all four follow-up intervals

A two-sample t-test was used to determine the exact difference between both surgical approaches. The results showed that the mean HP scores of CY group were significantly higher at 1 month follow-up (t=-2.50, df=20, 95% CI: -44.75 to -4.05, two-tailed P=0.021), as well as at the 3-month follow-up (t=-2.84, df=20, 95% CI: -40.96 to -6.29, two-tailed P=0.01), but not at the 6-month follow-up (t=-1.33, df=20, 95% CI: -31.22 to 6.87, two-tailed P=0.197) or the 12-month follow-up (t=-1.95, df=20, 95% CI: -42.10 to 1.38, two-tailed P=0.065); see Table 5-5

Table 5-5 Two-sample t-test to determine exact differences between both surgical approaches

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-Tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Percentage of HP 1 month postoperative	Equal variances assumed	.000	.985	-2.50	20	.021	-24.40	9.76	-44.75	-4.05
	Equal variances not assumed			-2.48	18.410	.023	-24.40	9.85	-45.06	-3.73
Percentage of HP 3 months postoperative	Equal variances assumed	.031	.862	-2.84	20	.010	-23.63	8.31	-40.96	-6.29
	Equal variances not assumed			-2.84	19.288	.010	-23.63	8.31	-41.00	-6.25
Percentage of HP 6 months postoperative	Equal variances assumed	.001	.973	-1.33	20	.197	-12.18	9.13	-31.22	6.87
	Equal variances not assumed			-1.32	18.297	.203	-12.18	9.23	-31.54	7.19
Percentage of HP 12 months postoperative	Equal variances assumed	.038	.848	-1.95	20	.065	-20.36	10.42	-42.10	1.38
	Equal variances not assumed			-1.92	17.671	.071	-20.36	10.60	-42.65	1.94

Table 5-6 Independent Samples t-test Effect Sizes

			95% Confidence Interval	
		Standardizer[a]	Point Estimate	Lower	Upper
Percentage of HP 1-month post-operative	Cohen's d	22.78373	-1.071	-1.961	-.158
	Hedges' correction	23.68507	-1.030	-1.886	-.152
	Glass's delta	24.05662	-1.014	-1.951	-.035
Percentage of HP 3-months post-operative	Cohen's d	19.40858	-1.217	-2.124	-.286
	Hedges' correction	20.17640	-1.171	-2.043	-.275
	Glass's delta	19.41130	-1.217	-2.200	-.189
Percentage of HP 6-months post-operative	Cohen's d	21.31952	-.571	-1.422	.293
	Hedges' correction	22.16295	-.549	-1.368	.282
	Glass's delta	22.64042	-.538	-1.398	.350
Percentage of HP 12-months post-operative	Cohen's d	24.34156	-.836	-1.705	.051
	Hedges' correction	25.30454	-.805	-1.640	.049
	Glass's delta	26.61246	-.765	-1.656	.161

a. The denominator used in estimating the effect sizes.
Cohen's d uses the pooled standard deviation.
Hedges' correction uses the pooled standard deviation, plus a correction factor.
Glass's delta uses the sample standard deviation of the control group.

5.4.3 Speech perception

The speech test was performed at 6- and 12-month follow-up visits. The mean pre-operative BKB score of the whole sample was (M=31.73, SD=25.48). The mean pre-operative BKB score of the RW group (M=33.5, SD=27.36) was not significantly higher (t=0.14, df=20, 95% CI: -20.70 to 20.20, two-tailed P=0.89) than the CY group (M=32.00, SD=21.42). The mean BKB score of the RW group at 6 months (M=53.5, SD=35.85) was not significantly higher (t=0.40, df=20, 95% CI: -25.15 to 37.05, two-tailed P=0.69) than the CY group (M=47.55, SD=33.51). At the 12-month review, the RW group (M=66.04, SD=31.30) was also not significantly higher (t=0.20, df=20, 95% CI: -24.94 to 30.23, two-tailed P=0.84) than the CY group (M=63.40, SD=33.37); see Table 5-8. Figure 5-4 shows the 95% CI of the speech perception scores in both groups, which did not show any significance at both follow-up intervals.

Table 5-7 Mean and standard deviation of BKB scores for each surgical group at all reviews

	Surgical Approach	N	Mean	Std. Deviation	Std. Error Mean
Pre-operative BKB score	RW	12	33.50	27.358	7.90
	CY	10	32.00	21.42	6.80
BKB score at 6 months	RW	12	53.50	35.85	10.35
	CY	10	47.55	33.52	10.60
BKB score at 12 months	RW	12	66.04	31.30	9.04
	CY	10	63.40	30.38	9.61

RW= round window, CY= cochleostomy

Table 5-8 Results of independent-samples t-test of BKB speech perception test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Pre-operative BKB score	Equal variances assumed	1.27	.273	.141	20	.889	.889	1.50	-20.70	23.70
	Equal variances not assumed			.144	19.695	.887	.887	1.50	-20.21	23.70
BKB score at 6 months	Equal variances assumed	.346	.563	.399	20	.694	5.95	14.90	-25.15	37.05
	Equal variances not assumed			.402	19.695	.692	5.95	14.81	-24.98	36.88
BKB score at 12 months	Equal variances assumed	.134	.718	.200	20	.844	2.64	13.23	-24.94	30.23
	Equal variances not assumed			.201	19.489	.843	2.64	13.19	-24.91	30.20

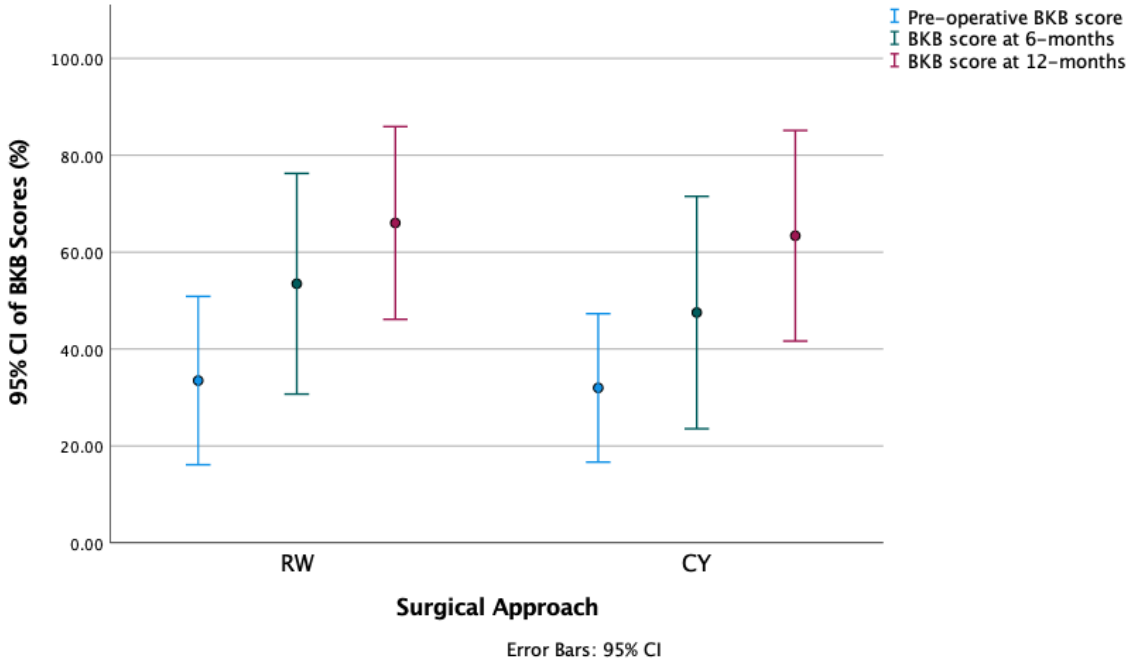

Figure 5-4 95% confidence intervals of speech perception mean scores in both groups.
RW= round window, CY= cochleostomy

5.4.4 **Radiology**

5.4.4.1 Accuracy of insertion (electrode scalar position)

The results of the CBCT showed all patients had full insertion, except for one patient who had one extra-cochlear electrode. The majority of patients (18 out of 22) had their electrode arrays placed correctly into the ST. Four of these 18 had some electrodes classified as possible scala tympani (PST). The remaining four patients of the 22 had some electrodes classified as possible scala vestibuli (PSV). One of these four had some channels classified as PST, and another one had some electrodes classified as definite electrode displacement into scala vestibuli (see Table 5-9 and Table 5-10).

The insertion accuracy was calculated based on the percentage of electrode contacts in each array that were DST in each patient. Since the accuracy of insertion was not normally distriputed, the Mann-Whitney test was utilised to evaluate the accuracy of electrode placement between both surgical approaches. The test revealed that the accuracy of electrode placement into the ST in the RW group was not significantly different from that of the CY group (U=42.00, z= -1.83 N1=12, N2=10, two-tailed P=0.169, r= -0.29).

Table 5-9 Number of patients in each classification category for the two surgical approaches.

	2=DST	1=PST	0=Uncertain	(-1) PSV	(-2) DSV	(-3) Extra-Cochlear	Total
RW	6 (50%)	3	0	3 (one repeated PST)	1 (and PSV)	1	12
CY	8 (80%)	1	0	1	0	0	10
Total	14 (63.63%)	4 (18.18%)	0	4 (18.18%)	1 (4.55%)	1 (4.55%)	

The five categories of electrode placement are: DST=electrodes inserted definitely into the ST, PST=possible scala tympani, PSV=possible scala vestibuli, DSV=definitely into the SV and extra-cochlear.

Table 5-10 Results of Mann–Whitney test assessing accuracy of insertion between both approaches

	Percentage of electrodes definitely at ST
Mann–Whitney U	42.00
Wilcoxon W	120.00
Z	-1.38
Asymp. Sig. (2-tailed)	.169
Exact Sig. [2*(1-tailed Sig.)]	.254[b]

a. Grouping variable: surgical approach.
b. Not corrected for ties.

5.4.4.2 Depth of insertion

This study included two types of electrode arrays: CO622/CO522 from Cochlear Corporation and SlimJ from Advanced Bionics. The mean linear depth of insertion for both devices was 21.87 mm (SD=2.08), ranging between 17.80 mm and 25.80 mm. The mean angular depth of insertion for both devices was 419.54 degrees (SD=46.85), ranging between 360° and 503°. No significant difference existed in the linear or angular depth of insertion between the two devices [(t= 0.14, df= 20, 95% CI: -1.78 to 2.03, P=0.89) and (t= -103, df=20, 95% CI= -44.98 to 40.74, P=0.92), respectively]. Table 5-11 shows the depth of insertion details of each device.

When comparing the linear depth of insertion between both surgical approaches, the mean depth of the CY group (M=22.57, SD=2.11) was not significantly different (t= -1.48, df=20, 95% CI: -3.09 to 0.522, two-tailed P=0.154) from the RW group (M=21.28, SD=1.95). Similarly, the mean angular depth of the CY group (M=434.10, SD=48.88) was not significantly different (t=-1.36, df=20, 95% CI: -67.71 to 14.34, two-tailed P=0.190) from the RW group (M=407.41, SD=43.37); see Table 5-13.

Table 5-11 The mean linear depth (mm) and angular depth (degrees) of insertion and standard deviation for both devices

	Device	N	Mean	Std. Deviation	Std. Error Mean
Angular depth of insertion (degrees)	AB	12	418.58	41.417	11.956
	CO	10	420.70	54.965	17.381
Linear depth of insertion (mm)	AB	12	21.9253	1.72849	.49897
	CO	10	21.8000	2.54165	.80374

Table 5-12 The mean and standard deviation of linear and angular insertion depth for both surgical approaches.

	Surgical Approach	N	Mean	Std. Deviation	Std. Error Mean
Angular depth of insertion (degrees)	RW	12	407.41	43.372	12.520
	CY	10	434.10	48.884	15.459
Linear depth of insertion (mm)	RW	12	21.2836	1.94990	.56289
	CY	10	22.5700	2.11453	.66867

Table 5-13 Result of independent sample t-test comparing angular and linear insertion depth between both approaches.

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-Tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Angular depth of insertion (degrees)	Equal variances assumed	.210	.652	-1.357	20	.190	-26.687	19.668	-67.713	14.340
	Equal variances not assumed			-1.342	18.254	.196	-26.687	19.893	-68.438	15.065
Linear depth of insertion (mm)	Equal variances assumed	.366	.552	-1.483	20	.154	-1.28637	.86733	-3.09558	.52285
	Equal variances not assumed			-1.472	18.623	.158	-1.28637	.87405	-3.11828	.54555

Table 5-14 Demographics and patient outcomes

No.	Demographics						
	Age	*Gender*	*Aetiology*	*Duration of deafness (y)*	*Ear*	*Surgical approach*	*Device*
1	44	F	Fever	39	Rt	RW	AB
2	44	F	Genetic	41	Lt	CY	AB
3	61	F	Unknown	33	Rt	RW	Co522
4	41	M	Unknown	35	Lt	RW	AB
5	65	F	Autoimmune	19	Lt	RW	AB
6	75	F	Unknown	40	Rt	CY	Co622
7	69	F	Unknown	28	Lt	RW	AB
8	56	M	Unknown	24	Lt	CY	Co622
9	32	M	Genetic	32	Rt	CY	Co522
10	69	F	Unknown	15	Rt	CY	AB
11	33	F	Autoimmune	33	Lt	CY	Co622
12	70	F	Unknown	40	Rt	RW	Co622
13	41	M	Genetic	39	Lt	RW	AB
14	71	F	Unknown	20	Rt	CY	AB
15	49	M	Genetic	41	Lt	RW	Co622
16	74	M	Genetic	65	Lt	CY	AB
17	83	M	Unknown	20	Lt	RW	Co622
18	28	M	Genetic	24	Lt	CY	AB
19	71	M	Genetic	31	Rt	CY	AB
20	54	F	Genetic	27	Rt	RW	Co622
21	71	M	Unknown	31	Lt	RW	Co622
22	73	F	Genetic	23	Rt	RW	AB
Mean	57.91	-	-	31.8	-	-	-
Std Dev.	±16.35	-	-	±10.88	-	-	-
	-	M=10 F=12	-		Rt.=10 Lt.=12	RW=12 CY=10	CO=10 AB=12
Total	-	22	-		22	22	22

M= male, F= female
Rt= right, Lt=left
RW= round window, CY= cochleostomy

Table 5-15 Cont. Demographics and patient outcomes

Electrode placement was assessed based on the number of electrodes in each scala (DST=definite scala tympani; PST=possible scala tympani; DSV=definite scala vestibuli; PSV=possible scala vestibuli). The HEARING group formula was used to calculate the percentage of HP (S%) and convert it into four categories; C=complete HP, P=partial HP, M=Minimal HP, TL=total loss of hearing.

No.	Insertion depth		Electrode placement								Speech perception (BKB)			HP (S value %, categorical)			
	Angular (degrees)	Linear (mm)	*2=DST*	*1=PST*	*0=uncertain*	*(-1) PSV*	*(-2) DSV*	*(-3) extra-cochlear*	*% of DST*	*% of possible ST/ SV*	*Pre-op (%)*	*6 months (%)*	*12 months (%)*	*1 month*	*3 months*	*6 months*	*12 months*
1	423	21	16	0	0	0	0	0	100	0.0	56	88	67	(44.44, P)	(22.22, M)	(55.56, P)	(55.6, p)
2	448	19.4	16	0	0	0	0	0	100	0.0	12	0	0	(37.04, P)	(29.63, P)	(29.63, P)	(40.7, P)
3	412	22.5	19	0	0	3	0	0	86.4	13.6	62	93	100	(54.00, P)	(62.00, P)	(48.00, P)	(40.0, P)
4	446	23	16	0	0	0	0	0	100	0.0	32	34	94	(0.00, TL)	(29.63, P)	(29.63, P)	(0.0, T)
5	417	22.2	15	1	0	0	0	0	93.8	6.3	6	78	96	(60.71, P)	(50.00, P)	(51.79, P)	(44.6, P)
6	408	23.8	22	0	0	0	0	0	100	0.0	12	35	54	(13.33, M)	(15.00, M)	(0.00, TL)	(3.3, M)
7	391	21	16	0	0	0	0	0	100	0.0	42	55	32	(36.67, P)	(18.33, M)	(23.33, M)	(1.7, M)
8	425	22.7	14	8	0	0	0	0	63.6	36.4	52	20	34	(62.75, P)	(39.22, P)	(41.18, P)	(2.0, M)
9	503	25.8	22	0	0	0	0	0	100	0.0	38	14	56	(34.62, P)	(46.15, P)	(34.62, P)	(23.1, M)
10	378	21.3	16	0	0	0	0	0	100	0.0	46	70	90	(72.22, P)	(74.44, P)	(84.44, C)	(84.4, C)
11	500	23.1	22	0	0	0	0	0	100	0.0	72	51	94	(60.00, P)	(65.00, P)	(34.92, P)	(37.5, P)
12	472	23	22	0	0	0	0	0	100	0.0	64	96	88	(18.52, M)	(0.00, TL)	(0.00, TL)	(7.4, M)
13	481	24.3	16	0	0	0	0	0	100	0.0	0	6	2	(53.66, P)	(43.90, P)	(48.78, P)	(53.7, P)
14	423	20.9	16	0	0	0	0	0	100	0.0	34	56	60	(70.67, P)	(69.33, P)	(66.67, P)	(66.7, P)
15	360	17.8	21	0	0	0	0	1	95.5	0.0	0	0	36	(18.52, M)	(18.52, M)	(25.93, P)	(11.1, M)
16	360	20	15	0	0	1	0	0	93.8	6.3	0	36	64	(106.67, C)	(60.00, P)	(33.30, P)	(33.3, P)
17	407	20.9	17	0	0	2	3	0	77.3	9.1	80	32	62	(0.00, TL)	(0.00, TL)	(0.00, TL)	(0.0, TL)
18	482	23.8	16	0	0	0	0	0	100	0.0	30	96	98	(48.44, P)	(48.44, P)	(53.13, P)	(50.0, P)
19	414	24.9	16	0	0	0	0	0	100	0.0	24	100	84	(48.72, P)	(30.77, P)	(35.42, P)	(61.5, P)
20	360	17.9	22	0	0	0	0	0	100	0.0	20	20	46	(28.99, P)	(5.80, M)	(2.90, M)	(2.9, M)
21	360	20.5	15	7	0	0	0	0	68.2	31.8	30	96	94	(5.56, M)	(22.22, M)	(38.89, P)	(0.0, TL)
22	360	21.3	4	11	0	1	0	0	25	75.0	10	44	76	(43.48, P)	(17.39, M)	(30.40, P)	(21.7, M)
Mean	419.54	21.86	-	-	-	-	-	-	-	-	32.81	50.80	64.84	41.46	34.90	35.13	29.15
Std Dev.	46.85	2.08	-	-	-	-	-	-	-	-	24.27	±34.12	±30.17	±25.48	±22.44	±21.71	±25.92
			No. of patients=22	No. of patients=4	No. of patients=0	No. of patients=4	No. of patients=1	No. of patients=1	No. of patients=14	No. of patients=7		-	-	-	-	-	-

5.5 Discussion

5.5.1 A brief summary of the results

This study aimed to evaluate which surgical approach was associated with better audiological and radiological outcomes. The audiological outcomes showed a better HP level in the CY group in the 1-, 3-, 6-, and 12-month follow-ups. This difference was statistically significant at the 1- and 3-month reviews. Regarding speech perception, the RW group scored higher, but this difference was not statistically significant. Radiological outcomes showed no statistically significant difference between both groups in the depth of insertion or accuracy of insertion into the ST.

5.5.2 Hearing preservation

Our findings indicate that the CY approach had superior HP at all follow-ups and that the difference was statistically significant at short-term follow-ups. These results are comparable to those of earlier systematic reviews and meta-analyses. Santa Maria et al. (2014) suggested the superiority of the CY approach, whereas Havenith et al. (2013) reported no significant difference, and Snels et al. (2019) reported no significant difference after 6 months. The findings of this study and previous systematic reviews are contradictory to current practice.

The early difference in the HP level may be attributable to the trajectory of the electrode array during the insertion procedure. The CY method provides a more direct route to the ST. When the electrode array is inserted through the RW approach, its trajectory is toward the modiolus, which raises the risk of intra-cochlear trauma (Clark et al., 1984). This finding has been reported since the early stages of cochlear implants. The practice of cochlear implant surgery has evolved over time. With the development of new, flexible, atraumatic arrays, the majority of research has demonstrated a considerable improvement in HP levels when using the RW approach, and despite the limited evidence, many surgeons have shifted their practice to RW (Santa Maria et al., 2014). The findings revealed that the level of HP deteriorated with time in both approaches, with the difference becoming insignificant at 6 months, which could be attributed to fibrosis and new bone formation (Nadol and Eddington, 2006, Li et al., 2007, Bas et al., 2012).

The surgical approach has been the topic of extensive debate in the scientific literature for a variety of reasons. Initially, the emphasis in the literature was on the outcome enhancement of the RW method. The homogeneity of electrode arrays was not accounted for in some comparisons between the two methods (Sun et al., 2015). Insufficient research has compared the two methods using the same contemporary electrode (Santa Maria et al., 2014). Additionally, substantial past research has examined the two approaches utilising CY when the RW is inaccessible (Arnoldner et al., 2010, Gstoettner et al., 2009).

Our study bridges the evidence gap in the literature and provides an unbiased comparison of the two techniques by considering the effect of other variables. This trial's preliminary results indicate that the CY group had a greater HP level in the short to medium term. These findings are interesting and suggest a new potential direction for contemporary surgical practice.

5.5.3 Speech

With regards to speech perception scores, our results show slightly better scores in the RW group, but this did not reach the level of significance at either the 6- or 12-month follow-ups. Our findings are in alignment with (Kang and Kim, 2013), who reported better speech performance in the RW group 12 months after the surgery, but it was not significantly different from the CY group. A recent double-blind randomised controlled trial conducted by Naderpour et al. (2020) compared the outcomes between both approaches in a paediatric population. This study's outcome measures did not include HP but rather "auditory performance" and "speech intelligibility". Within 12 months, they found no significant difference in the auditory performance scores between the two techniques. In addition, they observed that the mean speech intelligibility score was significantly higher in the RW group after 3, 6 and 9 months of assessment, but not at 12 months. Another recent RCT assessed speech and sound perception in children using a the same tool and found no significant difference between the two groups when assessed 6 months after surgery (Shishodia and Saurav, 2021).

Another study reported no significant difference between patients in both groups in tone, vowel, constant, disyllable and sentence perception 12 months after the surgery

(Cheng et al., 2018). Many other studies have reported no significant difference in speech perception between both approaches (Adunka et al., 2014, Demir et al., 2021, Rajput and Nilakantan, 2019, Cheng et al., 2018). However, Elafandi et al. (2020) reported significantly better speech perception scores in the RW groups in the long term (24–36 months post-implantation). Notably, that study used contour advanced electrode array and a CY approach in conditions of difficult visualisation. The long-term outcome is another aspect that needs to be addressed in future studies.

5.5.4 **Radiology**

5.5.4.1 Depth of insertion

Our findings reveal no statistically significant difference between the two surgical techniques in the linear or angular depth of insertion. Using CBCT scanning, Fan et al. (2018) observed no significant difference in the linear or angular depth of insertion between the two techniques, which is consistent with our findings. O'Connell et al. (2016a), Hassepass et al. (2015) and Wanna et al. (2015), among others, used lateral-wall arrays and reported comparable findings.

5.5.4.2 Accuracy of insertion (elctrode scalar position)

Intra-cochlear electrode trauma varies in its degree and sevesrity. Eshraghi et al. (2003) classified intracochlear trauma into four domains: (1) basilar membrane elevation, (2) rupture or disruption of the basilar membrane or spiral ligament, (3) electrode crossing from ST to SV and (4) fracture of the spiral lamina or modiolus or tearing of SV. Hoskison et al. (2017) conducted a systematic review to assess intra-cochlear trauma and reported that grade 3 was the only kind of trauma that had been reported by clinical radiological studies; histological studies are more capable of describing other grades of trauma. The assessment of electrode trauma in histological studies revealed that 65.4% of cases were in grade 3, whereas categories 1, 2 and 4 were seen in 11.5% each. Postoperative audiological changes could result from any kind of trauma.

In this trial, we used atraumatic electrode arrays, which resulted in no significant difference in intracochlear trauma between approaches. A recent study conducted by Fan et al. (2018) used a standard-length lateral-wall Med-EL array to compare electrode placement in 24 paediatric patients and reported no significant difference

between both approaches. Hoskison et al. (2017) reported in their systematic review that electrode trauma existed in 30% of CY candidates and 20% of RW candidates. However, they believed that this finding is limited because the majority of research (61.1%) reported electrode injuries without specifying the insertion method.

Another older retrospective study reported a higher chance of ST insertion in the RW group (Wanna et al., 2015). The limitation of these studies is the large difference in candidate numbers between both arms because they used CY only in challenging cases where the RW was not accessible. They used rotational CT scanning, which is less accurate than CBCT, and the latter publication used heterogeneous arrays (pre-curved, lateral-wall and mid-scala) from all three manufacturers.

The main limitation of previous studies is the bias of surgeon selection or RW orientation/ accessibility. Randomisation in this study overcomes this limitation, and that could be one of the reasons for our results being different. The ease of visualisation of the round window membrane (RWM) and its position, size, shape and orientation vary widely among patients, which remains a challenge for soft surgeries. Unfavourable RW conditions might influence the outcome of the surgery when using either approach (Zhou et al., 2014, Bae et al., 2019), and the severity of intra-cochlear trauma could be related to this. Many studies have been published about the feasibility of RW insertion in all patients, even in difficult visualisation conditions (Jwair et al., 2021, Stuermer et al., 2021, Al-Muhaimeed and Abdelwahed, 2015, Bae et al., 2019). Successful RW insertion does not mean smooth insertion, and it should not be an aim by itself (Bae et al., 2019). The desire to achieve a RW approach in conditions of difficult visualisation might lead to trauma to the corda tympani nerve or fallopian canal due to over-drilling to expose the RW (Jwair et al., 2021).

The CY procedure has been through many changes over time, and not all surgeons use the same approach or location of drilling. This should be considered when reading the literature. Moreover, this procedure might be affected by surgeons' skills, landmarks and the anatomy of the cochlea (Badr et al., 2018, Briggs et al., 2005). The most accurate location for CY is anterior-inferior to the RWM. The correct CY location in relation to the RW is critical to avoid SV insertion or any cochlear trauma.

The current practice uses CY in difficult conditions when RW is not feasible, which results in a higher chance of trauma. This may be one of the reasons that our results differ from those of earlier studies. Randomisation in this study eliminated the bias of the anatomy effect. These findings suggest that the insertion approach should not be generalised to all patients based on the surgeon's practice only. Moreover, the findings confirm and emphasise the importance of RW anatomy and orientation, as reported in previous studies (Pringle and Konieczny, 2021, Zhou et al., 2014). Previous research has examined the influence of the variety of RW anatomy and reported that CY and ERW are less traumatic when the RW anatomy is favourable (Zhou et al., 2014).

Guidelines are needed to determine the appropriate surgical approach based on the anatomical orientation of the cochlea and not on the possibility of RW insertion. The advantage and disadvantages of both approaches should be weighted to determine the optimal insertion route for each patient. Preoperative imaging and robotic insertion might help smoother insertion and better HP.

5.5.5 Strengths and limitations

To our knowledge, this is the first randomised double-blinded trial investigating the effect of the surgical approach in the adult population. The topic of HP is multifactorial and has many limitations in the literature. The design of this study helped to minimise bias and investigate the topic more accurately. This study had well-defined inclusion and exclusion criteria and a management protocol that was used with all patients. Randomising patients between approaches helped to remove the effects of surgeon selection and anatomical variation. This could be one of the reasons for our results being different from previous studies where CY was used only when RW was not achieved. Finally, this trial used CBCT, which is known for its high resolution and accuracy when identifying electrode placement.

This study has some limitations. First, it was interrupted by the COVID-19 pandemic, which resulted in very limited missing data, handled with multiple imputation. The original dataset was analysed and compared to the imputed dataset; the result did not show any difference in the level of significance of any of the objectives. Second, the findings of this study represent the preliminary outcomes only because it was possible to only recruit two thirds of the sample before being interrupted by COVID-19.

However, this trial is ongoing, and research continuation after COVID-19 will help us address this limitation.

5.5.6 Future direction

The fact that the CY approach resulted in better HP encourages further research. Additional research on radiological, histological and animal models could aid in gaining a deeper understanding of the topic. This trial led us towards optimising and redefining the soft-surgical approach. The future direction of this study if we performed it again would include a postoperative questionnaire to assess the degree of difficulty with the RW orientation and visualisation during surgery using the visibility classification method outlined by (Stuermer et al., 2021). This would allow us to correlate insertion difficulties with the accuracy of electrode placement and HP level. In addition, it would be interesting to compare the outcomes of unfavourable RW conditions between the extended RW, CY and RW approaches.

5.6 Conclusion

Randomisation in this trial overcame the limitation of unfavourable RW conditions and surgeon selection of the insertion approach. An electrode array could be inserted successfully with either surgical approach because no significant difference was found in electrode placement, depth of insertion or speech perception. The CY approach had better HP levels than the RW approach. This difference was noticed from the first follow-up. This could be related to the minor trauma resulting from the electrode trajectory towards the modiolus during RW insertion. Even though the CY approach had better initial HP, no significant difference existed between both approaches 6 months after the surgery. Long-term outcomes are essential to a complete understanding of the topic and will help us reach a clearer conclusion.

Chapter 6 : A randomised controlled trial evaluating the effect of depth of electrode array insertion and position on audiological outcomes: RCT part 2

The randomised controlled trial (RCT) are presented in two chapters: chapter 5 and chapter 6. The first part of the RCT (chapter 5) aimed to compare the outcomes of round window versus cochleostomy. This chapter presents the second part and aims to investigate the relationship between radiological (electrode position and insertion depth) and audiological (HP and speech perception) outcomes.

Abstract

Introduction

The relationship between of electrode array insertion depth, accuracy of array placement, and audiological outcomes remains an important research question. Despite the potential advantages of full cochlear coverage, the depth of insertion is debated in terms of hearing preservation (HP) surgery, speech perception, and intra-cochlear trauma. Surgeons face the dilemma of whether to have shallow insertion for possibly better HP or deeper insertion for better cochlear coverage. Most previous research investigated this question using electrodes of various lengths and addressed the influence of the electrode array more than the surgery itself.

Objective

This study aims to investigate the relationship between the depth of insertion, electrode array position in the cochlea, HP, and speech perception when using medium-length electrode arrays and soft cochlear implantation (CI) surgery.

Method

This prospective study recruited post-lingual CI candidates with moderate-length lateral-wall CI arrays (CI522/622 and AB SlimJ). HP was assessed at 1, 3, 6, and 12 months after surgery. Speech perception for all subjects was assessed at 6 and 12 months after surgery. Array position and insertion depth were assessed between 1 and 2 weeks after surgery using cone-beam computed tomography (CBCT). The position was classified into six categories: definite scala tympani (DST), possible scala tympani (PST), possible scala vestibuli (PSV), definite scala vestibuli (DSV), uncertain, and extra-cochlear.

Results

The study comprised 22 subjects: 10 males and 12 females. The mean age of the subjects was 57.91 years (SD=16.36). The mean angular depth of insertion is 419.54° (SD=46.85) (min=360°, max=503°), and the mean linear insertion depth was 21.87mm (2.08) (min=17.80 mm, max= 25.80 mm).

The results revealed seven cases with possible dislocation, one classified as DSV, and the other classified as PST or PSV. The only case with definite dislocation lost all residual hearing and had a below-average speech perception score. Statistical analysis revealed no significant correlation between the other degrees of trauma, speech perception, and HP.

Moreover, the statistical analysis revealed a positive, moderate correlation between the depth of insertion and the accuracy of insertion (proportion of electrodes DST); most patients with possible dislocation had a depth of insertion less than the mean. The statistical analysis revealed no significant correlation between the accuracy of insertion, HP, or speech perception score, and no significant correlation between the insertion depth, HP, or speech perception score.

Conclusion

Electrode dislocation between cochlear scalae has a negative effect on patient hearing outcomes; however, the effect of minor trauma is not clear. The standard soft surgical approach in this study limited the number of dislocated electrodes. The length of the electrode array and the depth of insertion should not be the main concerns of HP surgery if there is no forced insertion beyond the point of resistance. Further research is needed to investigate the relationship between the nature and severity of trauma on patient outcomes.

6.1 Introduction

Minimising intra-cochlear trauma is critical during cochlear implantation (CI) surgery, as it has been shown to correlate with better audiological outcomes and allows patients to benefit from future innovations (Gantz et al., 2005, Gfeller et al., 2006). Electrode array trauma has been classified into various degrees depending on the severity and nature of damage (Eshraghi et al., 2003), as explained in detail in the previous chapter (Section 5.4.4.1). Scalar electrode dislocation from the scala tympani (ST) to the scala vestibuli (SV) is the most common type of trauma in clinical studies, and it is considered one of the most damaging to residual hearing (RH) (O'Connell et al., 2016a, Wanna et al., 2015).

6.1.1 Trauma and CBCT

Advancements in radiological modalities allow for accurate assessment of electrode placement in vivo. Cone-beam computed tomography (CBCT) is a modern modality that has produced accurate results in many clinical studies. CBCT images are more precise than conventional CT scans regarding prediction of the location of electrode arrays in the cochlea (Saeed et al., 2014, Ruivo et al., 2009, Boyer et al., 2015). Histological studies remain the gold standard to assess less severe traumas; moreover, they are limited to anatomical findings. In contrast, radiological studies allow for correlation between radiological and audiological findings (speech perception and hearing preservation [HP]).

6.1.2 Radiological and audiological outcome correlations

Many factors play a role in electrode trauma and HP; depth of insertion is one of the debated factors. Previous studies have shown a positive correlation between the depth of insertion and increased risk of trauma, electrode dislocation, and loss of RH (Suhling et al., 2016, Jurawitz et al., 2014, Svrakic et al., 2016). In contrast, other studies have shown no significant correlation between the depth of insertion and HP (Nordfalk et al., 2016, Skarzynski et al., 2009, Erixon et al., 2012, Wanna et al., 2015). Many studies have investigated the relationship between depth of insertion and speech perception; however, the findings are inconsistent. Some studies found positive (O'Connell et al., 2016c, O'Connell et al., 2016a), negative (Finley et al., 2008), or no correlation (Holden et al., 2013, van der Marel et al., 2015, Kos et al.,

2005), and others suggested that deeper electrode insertion covers the low-frequency range, improves low-pitch sounds, and improves speech perception (Faulkner et al., 2006). Other studies reported apical-frequency pitch confusion (Gani et al., 2007) and reduced stimulation of the basal turn following over-insertion.

A recent meta-analysis published by Heutink et al. (2019) reported that the evidence supporting the positive influence of depth of insertion on speech perception was weak and that it was difficult to draw a conclusion on this relationship. According to Heutink et al. (2019), there are three main limitations of the existing literature: first is the variability between surgical protocols, as some studies tended to have a full insertion in all cases while others stopped at the first resistance point; second, most studies used electrodes of various lengths, which led to evaluation of the effect of the electrode rather than the surgery; and third, most studies reported only short-term outcomes. Short-term studies support the relationship more than long-term studies, which could be explained by neural plasticity. Insertion with long arrays helps match the tonotopic map of the cochlea and improve speech perception immediately after surgery (Hochmair et al., 2003), while in shorter-depth insertion, the brain requires time to adapt (Reiss et al., 2007).

The depth of insertion has been a concern for specialists and manufacturers for many years. All surgeries aim for full and smooth electrode array insertion into the ST. Many electrode arrays have been designed in various lengths to match the clinical needs of patients and to improve their outcomes; however, anatomical variation between patients remains a challenge. Pre-operative radiological assessment can help estimate the depth of the cochlear canal and aid in the selection of suitable electrodes. Unfortunately, electrode resistance can be experienced under many conditions: anatomical variations, narrowing of the cochlear canal, and ossification or buckling and bending of the electrode array. Electrode enforcement beyond the resistance point can lead to intra-cochlear trauma and affect patient outcomes (Adunka and Kiefer, 2006).

While implantation with longer arrays provides better coverage of the cochlea, it is associated with a higher risk of trauma. In contrast, implantation with very-short electrodes might show better HP but does not cover a sufficient area of the cochlea if the RH is lost in the future (Jurawitz et al., 2014). Atraumatic moderate-length lateral-wall (LW) electrode arrays are currently the most common arrays as they balance the risks and advantages in most cases. However, insertion depth still varies between patients for the previously mentioned reasons. The current study aims to investigate radiological and audiological outcomes when using a moderate-length LW electrode array, soft CI surgical approach, and not enforcing electrode insertion beyond the first point of resistance.

6.2 Objectives

This chapter aims to evaluate the relationship between HP, speech perception scores, and radiological findings, specifically the angular and linear depth of insertion and the accuracy of electrode placement.

Objectives:

1. To investigate the relationship between the insertion depth and the accuracy of electrode insertion into the ST (DST).
2. To investigate the relationship between the depth of insertion and BKB scores in quiet.
3. To investigate the relationship between the depth of insertion and the level of HP.
4. To investigate the relationship between the accuracy of electrode insertion into the ST (DST), the level of HP, and BKB scores in quiet.

6.3 Method

This study used the same methods and outcome measures as those used in the previous chapter (see Section 5.3).

6.4 Results

6.4.1 Demographics

The sample population of this chapter is the same as that of the previous chapter. The demographic characteristics were previously explained in the first part of the randomised control trial (Section 5.4.1).

6.4.2 The relationship between accuracy of electrode insertion and depth of insertion

All patients had full electrode insertion, except one. Seven out of the twenty-two patients had some degree of dislocation: one was classified as DSV, while the other six were classified as PST/PSV (Table 6-5). The mean angular depth of insertion was 419.54 ± 46.85°(range: 360–503°), while the mean linear depth of insertion was 21.86 ± 2.08 mm (range: 17.80–25.80 mm). The mean angular depth of insertion was 420.70° (SD=54.96) for Cochlear CO622/522 devices and 418.58° (SD=41.42) for Advanced Bionic SlimJ, while the mean linear depths were 21.80 mm (SD=2.54) and 21.92 mm (SD=1.73), respectively. The linear and angular insertion depths were not significantly different between electrodes ([(t= 0.14, df= 20, 95% CI: -1.78 to 2.03, P=0.89) and (t= -103, df=20, 95% CI= -44.98 to 40.74, P=0.92), respectively]. The difference in insertion depth between surgical approaches was not significant, as reported and discussed in the previous chapter.

The Shapiro–Wilk test was used to assess the normality of the data. As the data were nonparametric, Spearman's test was used to assess the correlations. The statistical analysis showed no significant correlation between the linear depth of insertion and the percentage of electrodes accurately inserted into the ST (rho = 0.317, df = 20, 95% CI [-0.13 - 0.66], p = 0.151). In contrast, the angular depth of insertion showed a significant moderate positive correlation with the accuracy of insertion (rho= 0.487, df= 20, 95% CI [0.07 – 0.76], p=0.022) (Table 6-1).

Table 6-1. Correlation between percentage of electrodeposition (DST) and depth of insertion.
The table shows a moderate positive correlation between the accuracy of insertion and angular depth.

			Angular depth of insertion (degree)	Linear depth of insertion (mm)
Spearman's rho	Percent of electrodes definitely at the ST	Correlation coefficient	.487*	.317
		Sig. (2-tailed)	.022	.151
		N	22	22

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

6.4.3 The relationship between depth of insertion and BKB scores

Speech perception was assessed post-operatively using the BKB test in quiet at two intervals. The first assessment took place at the 6-month follow-up, and the second assessment took place at 12-month follow-up. The mean BKB score was 50.8% (SD=34.11) at the 6-month and 64.84% (SD=30.20) at the 12-month follow-up. Data were assessed for normality using the Shapiro–Wilk test. As the data were parametric and normality distributed, the Pearson's correlation test was used. The results of Pearson's test showed that there was no significant relationship between the BKB scores at 6-month follow-up and linear depth of insertion (r=0.26, df= 20, p=0.25) or angular depth of insertion (r= -0.013, df=20, p=0.95). The 12-month follow-up scores showed no significant correlation with linear depth of insertion (r=0.26, df= 20, p=0.24) or angular depth of insertion (r= -0.004, df=20, p=0.98).

Table 6-2. Correlations between the depth of insertion and BKB scores.

		Angular depth of insertion (degree)	Linear depth of insertion (mm)
BKB score at 6 months	Pearson's correlation	-.013	.256
	Sig. (2-tailed)	.954	.250
	N	22	22
BKB score at 12 months	Pearson's correlation	-.004	.260
	Sig. (2-tailed)	.984	.242
	N	22	22

**. Correlation is significant at the 0.01 level (2-tailed).

6.4.4 The relationship between the depth of insertion and level of HP

HP was assessed at four intervals: 1-, 3-, 6-, and 12-months postoperatively. The formula described by Skarzynski was used to assess the level of HP, which ranged from 0 to 100. The means of HP of the 1-, 3-, 6-, and 12-month follow-up intervals were 41.46% (SD=25.48), 34.90% (SD=22.44), 35.13% (SD=21.71), and 29.15% (SD=25.92) respectively. Figure 5.2. in the previous chapter presents the HP level at

each follow-up. The Shapiro–Wilk test was used to assess the normality of the data, revealing normally distributed data. Because the data was parametric and normally distributed, Pearson's correlation test was used. The results of Pearson's correlation test showed that there was no significant correlation between angular depth of insertion and HP at 1-month follow-up (r= 0.003, df= 20, p=0.991), 3-month follow-up (rho= 0.23, df= 20, p=0.31), 6-month follow-up (rho= 0.068, df= 20, p=0.76), and 12-month follow-up (r= 0.19, df= 20, p=0.39).

In addition, no significant correlation was observed between linear depth of insertion and HP at 1-month follow-up (r= 0.05, df= 20, p=0.83), 3-month follow-up (r= 0.24, df= 20, p=0.28), 6-month follow-up (r= 0.13, df= 20, p=0.58), and 12-month follow-up (r= 0.19, df= 20, p=0.40).

Table 6-3. Correlation between depth of insertion and level of HP.

		Percentage of HP 1 month postoperatively	Percentage of HP 3 months postoperatively	Percentage of HP 6 months postoperatively	Percentage of HP 12 months postoperatively
Angular depth of insertion (degrees)	Pearson's correlation	.003	.228	.068	.192
	Sig. (2-tailed)	.991	.308	.763	.393
	N	22	22	22	22
Linear depth of insertion (mm)	Pearson's correlation	.049	.242	.126	.188
	Sig. (2-tailed)	.830	.278	.577	.402
	N	22	22	22	22

6.4.5 The relationship between the accuracy of electrode insertion into the scala tympani (DST), PTA scores, and BKB scores

The association between the accuracy of insertion (DST) and HP was examined. Spearman's test was the test of choice as the data were nonparametric. The results showed that there was no significant correlation between the percentage of electrodes accurately inserted into ST and HP at 1-month follow-up (rho= -0.034, df= 20, p=0.88), 3-month follow-up (rho= 0.1, df= 20, p=0.67), 6-month follow-up (rho= - 0.01, df= 20, p=0.98), and 12-month follow-up (rho= 0.37, df= 20, p=0.85).

The association between the accuracy of insertion (DST) and BKB was examined using Spearman's test. The results showed that there was no significant correlation between the percentage of electrodes accurately inserted into the ST and BKB scores at 6-month follow-up (rho= 0.014, df= 20, p=0.95) and 12-month follow-up (rho= - 0.16, df= 20, p=0.48).

Table 6-4. Correlations between the accuracy of insertion and the level of HP and BKB scores.

			Percentage of electrodes definitely at the ST	BKB score at 6 months	BKB score at 12 months	Percentage of HP 1 month postoperatively	Percentage of HP 3 months postoperative	Percentage of HP 6 months postoperative	Percentage of HP 12 months postoperative
Spearman's rho	Percentage of electrodes definitely at the ST	Correlation coefficient	1.000	.014	-.161	-.034	.097	-.007	.371
		Sig. (2-tailed)	.	.951	.475	.880	.668	.977	.089
		N	22	22	22	22	22	22	22

**. Correlation is significant at the 0.01 level (2-tailed).

6.5 Discussion

The depth of electrode array insertion remains a concern for CI surgeons; they must decide whether to choose longer electrode arrays with full coverage or shorter electrodes with shallower insertion and increase the possibility of HP (Dillon et al., 2019). This study aimed to establish whether differences in insertion depth influenced electrode location, speech perception, and HP when using homogeneous moderate-length electrode arrays. Moderate-length LW electrode arrays are currently the most common. This study used a soft surgical protocol in all cases. Electrode arrays were inserted fully or to the first point of resistance in all patients, which should be considered when interpreting our findings; forced insertion beyond this point could result in intra-cochlear trauma (Adunka and Kiefer, 2006).

All patients in our study had full insertion, except one, with one extra-cochlear electrode. Only one patient had electrode dislocation to the SV (classified as DSV), and six patients were classified as PST or PSV. The results did not show a significant correlation between depth of insertion and electrode dislocation, HP, or speech perception scores.

6.5.1 Depth of insertion and accuracy of insertion

The relationship between the angular depth and accuracy of insertion has been investigated in earlier studies. Our results showed a moderate positive correlation between the accuracy of electrode position and angular insertion depth. Most of the earlier studies that evaluated this correlation used a variety of electrode arrays, whereas we used homogeneous moderate-length electrode arrays. A study by (O'Connell et al., 2016b) used CI422 and CI512 and reported no significant relationship between angular depth of insertion and electrode location in either array.

Another study by (O'Connell et al., 2016a) used pre-curved and LW arrays from three manufacturers: MED-EL (ME), Advance Bionics (AB), and Cochlear Corporative (CO), and reported no correlation between depth and dislocation. Interestingly, they noted that patients with electrode dislocation lost their hearing and had shallower insertion

than other patients. O'Connell et al. (2016a) suggested that shallow insertion in these conditions could result from the resistance surgeons faced when the array deviated from the ST. The first point of resistance could be encountered at any stage of the insertion process, indicating possible trauma (Adunka and Kiefer, 2006). Another study by Wanna et al. (2015) used a variety of electrodes from Cochlea Corp., Advanced Bionics, and MED-EL, including LW, perimodiolar, and mid-scala devices. According to the study, the insertion depth of the seven implants with scalar excursion into the SV was shallower than the sample mean.

The observations reported by O'Connell et al. (2016a) and Wanna et al. (2015) support our findings. Exploration of the data showed that electrode displacement did not occur in any patients with deep angular insertion. Table 6-5 shows that all cases with possible dislocation did not have a deep angular insertion depth. Moreover, most of them (6 out of 7 patients) had a shorter angular depth of insertion than the mean of the whole sample (419.54°). Similarly, the only patient classified as DSV (patient no. 17) had a shallower angular insertion depth than the mean. This finding indicates that the first point of resistance could be encountered at any stage of the insertion process and that it indicates possible trauma. Enforcement of deeper insertion beyond the first point of resistance is correlated with a higher probability of electrode dislocation, as shown in previous studies (Adunka and Kiefer, 2006).

Controlled depth of insertion

Despite the positive effect of deep insertion and complete cochlear coverage (O'Connell et al., 2016a, Rivas et al., 2017), previous research has shown positive correlations between deep electrode insertion and intra-cochlear trauma (Finley et al., 2008, Adunka and Kiefer, 2006). Adunka and Kiefer (2006) reported a significant difference in the severity of trauma between cases of forced insertion versus soft insertion. The general correlation between depth of insertion and electrode dislocation might be inaccurate if insertion resistance is not controlled for. Many patients in our sample had deep insertion and did not have any degree of dislocation. Electrode resistance is critical when studying the depth of insertion and electrode location.

The perception of resistance during electrode insertion indicates possible trauma, which requires immediate termination of insertion. As shown in our results, application of a soft surgical approach has a positive influence on HP and minimises trauma. This observation may explain why only one out of the seven patients who had a possible trauma was classified as DSV. Moreover, patient no. 15, who had incomplete insertion, did not have any electrode displacement. This highlights that depth of insertion is not the main risk factor for intra-cochlear trauma; forcing the electrode array beyond the first point of resistance appears to be the main cause of trauma. Balance between electrode resistance and the insertion depth helps to achieve optimum outcomes.

Table 6-5. Insertion depth in patients with possible electrode displacement.

Pt. no.	ADI	LDI	Electrode type	No. of channels	% of DST	% of possible dislocation	Intra-cochlear classification (Number of electrodes)					
							(2) DST	(1) PST	(0) uncertain	(-1) PSV	(-2) DSV	(-3) extra-cochlear
3	412	22.5	Co622	22	86.4	13.6	*19*	-	-	3	-	-
5	417	22.2	AB	16	93.8	6.3	*15*	1	0	0	0	0
8	425	22.7	Co622	22	63.6	36.4	*14*	8	-	-	-	-
15	360	17.8	Co	22	95.45	-	*21*	-	-	-	-	1
16	360	20	AB	16	93.8	6.2	*15*	-	-	1	-	-
17	407	20.9	Co	22	77.3	9.1	*17*	-	-	2	3	-
21	360	20.5	Co	22	68.2	31.8	*15*	7	-	-	-	-
22	360	21.3	AB	16	25	75	4	11	1	-	-	-

ADI= angular depth of insertion, LDI= linear depth of insertion.
DST= definite scala tympani, PST= possible scala tympani, PSV= possible scala vestibuli, DSV= definite scala vestibuli.
Mean ADI of the whole sample= 419.54 ±46.85 degrees (min=360, max=503), and the mean LDI = 21.86 ± 2.08mm (min=17.80 mm, max= 25.80 mm).

6.5.2 Depth of insertion and hearing preservation

Most studies investigated depth of insertion using electrodes of various lengths. The findings of these studies were inconsistent; some reported better HP with shallower insertion (Suhling et al., 2016, Jurawitz et al., 2014, Svrakic et al., 2016), while others reported no correlation between depth of insertion and HP (Skarzynski et al., 2009, Erixon et al., 2012, Wanna et al., 2015, Nordfalk et al., 2016). A recent study conducted by Suhling et al. (2019) compared the level of HP among six electrode arrays from different manufacturers. They reported that HP was achieved with all electrodes; moreover, shorter arrays had better levels of HP. Interestingly, they noted variability in HP for the same length arrays from different manufacturers. This inconsistency could be related to variation between the types and lengths of electrode arrays and the surgical protocol of electrode insertion between studies. Moreover, the type and severity of intra-cochlear trauma might vary between patients and may thus influence HP.

This relationship was investigated in very few studies that used the same electrode. An early study by Erixon et al. (2012) investigated this relationship using Flex^{EAS24} for all patients, except one. The depth of insertion in this study ranged between 300° and 540° (17.4–28.5 mm) and no significant correlation was reported with the level of HP. In general, the level of HP is related to the incidence of trauma (Balkany et al., 2006). A temporal bone study conducted by Adunka and Kiefer (2006) could help us understand this relationship. This study used electrodes of the same length and investigated the effect of insertion depth on intra-cochlear trauma. The findings of the study suggested that the main reason for trauma was not the depth but rather forced insertion beyond the first point of resistance when aiming for deep insertion.

Our results showed that differences in the depth of insertion when employing a soft surgical protocol and limiting the insertion to the resistance point when using a moderate-length electrode did not affect audiological outcomes. Therefore, preserving RH should not be a concern when choosing the length of the electrode array. However, surgeons should not exceed the resistance point to minimise the possibility of intra-cochlear trauma and loss of RH.

6.5.3 Depth of insertion and BKB scores

Previous reports on the relationship between angular depth of insertion and speech perception are inconsistent (Chakravorti et al., 2019, Heutink et al., 2019). In their systematic review, Heutink et al. (2019) related these inconclusive results to the variations between electrode lengths and speech perception tests that were used in the literature. This limitation was overcome in our study. The use of homogenous electrode length minimised differences between patients and ruled out the effect of the electrode array. The results showed that small differences in the depth of insertion had no significant effect on speech perception at the 6-month or 12-month follow-up. However, forcing insertion beyond the resistance point could result in severe intra-cochlear trauma, as discussed earlier.

Heutink et al. (2019) conducted a systematic review to investigate the relationship between insertion depth and speech perception at or 1 year after surgery. The study reported that the body of existing evidence at the time did not support this relationship, as the level of the available evidence was weak and no randomised trials had investigated this topic. Moreover, they reported that the positive relationship between depth of insertion and speech perception was mainly in short-term studies. The relationship was supported by 40% of the short-term (less than 1 year) studies and only 17% of the long-term studies. Finally, the study mentioned that the main reason for differences in depth of insertion in the literature was variation in the lengths of the arrays used, rather than anatomical or surgical reasons.

Many studies evaluated the effect of insertion depth by comparing electrodes of various lengths. For example, Chakravorti et al. (2019) conducted a study investigating this relationship using a wide variety of pre-curved and LW arrays from the three manufacturers, CO, MD, and AB. The study used an algorithm to automate image analysis. They reported that better speech scores (BKB and CNC [consonant-nucleus-consonant]) were correlated with deeper insertion of the LW arrays. Moreover, pre-curved arrays produced better speech scores (CNC) with shallower insertion. The

main limitation of this study was that the testing interval was not consistent across patients, as it ranged between 2 months and 16 years.

O'Connell et al. (2016c) used LW arrays at three different lengths (MED-EL Flex28 [28 mm], MED-EL Flex24 [24 mm], and MED-EL Standard [31.5 mm]). The study reported better levels of speech perception in patients with deeper insertion 12 months post-surgery. Canfarotta et al. (2021) reported better CNC scores in patients implanted with longer MED-EL arrays (31.5 mm) than patients implanted with medium-length arrays (24 mm). Both studies reported a positive correlation between speech perception and longer electrode arrays. Due to the variation in the lengths of electrode arrays in these studies, their results cannot be generalised or compared to the results of our study, as they measured the effect of electrode array more than the surgery. Moreover, this positive outcomes might have been influenced by electrode separation, channel interaction, tonotopic organisation, or alignment with the spiral ganglions (Yukawa et al., 2004).

A study by Rivas et al. (2017) reported a positive correlation between the scores of speech perception and an increase in the depth of insertion up to 500°; deeper insertion beyond this point could not positively affect patient outcomes. The correlation between depth of insertion and speech perception remains challenging to address. Even though, based on our findings, we suggest that minimal differences in depth of insertion when using arrays with homogeneous length do not significantly influence audiological outcomes, deeper traumatic insertion beyond the resistance point could result in a negative effect.

Table 6-6. Audiological outcomes of patients with possible electrode dislocation.

Pt. no.	Angular depth	Linear depth	Electrode type	No. of channels	% of DST	% of possible dislocation	Electrode placement						BKB scores (%)		Percentage of hearing preservation (S value%, categorical)			
							(2) DST	(1) PST	(0)	(-1) PSV	(-2) DSV	(-3) extra-cochlear	6 months	12 months	1 months	3 months	6 months	12 months
3	412	22.5	Co622	22	86.4	13.6	19			3			93	100	(54.00, P)	(62.00, P)	(48.00, P)	(40.0, P)
5	417	22.2	AB	15	93.8	6.3	15	1					78	96	(60.71, P)	(50.00, P)	(51.79, P)	(44.6, P)
8	425	22.7	Co622	22	63.6	36.4	14	8					20	34	(62.75, P)	(39.22, P)	(41.18, P)	(2.0, M)
15	360	17.8	Co	22	95.45	-	21					1	0	36	(18.52, M)	(18.52, M)	(25.93, P)	(11.1, M)
16	360	20	AB	16	93.8	6.2	15			1			36	64	(106.67, C)	(60.00, P)	(33.30, P)	(33.3, P)
17	407	20.9	Co	22	77.3	9.1	17			2	3		32	62	(0.00, TL)	(0.00, TL)	(0.00, TL)	(0.0, TL)
21	360	20.5	Co	22	68.2	31.8	15	7					96	94	(5.56, M)	(22.22, M)	(38.89, P)	(0.0, TL)
22	360	21.3	AB	16	25	75	4	11	1				44	76	(43.48, P)	(17.39, M)	(30.40, P)	(21.7, M)

ADI= angular depth of insertion, LDI= linear depth of insertion
DST= definite scala tympani, PST= possible scala tympani, PSV= possible scala vestibuli, DSV= definite scala vestibuli
The HEARING group formula was used to calculate the percentage of HP (S%) and convert it into four categories; C=complete HP, P=partial HP, M=Minimal HP, TL=total loss of hearing.
Mean ADI of the whole sample = 419.54± 46.85 degrees, and mean LDI = 21.86± 2.08
The mean HP at: 1month= 41.46 ± 25.48%, 3 months= 34.90± 22.44%, 6 months= 35.13 ±21.71%, 12 months= 29.15 ±25.92%.
The mean BKB score at 6 months= 50.80 ±24.12%, 12 months= 64.84 ±30.17%

6.5.4 The accuracy of insertion and hearing preservation and BKB scores

The aim of electrode insertion in CI surgery is successful ST placement, especially in patients with RH. Electrode displacement from the ST to the SV indicates trauma and crossing through the basilar membrane (BM). Intra-cochlear trauma was classified by Eshraghi et al. (2003) into four degrees, as explained in the previous chapter (Section5.5.4.2). Electrode dislocation from the ST to the SV is considered severe trauma. The disruption caused by electrode displacement might traumatise the BM, Reissner's membrane, osseous spiral lamina, or spiral ligament (Eshraghi et al. (2003).

The results of this study revealed seven cases with possible trauma, six of which were classified as PSV/PST, which is less severe than electrode dislocation. Only one patient (no. 17) had definite dislocation and was classified as DSV; this patient lost all RH. The BKB scores of the same patient were 32% and 62% for the 6-month and 12-month follow-up, respectively. Other patients with less severe trauma, classified as (PSV/PST), did not significantly correlate with HP or BKB scores (Table 6-6).

6.5.4.1 Accuracy of insertion and hearing preservation

Morrel et al. (2020) reported findings that were in line with ours. They found that electrode dislocation had a negative impact on the level of HP at the low-frequency range but had no impact on speech perception scores. Moreover, Adunka et al. (2005), Boyer et al. (2015), O'Connell et al. (2016c), and Wanna et al. (2015) reported a significant relationship between ST placement and HP. Wanna et al.'s study reported that all patients with scalar dislocation lost all RH, and 43% of patients with full ST placement lost their RH after some time. This delayed loss of RH could be related to minor trauma that cannot easily be assessed in clinical studies (Hoskison et al., 2017). Other possible reasons for delayed loss of RH are fibrosis, ossification, and progression of the disease aetiology.

6.5.4.2 Accuracy of insertion and BKB scores

Regarding speech perception and electrode dislocation, previous studies showed that patients with full ST insertion performed better on speech perception tests than

patients with electrode displacement (O'Connell et al., 2016a, Finley et al., 2008, Holden et al., 2013). Our study had a single case of electrode dislocation, and the speech perception of this patient was just below the average of the whole sample at 6- and 12-month follow-up. In contrast, statistical analysis did not show a significant correlation when considering less severe degrees of trauma (PST and PSV). In line with this finding, a recent study published by Morrel et al. (2020) investigated this relationship and reported no significant correlation between speech perception and accuracy of insertion.

When comparing our findings with existing literature, it seems that the effect of confirmed electrode dislocation to the SV on the level of HP is clear; however, there is no clear correlation with other degrees of trauma. The inconsistencies observed in the literature might be related to the nature and severity of the intra-cochlear trauma, the number of dislocated or possibly dislocated electrodes, the affected parts of the cochlea, and the accuracy of the radiological devices used to assess electrode placement. Despite the advancement of radiological modalities, clinical assessment of minor trauma remains limited. The combination of clinical and histological studies in the form of post-mortem studies might help to reach to more accurate conclusion regarding this issue (O'Connell et al., 2016d).

6.5.5 Strength and limitation

The current study has many strengths. The main strength of this study was the prospective design that helped to control the effect of surgical protocol, electrode type, and medical regimen. Second, this study had a standardised surgical protocol that was applied equally in all patients. Third, this study used a soft surgical approach, aiming for fully atraumatic insertion in all patients, which aligned with current practices. Fourth, this study used homogenous, atraumatic LW electrodes, which excluded the influence of electrode arrays and increased the accuracy of the findings and their relevance to the surgical procedure and its impact on the insertion accuracy and depth between patients. Finally, this study used CBCT scans, which have very low artefacts and high accuracy compared with conventional CT scans.

The current study has several limitations. First, because of the soft surgery protocol and limiting the insertion to the first point of resistance, the incidence of intra-cochlear trauma was low. The lack of trauma and dislocated electrodes limited the analysis of correlations between variables. This is one of the main difficulties when studying this subject and more accurate results would require a larger sample size. Second, this study did not account for differences in coding strategies when analysing patient performance and BKB scores. The level of speech perception was measured at 6 and 12 months postoperatively to minimise the effect of mapping. At the assessment time, most maps were stable, and patients had adapted to them. Third, this study was interrupted by coronavirus disease 2019 (COVID-19), which restricted the sample size. This chapter shows the interim results of the study; the final results will be reported once the whole sample has been recruited. Moreover, the study was limited to a short- and mid-term duration of follow-up. Long-term duration remains an area of future research.

6.6 Conclusion

The results of this study concluded the effects of insertion depth and electrode position on patient outcomes when using moderate-length electrode arrays with soft CI surgery and limiting the insertion depth to the first point of resistance.

The application of soft surgery limits the severity of intra-cochlear trauma. The severity of intra-cochlear trauma varied between patients. The findings of this study suggest that electrode dislocation between the ST and the SV has a clear association with negative outcomes. Electrode dislocation to the SV was noted in one patient and led to total loss of RH and a below-average BKB score. No statistical significance was noted between less severe degrees of trauma (PST/PSV) and audiological outcomes. Studying the effect of the nature and severity of trauma is limited in clinical studies. Future histological studies are needed to explore the effect of this variable on patient outcomes in the form of clinical post-mortem studies.

No significant correlation was found between insertion depth and HP or BKB scores. Deep angular insertion did not increase the risk of electrode trauma. In contrast, most patients with possible electrode array dislocation (classified as PST/PSV) had a shallower depth of insertion than the mean of the whole sample. Therefore, the length

of the electrode array and the depth of insertion should not be the main concerns of HP surgery as long as there is no resistance during the insertion process.

Chapter 7 : General discussion and conclusion

The last chapter of this thesis provides a general discussion of the overall results.

7.1 General aims revisited

The main objective of the research carried out in this thesis was to evaluate the relationship between the surgical approach of electrode array insertion (RW versus CY) and HP. Furthermore, the relationship between HP and selected variables, including the cochlear size, electrode position, and angular and linear insertion depth was investigated. To achieve the goals of this thesis, four projects were conducted. Project 1 (Chaptr 2) was a systematic review of all available published data regarding HP in patients who had received modern atrumatic lateral-wall cochlear implant arrays. Project 2 (Chapter 3) was a retrospective study that investigated the relationship between electrode dislocation, cochlear size, insertion depth, surgical approach and HP. Project 3 (Chapter 4) was a survey that assessed the current surgical practice for HP among consultant cochlear implant surgeons in the United Kingdom. Project 4 (Chapter 5 and 6) was a randomised controlled clinical trial with two parts. The first part evaluated the effect of the surgical approach of electrode insertion (RW and CY) on the level of HP, speech perception, intra-cochlear electrode array placement, and insertion depth. The second part of the project investigated the relationship between radiological and audiological outcomes, which included angular insertion depth, electrode array placement, HP and speech perception.

7.2 Summary and general discussions of the systematic review (chapter 2)

The systematic review of published studies on HP in cochlear implants assesses and investigates the relationship between the surgical approach and HP in individuals implanted with modern atraumatic lateral-wall electrode arrays. The residual hearing preservation in cochlear implantation is multifactorial, and isolating the effect of all variables is difficult. Moreover, the reporting of some variables is lacking in the literature. We found a large amount of variation in HP definitions and the method of calculating HP, which is one of the main reasons for the conflicting findings in the literature. Two previous systematic reviews (Havenith et al., 2013, Causon et al., 2015) and two meta-analyses (Snels et al., 2019, Santa Maria et al., 2014) reviewed this subject and their findings were conflicting. The results of our systematic review

showed that HP could be achieved with both surgical approaches, and no superiority of either approach was noted. This finding aligns with Havenith et al. (2013) and Snels et al. (2019).

Most of the studies we examined showed the possibility of HP with both medium (20–25-mm) and long (>25-mm) electrode arrays with both approaches. Very few studies showed better HP with shorter electrodes. Most studies assessed the level of HP within the first 12 months postoperatively. The findings revealed that HP deteriorated over time, whilst some studies demonstrated good long-term stability. The studies that compared both surgical approaches used various follow-up intervals ranging between 1 and 12 months, and all of them reported no significant difference between both approaches.

One of the main limitations in the literature is the indication for each surgical approach. Apart from one study, all of the studies included in our analysis stated that the CY approach was used as an alternative if the RW was not feasible. The placement of the CY is determined in relation to the RW. Less favourable orientation of the RW might affect the accuracy of CY insertion. Therefore, the results of the CY approach might be skewed for that reason.

This review was important to identify the gaps in the literature and understand the reasons for debate, as well as to emphasise the need of designing a prospective study that can control the effect of most of the other variables.

7.3 Summary and general discussion of the retrospective study (chapter 3)

The second project was a retrospective cohort study that used the CBCT scan to assess the electrode position. This study aimed to compare the outcomes of both surgical approaches and investigate the relationship between the electrode position, cochlear size, insertion depth and HP. The study revealed a big difference between the patient populations of the two surgery groups, which may be attributable to the practice of some surgeons. For that reason, it was not possible to statistically compare the incidence of trauma or the level of HP between approaches. However, none among the CY group had electrode displacement. In comparison, 6/35 patients in the RW group had a possibility of displacement.

Most patients in our sample had complete HP, followed by partial HP and then minimal HP. The results showed a significant correlation of electrode position with the level of HP. The proportion of electrodes compressing or bulging the basilar membrane (classified as possible ST) appears to affect the level of HP. This suggests that trauma is not limited to electrode dislocation between scala, but that even minor trauma may affect HP. On the other hand, no correlation was found between the number of extra-cochlear electrodes and the level of HP.

The cochlear size can be determined based on the diameter of the basal turn and can be divided into three sizes. The assessment of cochlear size showed the majority of patients had small cochleae (59.4%), followed by medium (34.4%) and then large cochleae (6.3%). The correlation between cochlear size and angular insertion depth was statistically significant among individuals with full insertion but not among those with incomplete insertion. However, neither the cochlear size nor the insertion depth showed a significant correlation with electrode position. Although identifying the cochlear size is useful for predicting the cochlear duct length and insertion depth, this information is not sufficient to preserve residual hearing. Because achieving complete insertion is not possible in all cases, the resistance felt during insertion may terminate the procedure at any depth. Insertion beyond this point may cause trauma and residual hearing loss. In our cohort, insertion was terminated at the first point of resistance, and no trauma occurred.

Due to the large difference in group sizes, this study was unable to evaluate the effect of the surgical approach. The same issue was noted in many previous retrospective studies (Guimaraes et al., 2015, Lee et al., 2010a, Gstoettner et al., 2009, de Carvalho et al., 2013). This highlights the necessity of the third and fourth projects. A prospective randomised controlled trial is required to compare the two surgical methods. Additionally, it is essential to comprehend surgeons' perspectives on HP operations, particularly in the absence of standardised HP practice.

7.4 Summary and general discussion of the survey study (chapter 4)

The third project of this thesis was a survey study designed to analyse the contemporary surgical practice of HP in cochlear implant patients in the United

Kingdom. The survey was directed at all consultant cochlear implant surgeons working for the NHS in the United Kingdom. This survey's findings reflect the experience of the majority (68%) of cochlear surgeons in the United Kingdom, who work in 80% of all cochlear implant centres in the United Kingdom.

The last survey in the United Kingdom was conducted in (2003) by Gibbin et al. At that time, the CY approach was the preferred approach because it was regarded as less traumatic. Comparing our findings to those of the previous study, the practices of cochlear implant surgeons have evolved. The findings of our study showed that the majority of surgeons agreed to use the lateral-wall array in HP cases and to insert the electrode via the RW approach in all cases. The majority used an ERW or CY approach only if the RW was not readily accessible. Moreover, most surgeons in our study agreed to use corticosteroids and antibiotics in both standard and HP cases. Local corticosteroids were used by 69% of surgeons in HP cases and 41% of surgeons in standard cases.

The practice of surgeons in the United Kingdom is similar to that in the United States when it comes to electrode selection, the route of insertion and the usage of corticosteroids. Although the majority of surgeons agreed to use intra-operative corticosteroids and antibiotics for HP patients, variations exist in pre- and postoperative protocols, and post-operative audiological assessments. In addition, there is no consensus regarding the indications for attempted HP. This outcome is consistent with our systematic review and highlights the need for a standardised protocol for HP operations. Such a protocol would enable national and worldwide comparisons of outcomes across cochlear implant centres.

7.5 Summary and general discussion of the randomised controlled trial, Part 1 (chapter 5)

The fourth study was a double-blind randomised controlled trial. The initial objective of the randomised controlled trial was to compare the audiological and radiological outcomes of both surgical approach. The study included 22 participants who were randomly assigned to either surgical approaches. At all follow-ups, the CY group had a higher mean HP level than the RW group. During early follow-up (1 and 3 months), this difference was statistically significant. At late follow-ups, the levels of the CY group remained higher, although the differences were not statistically significant. The

trajectory of the electrode array when implanted using either strategy is a likely contributing factor to the change in HP. The CY technique provides linear access to the ST, whereas the RW route is more traumatic due to the electrode's trajectory toward the modiolus, which redirects the electrode. At a late stage, fibrosis and new bone formation, which may contribute to the decrease in the difference between the two groups.

The outcome of our study is comparable to early systematic reviews' findings. Santa Maria et al. (2014) suggested in their meta-analysis that the CY approach is a less traumatic insertion, and the findings of the systematic review conducted by Havenith et al. (2013) suggested no significant difference between both approaches. Several other studies found the opposite; however, the results of the majority of these studies are skewed because the CY technique was used in an unfavourable RW orientation or visibility, which increases the risk of trauma with either approach. The randomisation in our study overcomes this issue, which may explain our findings.

Regarding speech perception, the RW group scored slightly higher than the CY group, but the difference was not statistically significant. This finding is consistent with the conclusions of two recent randomised controlled trials in paediatric populations (Naderpour et al., 2020, Shishodia and Saurav, 2021). Finally, the insertion depth and the accuracy of electrode placement were assessed and compared between approaches, and no significant differences were found. Therefore, both approaches provide sufficient coverage for the cochlea and are sufficiently effective in enhancing patients' abilities. Finally, deterioration in HP levels over time was observed in both groups, which necessitates additional investigation into the long-term outcomes and residual hearing stability.

7.6 Summary and general discussion of the randomised controlled trial, part 2 (chapter 6)

The second part of the trial aimed to investigate the correlations between the radiological (insertion depth and the accuracy of electrode placenet) and audiological (HP and speech perception scores) outcomes. This study used homogeneous atraumatic lateral-wall arrays of similar length. The electrode position was assessed in all cases and revealed one case with definite electrode dislocation to the SV who lost all residual hearing and had BKB score just below the average of the whole

sample. All the other cases had ST insertion, but seven had some electrodes classified as PST or PSV. No significant correlation was found between the electrode position of minor truamas (PST and PSV), HP and BKB score.

Even though the radiological pictures of this investigation and the retrospective analysis were evaluated by the same expert physicians using the same methodology, their findings are different concerning minor trauma and HP. Identifying the electrode position cannot explain exactly what happens at the histological level. The severity of cochlear trauma was classified in early histological studies (Eshraghi et al., 2003), and the severity of electrode trauma indicates the patient's outcome. Electrode dislocation is considered a severe trauma and leads to the loss of residual hearing. Although patients seem to have the same electrodes at the same position on the images, we do not know precisely what happens at the histological level, which may involve disruption of the scale media or bulging or tearing of the basilar membrane. Histological studies continue to be the gold standard for assessing trauma, despite their limitations and inability to include clinical findings. Future research may involve post-mortem examinations to help us gain a greater understanding of the relationship between the severity of trauma and audiological outcomes.

Morover, our results showed a significant negative relationship existed between the accuracy of electrode position and angular insertion depth. All cases involving electrode dislocation had a shallower insertion depth than the mean. In this study, insertion was halted at the first spot of resistance. Therefore, shallow insertion may result in electrode resistance conditions. This finding is comparable to prior research; O'Connell et al. (2016a) and Wanna et al. (2015) observed that electrode dislocation occurred in patients whose insertion depth was shorter than the sample mean. As per prior studies, electrode resistance may indicate trauma (Adunka and Kiefer, 2006). Fortunately, the majority of patients in our study did not exhibit definite scalar distortion because the insertion procedure was terminated at the first site of resistance, but they did have some electrodes classified as PST or PSV. We anticipate dislocation if the array was forced deeper into the cochlea. On the other hand, many patients in our sample had deep insertion without dislocation. Therefore, insertion resistance is a critical variable when examining the insertion depth and electrode position, and should be considered carefully when using cochlear duct length as guidance.

No significant correlation existed between insertion depth and HP. The majority of research examining the association between insertion depth and HP has used electrodes of varying lengths, and their results are controversial among those who support the relationship (Suhling et al., 2016, Jurawitz et al., 2014, Svrakic et al., 2016) and those who indicate no relationship (Skarzynski et al., 2009, Erixon et al., 2012, Wanna et al., 2015, Nordfalk et al., 2016). HP could be affected by variations in electrode type, length and surgical technique, which vary between these studies. In addition, the type and severity of trauma might vary among patients, as does its effect on HP. On the other hand, some research that studied this relationship and employed homogenous electrodes showed no significant difference (Erixon et al., 2012). In general, HP is associated with the incidence of trauma (Balkany et al., 2006), and we think that deep insertion does not necessarily result in trauma and loss of residual hearing (Adunka and Kiefer, 2006).

Similarly, no significant correlation was found between the insertion depth and speech perception scores. Our findings are comparable to the conclusion of a recent systematic review by Heutink et al. (2019). The authors concluded that the available evidence does not support this relationship. Furthermore, they found that variations in electrode types and lengths, and not anatomical or surgical variances, account for the majority of disparities in the literature regarding insertion depth. Therefore, the positive correlation in some earlier studies might be attributable to electrode separation and channel interaction, the tonotopic organisation, and alignment with spiral ganglions (Yukawa et al., 2004). However, in our study, we measured speech perception scores when using homogeneous electrodes, which resulted in less prominent differences in insertion depth between patients.

Variability between electrode types and lengths appears to be one of the limitations of the literature when correlating insertion depth and audiological outcomes. This study overcame this limitation by controlling the type of electrode. Therefore, our results showed that the depth of insertion had no effect on HP and speech perception when using an atraumatic lateral-wall electrode array with a moderate length and using a soft-surgical protocol where the insertion was limited to the resistance point. Future studies are required to examine these correlations utilising electrode arrays with longer lengths.

7.7 Conclusion

This thesis investigated the impact of surgical procedures on HP. Cochlear implant practice has undergone numerous modifications. Very few CY cases have been reported in recent medical literature, making comparison difficult. The majority of surgeons in the United Kingdom currently employ the RW technique as the standard procedure and the CY approach as an alternative, which is a significant limitation of retrospective investigations. The results of the randomised controlled study presented in this thesis showed that the CY approach gave significantly superior HP in the short term, however no significant difference was observed in HP or BKB scores at 6 and 12 months' follow-up. These results give the surgeons the confidence to switch to a CY approach when RW access is difficult. The depth of insertion should not be the main concern when preserving hearing. However, the resistance felt during the insertion process should be considered carefully because it may indicate trauma. Finally, national and international evidence-based guidelines are needed to standardise the practice of HP surgeries and ensure the quality of cochlear implant surgery. Future research collaborations between surgeons and researchers, coordinated by the BCIG, will help in achieving this objective.

Chapter 8 : Strengths and limitations

This chapter highlights the strengths and limitations of this body of work.

Each chapter of this thesis discusses the strengths and limitations of each project. Overall, this thesis tried to study the impact of the surgical approach (RW versus CY) while controlling other variables. Conducting the systematic review gave us a broad understanding of the limitations in the current literature and helped us to design our protocol for the prospective trial. The strengths of the systematic review are that it covered all published literature in English between 1980 and 2017, and the investigation exclusively considered the outcomes of the modern atruamtic lateral-wall electrode arrays, which are the most widely used electrodes and relevant to current practice.

The survey study helped us to bridge the gap in our knowledge about this topic and consider the opinions and practices of cochlear implant surgeons in the United Kingdom. The strength of this survey comes from its target group because it was directed only to cochlear implant consultant surgeons. Previous surveys included the opinions of trainees and consultants. In addition, our survey had a high response rate (68% of surgeons and 80% of centres), so it represents the general practice in the United Kingdom.

In this thesis, both retrospective and prospective research investigated electrode conditions using CBCT scanning, one of the most precise radiological modalities. Moreover, our investigations had excellent control over the electrode type since all of the electrodes included in these studies were atraumatic lateral-wall electrodes of moderate length. Our prospective study is the first randomised controlled trial to investigate this topic in the adult population. As discussed in the systematic review, most published literature had a retrospective design and limitations related to the control of confounding factors. In our double-blinded randomised controlled trial, we had a well-established protocol to assure equal management of all candidates and eliminate the effect of other variables. Therefore, this study has a high level of

evidence and provides novel findings, revealing that the HP outcomes of both approaches are comparable.

Although the study had a sample power calculation, it was not possible to recruit the whole sample due to the COVID-19 pandemic and the timeframe of my research. The study has resumed, and the final result will be published at the end. Other limitations of this study include some missing data because some patients could not attend some of their appointments during COVID-19. This study had multiple assessment intervals to assess change over time, but it was limited to short- to midterm findings (1–12 months). Lastly, the speech discrimination test in our study was conducted only in quiet because it covered the first year of rehabilitation. Speech in noise has to be considered in the future as it represents patients' ability to discriminate speech in difficult conditions.

Chapter 9 : Implications and future research direction

This chapter will discuss some implications and future research directions. Several implications for the research community and policymakers can be derived from the studies presented in this thesis. First, the practice of HP cochlear implantation surgery involves multiple variables that may affect patient outcomes, yet no standard protocol exists for conducting this surgery. The importance of this point increased with the easing of candidacy criteria, which increased the number of patients with significant residual hearing. This thesis began the process of standardising this procedure by illustrating the current practice, including electrode selection, surgical steps, medical regimens and audiological follow-ups. Standardising this procedure will enhance cochlear implant results, patient experience and device benefit.

Second, this thesis proposes a re-evaluation of the standard surgical procedure, in which the RW is performed as the standard approach and CY as an alternative. There is a need for an attempt to identify the optimal surgical approach for each patient. If this study were repeated, I would include a surgical questionnaire to determine the RW's visibility, orientation and accessibility. Afterwards, when employing either the RW or CY technique, a correlation between these variables and the level of HP must be determined. Third, the insertion force must be considered more carefully. Human hands are limited to sensing minor degrees of resistance. Therefore, future research needs to focus on an automated insertion device with a force sensor. Force sensors are able to measure contact forces below the rupture threshold of the cochlea's internal structure. This device could aid in terminating the insertion at the point of resistance, preserving more hearing.

Some aspects were limited in this thesis and need to be explored in future research. Future studies may explore HP in larger sample sizes and different age groups, considering that the majority of cochlear implant recipients are young and may require multiple implants in their lifetimes. Future research on HP must incorporate long-term follow-ups. Longitudinal studies are needed to evaluate the stability of HP, provide a deeper understanding and determine the superior approach. In addition, the long-term preservation of intra-cochlear structures allows patients to benefit from future therapeutic advancements. The postoperative practice of audiology for cochlear implant patients with preserved hearing is yet another area of research. Future

research should also investigate the practical benefits of hearing protection, such as hearing in noise and music appreciation.

Appendixes

Appendix 1 : Data base search strategy and MeSH terms

1. exp Cochlear Implants/
2. exp Cochlear Implantation/
3. (cochlea$ adj2 implant$).mp. [mp=title, abstract, original title, name of substance word, subject heading word,
keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier,
synonyms]
4. (cochlea$ adj2 prosthe$).mp. [mp=title, abstract, original title, name of substance word, subject heading word,
keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier,
synonyms]
5. 1 or 2 or 3 or 4
6. exp Round Window, Ear/
7. (round adj2 window).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword
heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8. 6 or 7
9. cochleostom$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading
word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
10. 5 and 8
11. 9 and 10
12. preserv$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading
word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
13. residual$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading
word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
14. 12 or 13
15. 11 and 14

Appendix 2: PICOS criteria for the systematic review

Inclusion and exclusion criteria were defined as follows:

- **Participants:** Cochlear implant patients of any age.

- **Intervention(s):** Cochlear implant surgery that aimed for hearing preservation and used modern atraumatic lateral-wall electrodes. The length of these electrodes has to be > 20 mm

- **Comparator(s)/Control:** Comparing the outcomes of cases with the round window insertion versus cochleostomy insertion.

- **Outcome(s):** The level of hearing preservation

- **S (Study Design):** Randomised and non-randomised studies, repeated measures, case reports, or cohort studies.

Appendix 3 Downs and Black Article Appraisal Tool

Table 1
Level of quality (excellent (26–28); good (20–25); fair (15–19); and poor (≤14))

Study	Score	Level of Quality	Study	Score	Level of Quality
(Adunka et al., 2013)	21	good	**(Erixon et al, 2015)**	19	fair
(de Carvalho et al., 2013)	16	fair	**(Fischer et al, 2015)**	14	Poor
(Erixon et al., 2012)	21	good	**(Hassepass et al., 2015)**	23	good
(Gstoettner et al., 2009)	16	fair	**(Helbig et al., 2011)**	18	fair
(Lee et al., 2010)	17	fair	**(Moteki et al., 2016)**	15	fair
(Brown et al., 2015)	15	fair	**(Santa Maria et al., 2013)**	21	good
(Mahmoud et al., 2014)	20	good	**(Skarzynski et al., 2014)**	15	fair
(Usami et al., 2011)	15	fair	**(Skarzynski et al., 2016)**	19	fair
(Usami et al., 2014)	17	fair	**(Suhling, et al., 2016)**	19	fair
(Radeloff et al., 2012)	14	Poor	**(Sun et al., 2015)**	21	good
(Arnoldner et al., 2010)	15	fair	**(Bruce, et al., 2011)**	16	fair
(Guimaraes et al., 2015)	21	good	**(adunka et al., 2014)**	18	fair
(Bruce et al., 2014)	19	fair			

Appendix 4 The questionnaire of the survey study

Survey of Cochlear Implants Surgical practice for hearing preservation in the UK

We are conducting a survey to understand the current surgical practice of CI in the UK.
This survey is to be completed by consultant surgeons.
Answers to this questionnaire should reflect personal practice and not your team/centre.
Your response is invaluable in helping us complete this research.

Definitions:

- Standard cases: any patients for cochlear implantation with definable / measurable air conduction hearing threshold on pure tone audiometry
- HP case/ EAS case: any patients with substantial amount of residual hearing and planned EAS cochlear implantation.

1. Duration of clinical practice in the cochlear implant field as consultant surgeon
   a. 1-5 years
   b. 6-10 years
   c. 11-15 years
   d. 16-20 years
   e. >20 years

2. When do you try to preserve residual hearing by using a hearing preservation protocol which might include certain devices, corticosteroids, antibiotics, hyaluronic acid or surgical technique?
   a. Normal to mild hearing loss at low frequencies (125Hz-1000Hz).
   b. Hearing threshold better than 60dB at any of low frequency rage (125Hz-1000Hz).
   c. Any measurable hearing.

Device selection:

1. Which electrode array do you routinely use for hearing preservation (HP) surgery?
   a. Hybrid electrode.
   b. Conventional length electrode, same length for all patients.
   c. Conventional length electrode, length determined by imaging findings.
   d. Conventional length electrode, length determined by preoperative hearing thresholds.

2. Which manufacturer do you prefer for hearing preservation (HP) cases? (Select one or more)
   a. Advanced Bionic.
   b. Cochlear Corp.
   c. MED-EL GmbH.
   d. Oticon
   e. No preference.

3. Which electrode array do you routinely use for standard cases?
   a. Lateral (straight) wall electrode
   b. Pre-curved electrode

4. Which electrode array do you routinely use for hearing preservation (HP) surgery?
   a. Lateral (straight) wall electrode
   b. Pre-curved electrode

Surgery

5. Corticosteroid regimen for standard cases? (Select one or more)
    a. Pre-operative Oral
    b. Pre-operative IV
    c. Intra-operative IV
    d. Intra-operative local
    e. Post-operative Oral
    f. None

6. Corticosteroid regimen for HP cases? (Select one or more)
    a. Pre-operative Oral
    b. Pre-operative IV
    c. Intra-operative IV
    d. Intra-operative local
    e. Post-operative Oral
    f. None

7. Antibiotic regimen for Standard cases? (Select one or more)
    a. Intra-operative IV
    b. Post-operative Oral
    c. Post-operative IV
    d. None
    e. Depends on the case.

8. Antibiotic regimen for HP cases? (Select one or more)
    f. Intra-operative IV
    g. Post-operative Oral
    h. Post-operative IV
    i. None
    j. Depends on the case.

9. Do you use Hyaluronic acid (Healon)?
    a. Yes, for all cases.
    b. Only HP cases.
    c. Only standard cases.
    d. No.

10. The speed of electrode insertion for standard cases?
    a. Less than 30 sec
    b. More than 30-60 sec
    c. More than 1 min.

11. The speed of electrode insertion for HP cases?
    a. Less than 30 sec
    b. Between 30-60 sec.
    c. More than 1 min.

Surgical approach of electrode insertion

12. Which surgical approach do you routinely use for electrode insertion for standard cases? (Select one or more)
    a. Round Window (RW)
    b. Extended round window (ERW)
    c. Cochleostomy (CY)

13. Which surgical approach do you prefer for HP?
    a. Round Window (RW)
    b. Extended round window (ERW)
    c. Cochleostomy (CY)

14. Do you use ERW or CY approach only if RW approach is not possible?
    a. Yes
    b. No

15. Which sentence describes your technique when drilling a cochleostomy
    a. Drill all the way to the cochlear duct
    b. Drill the bone only and use a hook or needle to open the membranous labyrinth.

16. How do you seal cochleostomy?
    a. Soft tissue (muscle or fascia).
    b. Fibrin glue.
    c. Either A or B.
    d. A and B
    e. No sealing

17. How do you seal the round window?
    f. Soft tissue (muscle or fascia).
    g. Fibrin glue.
    h. Either A or B.
    i. A and B
    j. No sealing

Audiology evaluation:

18. Do you use any kind of intraoperative monitoring (AIM/ECohG)?
    e. Yes
    f. No

19. Routine unaided post-operative PTA?
    a. Yes, for all patients.
    b. Just for EAS
    c. For any patient with residual hearing.

20. Timing of unaided post-operative assessment?
    a. Only once post-operative
    b. Every 3 months
    c. Every 6 months
    d. Every 12 months
    e. Every visit to the audiology clinic

21. Additional comments (optional free text)

Appendix 5 Participant consent form for the RCT

CENTRE FOR AUDITORY RESEARCH,
UCL EAR INSTITUTE
332, Gray's Inn Rd London WC1X 8EE UK
Tel: 020 7679 8983
Fax: 020 7679 8990

University College London Hospitals NHS
NHS Foundation Trust

PARTICIPANT CONSENT FORM

Title of Project:
Round window versus cochleostomy electrode array insertion with lateral wall atraumatic electrode: a prospective randomised clinical study
Chief Investigator: Prof Shakeel Saeed (UCL)
PhD researcher: Ibrahim Busaad (UCL)

	Initials
1. I confirm that I have read and understand the information sheet dated 2/05/2018 (Version 2) for the above study and have had the opportunity to ask questions.	☐
2. I understand that I can refuse to enter the study, without giving any reason and without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from UCL Ear Institute, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I am happy to enter the study and be randomised to which surgical technique I undergo during surgery. I understand all data will be collected anonymously.	☐
5. I am happy to be part of the study.	☐

_____	_____	
Name of Patient	Date	Signature
_____	_____	
Name of Person taking consent	Date	Signature

Appendix 6 Participant information sheet for the RCT

CENTRE FOR AUDITORY RESEARCH,
UCL EAR INSTITUTE
332, Gray's Inn Rd London WC1X 8EE UK
Tel: 020 7679 8983
Fax: 020 7679 8990

PARTICIPANT INFORMATION SHEET.....VERSION 2 (2/05/2018)

Title of Project:

Round window versus cochleostomy electrode array insertion with lateral wall atraumatic electrode: a prospective randomised clinical study

Dear Madam/Sir

You are invited to participate in a research project being conducted by NHS and sponsored by University College London (UCL). This information sheet describes the project. Please read this sheet carefully and be confident that you understand its contents before deciding whether to participate. If you have any questions about the project, please ask us (see contact details below).

Your participation will be a valuable addition to our research and very useful to those people who work in the field of cochlear implants.

What is the project about?
As a routine part of cochlear implantation, a hole is made in the hearing organ (cochlea) to insert the cochlear implant. There is considerable debate about where the best place in the ear is to make this hole, in the round window (a natural opening in the cochlear) or near to the round window (cochleostomy). Both approaches are routinely used across the world in cochlear implant centres. We are conducting a study to determine which of these places is best to keep as much of the remaining 'natural' hearing as possible when having a cochlear implant.

What is the purpose of the study?

A cochlear implant is a device that is inserted into the cochlea (the hearing organ) to stimulate it electrically and provide the sensation of sound. It is used in people who have severe hearing loss at higher frequencies. Higher frequencies tend to be important for hearing speech. Some people with hearing loss like this still have lots of hearing at lower frequencies. This can be very important, particularly with things like hearing music. The

question we want to answer is how can we do a cochlear implant operation while keeping as much of the low frequency hearing as possible.

The two ways that cochlear implants are put into the inner ear are called ‘round window’ and ‘cochleostomy’. A ‘round window’ insertion involves drilling around a soft opening of the cochlea and then opening this soft area. It has the advantage of going into what is almost a ‘natural opening’ in the ear. However, it can be difficult to reach, and it might be that by changing the ‘natural opening’ of the ear, we also change the way sound works in the ear.

A ‘cochleostomy’ involves using a small drill to make a hole in the side of the cochlea, and placing the cochlea implant through the hole. This has the advantage of being more straightforward to access, and going directly to the hearing parts of the cochlea, but as it does not go through a ‘natural opening’ it can be more difficult to find the best part of the hearing organ to put the implant.

Both techniques are very commonly used throughout the UK, and indeed across the world, and whichever technique you have will allow you to use a cochlear implant normally.

Why have you been invited?

You have been invited because you are being assessed, or have been offered a cochlear implant, and you have some remaining ‘natural’ hearing. We recommend maintaining ‘natural’ hearing even when you have a cochlear implant as the ‘natural’ and electrical hearing can work well together.

Before you agree, we would like you to understand what the research project is about. One of the research team will go through the information sheet with you and answer any questions you may have. Talk to other people about the work and your contribution to it, if you wish. Once you have had time to consider the research project, a member of the research team will ask if you would like to be part of the study. If you are happy to proceed, you will be enrolled in the study.

Will this use up your time?

You would be assessed frequently during your first year, all of these assessments are part of routine practice in our centre for patients who receive cochlear implants. For the duration of your first year with a cochlear implant, we will use the data from your appointments to determine how much the cochlear implant is helping your hearing. After this point, your involvement with the study will end, but your ongoing cochlear implant care will continue as it would if you were not part of the study.

Cochlear implantation does require a significant time commitment, but as all the care you receive will be as it would be if you were not participating in the study, there will not be any further demands on your time.

Do you have to take part?

It is up to you to decide whether you wish to take part. If you do not, then your cochlear implant assessment, operation, and aftercare will proceed as planned. A decision not to

take part will make no difference to the surgical procedures or to the standard of care you will receive.

It is important to note that we are undertaking this study using a particular cochlear implant, that we most commonly use when we want to keep as much 'normal' hearing as possible. If you choose to be implanted with a different device for other reasons, you will not be able to continue in the study.

What are the risks to you?

Prior to recommending cochlear implantation, the clinical team will have performed a full assessment of your current hearing, and your suitability for cochlear implantation. During this time, they will have discussed with you the benefits and risks of implantation. They will only proceed with cochlear implantation if they think it is in your best interests, and you agree, having considered the information they have given you.

The great majority of patients who undergo implantation benefit significantly from the improved hearing that implants can provide to those with severe and profound hearing loss. However, insertion of cochlear implants does carry risks. These risks are small, and complications associated with cochlear implants are rare. Your involvement in this study will not affect these risks. Risks associated with the operation include infection, bleeding, scarring, dizziness, device failure, loss of residual hearing, and very rarely taste disturbance or weakness of one side of the face (when they do occur these are usually temporary).

These risks will be the same whether you choose to enter the study or not. The procedure you undergo, whichever technique is used, will be a routine cochlear implant procedure.

Will your involvement be kept confidential?

After the operation, in the research database you will be identified only by a number assigned by those people who are treating you. All data that is made public will be entirely anonymous even after publication.

Will you find out which surgical technique you underwent?

For the duration of the study, the intention is that you will not know which technique you underwent, in case that changes your opinion of the operation or your hearing. The details of your operation will, however, be available to all those people treating you. If you wish to know the details of the operation, then you can be told after the completion of the study.

Who is carrying out the research?

The study is being conducted by University College London in conjunction with the Cochlear Implant Department at the Royal National Throat Nose and Ear Hospital.

This study is part of PhD student research project. The research project has received a grant from Med-El, who produce the cochlear implant we use frequently when attempting to preserve hearing.

Who has reviewed the study?

This study is currently under review. This study has been reviewed by NHS ethics committee and has been sponsored by UCL.

What if something goes wrong?

Complications associated with cochlear implants are rare. Both techniques for cochlear implant insertion used in this trial are used in routine clinical practice. Complications will therefore be managed in the same way whether you are a part of the trial or not. The management of these complications will also not be affected by the technique used for your operation.

If, before the trial has ended, it becomes clear that one technique is clearly superior to the other, then the trial will be stopped, and the results will be published.

Further information and contact details

If you need any further information **on the research project** please feel free to contact any one of us:

Chief Investigator: Prof Shakeel Saeed: e-mail shakeel.saeed@ucl.ac.uk;
Tel 020 7915 1593
PhD researcher: Ibrahim Busaad: e-mail Ibrahim.saad.12@ucl.ac.uk

If you have any issues associated with your clinical care, you can contact the cochlear implant department:

cioffice@uclh.nhs.uk

Or alternatively the Patient Advice and Liaison Service (PALS)

pals@uclh.nhs.uk or 02034573002

Our address is at the top of this information sheet.

If you need further information or advice about the surgery and what it involves, members of your clinical care team will be happy to provide it.

We hope that you will consent to enter the study, so we can determine the best way of performing these operations, and help other people receiving cochlear implants throughout the world**.**

Thank you for taking the time to read this information sheet and for entering the study if you decide to do so.

References

Abi Zeid Daou, C. & Bassim, M. 2020. Hyaluronic acid in otology: Its uses, advantages and drawbacks - a review. *Am J Otolaryngol,* 41**,** 102375.

Addams-Williams, J., Munaweera, L., Coleman, B., Shepherd, R. & Backhouse, S. 2011. Cochlear implant electrode insertion: In defence of cochleostomy and factors against the round window membrane approach. *Cochlear Implants Int,* 12 Suppl 2**,** S36-9.

Adunka, O., Gstoettner, W., Hambek, M., Unkelbach, M. H., Radeloff, A. & Kiefer, J. 2004a. Preservation of basal inner ear structures in cochlear implantation. *ORL J Otorhinolaryngol Relat Spec,* 66**,** 306-12.

Adunka, O. & Kiefer, J. 2006. Impact of electrode insertion depth on intracochlear trauma. *Otolaryngol Head Neck Surg,* 135**,** 374-82.

Adunka, O., Kiefer, J., Unkelbach, M. H., Lehnert, T. & Gstoettner, W. 2004b. Development and evaluation of an improved cochlear implant electrode design for electric acoustic stimulation. *Laryngoscope,* 114**,** 1237-41.

Adunka, O., Kiefer, J., Unkelbach, M. H., Radeloff, A. & Gstoettner, W. 2005. Evaluating cochlear implant trauma to the scala vestibuli. *Clin Otolaryngol,* 30**,** 121-7.

Adunka, O. F. & Buchman, C. A. 2007. Scala tympani cochleostomy i: Results of a survey. *Laryngoscope,* 117**,** 2187-94.

Adunka, O. F., Dillon, M. T., Adunka, M. C., King, E. R., Pillsbury, H. C. & Buchman, C. A. 2013. Hearing preservation and speech perception outcomes with electric-acoustic stimulation after 12 months of listening experience. *Laryngoscope,* 123**,** 2509-15.

Adunka, O. F., Dillon, M. T., Adunka, M. C., King, E. R., Pillsbury, H. C. & Buchman, C. A. 2014. Cochleostomy versus round window insertions: Influence on functional outcomes in electric-acoustic stimulation of the auditory system. *Otol Neurotol,* 35**,** 613-8.

Ahmed, S., Sheraz, S., Malik, S. A., Ahmed, N. R., Malik, S. A., Farooq, S., Raheem, A., Basheer, F. & Nayyar, Z. A. 2018. Frequency of congenital hearing loss in neonates. *J Ayub Med Coll Abbottabad,* 30**,** 234-236.

Al-Muhaimeed, H. S. & Abdelwahed, H. Y. 2015. Difficult cochleostomy in the normal cochlea. *The Egyptian Journal of Otolaryngology,* 31**,** 149-155.

Anne, S., Ishman, S. L. & Schwartz, S. 2016. A systematic review of perioperative versus prophylactic antibiotics for cochlear implantation. *Ann Otol Rhinol Laryngol,* 125**,** 893-899.

Appachi, S., Schwartz, S., Ishman, S. & Anne, S. 2018. Utility of intraoperative imaging in cochlear implantation: A systematic review. *The Laryngoscope,* 128**,** 1914-1921.

Arnoldner, C., Helbig, S., Wagenblast, J., Baumgartner, W. D., Hamzavi, J. S., Riss, D. & Gstoettner, W. 2010. Electric acoustic stimulation in patients with postlingual severe high-frequency hearing loss: Clinical experience. *Adv Otorhinolaryngol,* 67**,** 116-24.

Aschendorff, A. 2011. [imaging in cochlear implant patients]. *Laryngo- Rhino- Otologie,* 90 Suppl 1**,** S16-21.

Aschendorff, A., Kromeier, J., Klenzner, T. & Laszig, R. 2007. Quality control after insertion of the nucleus contour and contour advance electrode in adults. *Ear Hear,* 28**,** 75s-79s.

Ashmore, J. F. & Kolston, P. J. 1994. Hair cell based amplification in the cochlea. *Current opinion in neurobiology,* 4**,** 503-508.

Avci, E., Nauwelaers, T., Lenarz, T., Hamacher, V. & Kral, A. 2014. Variations in microanatomy of the human cochlea. *J Comp Neurol,* 522**,** 3245-61.

Badr, A., Shabana, Y., Mokbel, K., Elsharabasy, A., Ghonim, M. & Sanna, M. 2018. Atraumatic scala tympani cochleostomy; resolution of the dilemma. *J Int Adv Otol,* 14**,** 190-196.

Bae, S.-C., Shin, Y.-R. & Chun, Y.-M. 2019. Cochlear implant surgery through round window approach is always possible. *Annals of Otology, Rhinology & Laryngology,* 128**,** 38S-44S.

Balkany, T. J., Connell, S. S., Hodges, A. V., Payne, S. L., Telischi, F. F., Eshraghi, A. A., Angeli, S. I., Germani, R., Messiah, S. & Arheart, K. L. 2006. Conservation of residual acoustic hearing after cochlear implantation. *Otology & Neurotology,* 27**,** 1083-8.

Barker, E. & Pringle, M. 2008. Survey of prophylactic antibiotic use amongst uk cochlear implant surgeons. *Cochlear Implants Int,* 9**,** 82-9.

Barrett, K. E., Barman, S. M., Boitano, S., Brooks, H. L. & Ganong, W. F. 2016. *Ganong's review of medical physiology / kim e. Barrett, phd, susan m. Barman, phd, scott boitano, phd, heddwin l. Brooks, phd,* New York, McGraw-Hill Education.

Bartling, S. H., Gupta, R., Torkos, A., Dullin, C., Eckhardt, G., Lenarz, T., Becker, H. & Stover, T. 2006. Flat-panel volume computed tomography for cochlear implant electrode array examination in isolated temporal bone specimens. *Otol Neurotol,* 27**,** 491-8.

Bas, E., Dinh, C. T., Garnham, C., Polak, M. & Van De Water, T. R. 2012. Conservation of hearing and protection of hair cells in cochlear implant patients' with residual hearing. *Anatomical Record (Hoboken, N.J.: 2007),* 295**,** 1909-27.

Basavaraj, S., Najaraj, S., Shanks, M., Wardrop, P. & Allen, A. A. 2004. Short-term versus long-term antibiotic prophylaxis in cochlear implant surgery. *Otol Neurotol,* 25**,** 720-2.

Battaglia, A., Lualhati, A., Lin, H., Burchette, R. & Cueva, R. 2014. A prospective, multi-centered study of the treatment of idiopathic sudden sensorineural hearing loss with combination therapy versus high-dose prednisone alone: A 139 patient follow-up. *Otol Neurotol,* 35**,** 1091-8.

Bench, J., Kowal, A. & Bamford, J. 1979. The bkb (bamford-kowal-bench) sentence lists for partially-hearing children. *Br J Audiol,* 13**,** 108-12.

Biedron, S., Westhofen, M. & Ilgner, J. 2009. On the number of turns in human cochleae. *Otology & Neurotology,* 30**,** 414-417.

Bjurström, S., Slepecky, N. & Angelborg, C. 1987. A histopathological study of the inner ear after the administration of hyaluronan into the middle ear of the guinea pig. *Acta Oto-Laryngologica,* 104**,** 62-65.

Blamey, P., Arndt, P., Bergeron, F., Bredberg, G., Brimacombe, J., Facer, G., Larky, J., Lindstrom, B., Nedzelski, J., Peterson, A., Shipp, D., Staller, S. & Whitford, L. 1996.

Factors affecting auditory performance of postlinguistically deaf adults using cochlear implants. *Audiol Neurootol,* 1**,** 293-306.

Blamey, P., Artieres, F., Baskent, D., Bergeron, F., Beynon, A., Burke, E., Dillier, N., Dowell, R., Fraysse, B., Gallego, S., Govaerts, P. J., Green, K., Huber, A. M., Kleine-Punte, A., Maat, B., Marx, M., Mawman, D., Mosnier, I., O'connor, A. F., O'leary, S., Rousset, A., Schauwers, K., Skarzynski, H., Skarzynski, P. H., Sterkers, O., Terranti, A., Truy, E., Van De Heyning, P., Venail, F., Vincent, C. & Lazard, D. S. 2013. Factors affecting auditory performance of postlinguistically deaf adults using cochlear implants: An update with 2251 patients. *Audiol Neurootol,* 18**,** 36-47.

Boyer, E., Karkas, A., Attye, A., Lefournier, V., Escude, B. & Schmerber, S. 2015. Scalar localization by cone-beam computed tomography of cochlear implant carriers: A comparative study between straight and periomodiolar precurved electrode arrays. *Otol Neurotol,* 36**,** 422-9.

Briggs, R. J. S., Tykocinski, M., Stidham, K. & Roberson, J. B. 2005. Cochleostomy site: Implications for electrode placement and hearing preservation. *Acta Oto-Laryngologica,* 125**,** 870-876.

British Society of Audiology 2011. Pure-tone air-conduction and bone-conduction threshold audiometry with and without masking: Recommended procedure. British Society of Audiology Reading, UK.

Brockmeier, S. J., Peterreins, M., Lorens, A., Vermeire, K., Helbig, S., Anderson, I., Skarzynski, H., Van De Heyning, P., Gstoettner, W. & Kiefer, J. 2010. Music perception in electric acoustic stimulation users as assessed by the mu.S.I.C. Test. *Adv Otorhinolaryngol,* 67**,** 70-80.

Brown, K. D., Melton, M. F., Shonfield, H., Kraskin, M. & Wolf, J. 2015. Preserved low-frequency hearing following 20-mm cochlear implantation. *Otology & Neurotology,* 36**,** 240-3.

Bruce, I. A., Bates, J. E., Melling, C., Mawman, D. & Green, K. M. 2011. Hearing preservation via a cochleostomy approach and deep insertion of a standard length cochlear implant electrode. *Otol Neurotol,* 32**,** 1444-7.

Bruce, I. A., Felton, M., Lockley, M., Melling, C., Lloyd, S. K., Freeman, S. R. & Green, K. M. 2014. Hearing preservation cochlear implantation in adolescents. *Otology & Neurotology,* 35**,** 1552-9.

Bruce, I. A. & Todt, I. 2018. Hearing preservation cochlear implant surgery. *Adv Otorhinolaryngol,* 81**,** 66-73.

Campbell, A., T. Dillon, M., Buchman, C. & Adunka, O. 2013. *Hearing preservation cochlear implantation*.

Canfarotta, M. W., Dillon, M. T., Buchman, C. A., Buss, E., O'connell, B. P., Rooth, M. A., King, E. R., Pillsbury, H. C., Adunka, O. F. & Brown, K. D. 2021. Long-term influence of electrode array length on speech recognition in cochlear implant users. *Laryngoscope,* 131**,** 892-897.

Carlson, M. L., Driscoll, C. L., Gifford, R. H., Service, G. J., Tombers, N. M., Hughes-Borst, B. J., Neff, B. A. & Beatty, C. W. 2011. Implications of minimizing trauma during conventional cochlear implantation. *Otology & Neurotology,* 32**,** 962-8.

Carlson, M. L., O'connell, B. P., Lohse, C. M., Driscoll, C. L. & Sweeney, A. D. 2018. Survey of the american neurotology society on cochlear implantation: Part 2, surgical and device-related practice patterns. *Otol Neurotol,* 39**,** e20-e27.

Causon, A., Verschuur, C. & Newman, T. A. 2015. A retrospective analysis of the contribution of reported factors in cochlear implantation on hearing preservation outcomes. *Otol Neurotol,* 36**,** 1137-45.

Cerini, R., Faccioli, N., Barillari, M., De Iorio, M., Carner, M., Colletti, V. & Pozzi Mucelli, R. 2008. Bionic ear imaging. *Radiologia Medica,* 113**,** 265-77.

Chakravorti, S., Noble, J. H., Gifford, R. H., Dawant, B. M., O'connell, B. P., Wang, J. & Labadie, R. F. 2019. Further evidence of the relationship between cochlear implant electrode positioning and hearing outcomes. *Otol Neurotol,* 40**,** 617-624.

Chandrasekhar, S. S., Rubinstein, R. Y., Kwartler, J. A., Gatz, M., Connelly, P. E., Huang, E. & Baredes, S. 2000. Dexamethasone pharmacokinetics in the inner ear: Comparison of route of administration and use of facilitating agents. *Otolaryngol Head Neck Surg,* 122**,** 521-8.

Chang, A., Eastwood, H., Sly, D., James, D., Richardson, R. & O'leary, S. 2009. Factors influencing the efficacy of round window dexamethasone protection of residual hearing post-cochlear implant surgery. *Hear Res,* 255**,** 67-72.

Cheng, X., Wang, B., Liu, Y., Yuan, Y., Shu, Y. & Chen, B. 2018. Comparable electrode impedance and speech perception at 12 months after cochlear implantation using round window versus cochleostomy: An analysis of 40 patients. *ORL J Otorhinolaryngol Relat Spec,* 80**,** 248-258.

Cho, H. S., Lee, K. Y., Choi, H., Jang, J. H. & Lee, S. H. 2016. Dexamethasone is one of the factors minimizing the inner ear damage from electrode insertion in cochlear implantation. *Audiology & Neuro-Otology,* 21**,** 178-86.

Choudhury, B., Fitzpatrick, D. C., Buchman, C. A., Wei, B. P., Dillon, M. T., He, S. & Adunka, O. F. 2012. Intraoperative round window recordings to acoustic stimuli from cochlear implant patients. *Otol Neurotol,* 33**,** 1507-15.

Cipolla, M. J., Iyer, P., Dome, C., Welling, D. B. & Bush, M. L. 2012. Modification and comparison of minimally invasive cochleostomy techniques: A pilot study. *Laryngoscope,* 122**,** 1142-7.

Clark, G. M., Pyman, B. C., Webb, R. L., Bailey, Q. E. & Shepherd, R. K. 1984. Surgery for an improved multiple-channel cochlear implant. *Ann Otol Rhinol Laryngol,* 93**,** 204-7.

Cohen, L. T., Xu, J., Xu, S. A. & Clark, G. M. 1996. Improved and simplified methods for specifying positions of the electrode bands of a cochlear implant array. *Am J Otol,* 17**,** 859-65.

Cohen, N. L. & Hoffman, R. A. 1991. Complications of cochlear implant surgery in adults and children. *Ann Otol Rhinol Laryngol,* 100**,** 708-11.

Cosetti, M. K. & Waltzman, S. B. 2011. Cochlear implants: Current status and future potential. *Expert review of medical devices,* 8**,** 389-401.

Cullen, R. D., Higgins, C., Buss, E., Clark, M., Pillsbury, H. C., 3rd & Buchman, C. A. 2004. Cochlear implantation in patients with substantial residual hearing. *Laryngoscope,* 114**,** 2218-23.

Cullington, H. E. & Zeng, F. G. 2011. Comparison of bimodal and bilateral cochlear implant users on speech recognition with competing talker, music perception, affective prosody discrimination, and talker identification. *Ear Hear,* 32**,** 16-30.

Cushing, S. L., Daly, M. J., Treaba, C. G., Chan, H., Irish, J. C., Blaser, S., Gordon, K. A. & Papsin, B. C. 2012. High-resolution cone-beam computed tomography: A potential tool to improve atraumatic electrode design and position. *Acta Oto-Laryngologica,* 132**,** 361-8.

Dalbert, A., Pfiffner, F., Hoesli, M., Koka, K., Veraguth, D., Roosli, C. & Huber, A. 2018. Assessment of cochlear function during cochlear implantation by extra- and intracochlear electrocochleography. *Front Neurosci,* 12**,** 18.

Dalbert, A., Rohner, P., Roosli, C., Veraguth, D., Huber, A. & Pfiffner, F. 2019. Correlation between electrocochleographic changes during surgery and hearing outcome in cochlear implant recipients: A case report and systematic review of the literature. *Otol Neurotol*.

Dallos, P. 1996. Overview: Cochlear neurobiology. *The cochlea***,** 1-43.

De Carvalho, G. M., Guimaraes, A. C., Duarte, A. S., Muranaka, E. B., Soki, M. N., Martins, R. S., Bianchini, W. A., Paschoal, J. R. & Castilho, A. M. 2013. Hearing preservation after cochlear implantation: Unicamp outcomes. *Int J Otolaryngol,* 2013**,** 107186.

De Seta, D., Mancini, P., Russo, F. Y., Torres, R., Mosnier, I., Bensimon, J. L., De Seta, E., Heymann, D., Sterkers, O., Bernardeschi, D. & Nguyen, Y. 2016. 3d curved multiplanar cone beam ct reconstruction for intracochlear position assessment of straight electrodes array. A temporal bone and clinical study. *Acta Otorhinolaryngol Ital,* 36**,** 499-505.

Demir, B., Yüksel, M., Atılgan, A., Ciprut, A. & Batman, C. 2021. Spectral resolution and speech perception after cochlear implantation using the round window versus cochleostomy technique. *J Laryngol Otol,* 135**,** 513-517.

Dietz, A., Gazibegovic, D., Tervaniemi, J., Vartiainen, V. M. & Lopponen, H. 2016. Insertion characteristics and placement of the mid-scala electrode array in human temporal bones using detailed cone beam computed tomography. *Eur Arch Otorhinolaryngol,* 273**,** 4135-4143.

Dillon, M. T., Buss, E., O'connell, B. P., Rooth, M. A., King, E. R., Bucker, A. L., Deres, E. J., Mccarthy, S. A., Pillsbury, H. C. & Brown, K. D. 2019. Low-frequency hearing preservation with long electrode arrays: Inclusion of unaided hearing threshold assessment in the postoperative test battery. *Am J Audiol***,** 1-5.

Dinh, C. T. & Van De Water, T. R. 2009. Blocking pro-cell-death signal pathways to conserve hearing. *Audiol Neurootol,* 14**,** 383-92.

Do, K., Baker, K., Praetorius, M. & Staecker, H. A mouse model of implantation trauma. International Congress Series, 2004. Elsevier, 167-170.

Downs, S. H. & Black, N. 1998. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health,* 52**,** 377-84.

Eastwood, H., Chang, A., Kel, G., Sly, D., Richardson, R. & O'leary, S. J. 2010. Round window delivery of dexamethasone ameliorates local and remote hearing loss produced by cochlear implantation into the second turn of the guinea pig cochlea. *Hear Res,* 265**,** 25-9.

Echteler, S. M., Fay, R. R. & Popper, A. N. 1994. Structure of the mammalian cochlea. *Comparative hearing: Mammals.* New York: Springer.

Elafandi, H., Khalifa, M. A. & Elguindy, A. S. 2020. Cochlear implantation outcomes with round window electrode insertion versus cochleostomy insertion. *Int J Pediatr Otorhinolaryngol,* 138**,** 110272.

Erixon, E., Kobler, S. & Rask-Andersen, H. 2012. Cochlear implantation and hearing preservation: Results in 21 consecutively operated patients using the round window approach. *Acta Otolaryngol,* 132**,** 923-31.

Erixon, E. & Rask-Andersen, H. 2013. How to predict cochlear length before cochlear implantation surgery. *Acta Oto-Laryngologica,* 133**,** 1258-65.

Erixon, E. & Rask-Andersen, H. 2015. Hearing and patient satisfaction among 19 patients who received implants intended for hybrid hearing: A two-year follow-up. *Ear & Hearing,* 36**,** e271-8.

Escude, B., James, C., Deguine, O., Cochard, N., Eter, E. & Fraysse, B. 2006. The size of the cochlea and predictions of insertion depth angles for cochlear implant electrodes. *Audiol Neurootol,* 11 Suppl 1**,** 27-33.

Eshraghi, A. A. 2006. Prevention of cochlear implant electrode damage. *Current Opinion in Otolaryngology & Head & Neck Surgery,* 14**,** 323-8.

Eshraghi, A. A., Ahmed, J., Krysiak, E., Ila, K., Ashman, P., Telischi, F. F., Angeli, S., Prentiss, S., Martinez, D. & Valendia, S. 2016. Clinical, surgical, and electrical factors impacting residual hearing in cochlear implant surgery. *Acta Oto-Laryngologica***,** 1-5.

Eshraghi, A. A. & Van De Water, T. R. 2006. Cochlear implantation trauma and noise-induced hearing loss: Apoptosis and therapeutic strategies. *Anat Rec A Discov Mol Cell Evol Biol,* 288**,** 473-81.

Eshraghi, A. A., Yang, N. W. & Balkany, T. J. 2003. Comparative study of cochlear damage with three perimodiolar electrode designs. *Laryngoscope,* 113**,** 415-9.

Esquia Medina, G. N., Borel, S., Nguyen, Y., Ambert-Dahan, E., Ferrary, E., Sterkers, O. & Grayeli, A. B. 2013. Is electrode-modiolus distance a prognostic factor for hearing performances after cochlear implant surgery? *Audiol Neurootol,* 18**,** 406-13.

Faccioli, N., Barillari, M., Guariglia, S., Zivelonghi, E., Rizzotti, A., Cerini, R. & Mucelli, R. P. 2009. Radiation dose saving through the use of cone-beam ct in hearing-impaired patients. *Radiologia Medica,* 114**,** 1308-18.

Fan, X., Xia, M., Wang, Z., Zhang, H., Liu, C., Wang, N., Hou, L., Li, C. & Xu, A. 2018. Comparison of electrode position between round window and cochleostomy inserting approaches among young children: A cone-beam computed tomography study. *Acta Otolaryngol,* 138**,** 815-821.

Farinetti, A., Ben Gharbia, D., Mancini, J., Roman, S., Nicollas, R. & Triglia, J. M. 2014. Cochlear implant complications in 403 patients: Comparative study of adults and children and review of the literature. *Eur Ann Otorhinolaryngol Head Neck Dis,* 131**,** 177-82.

Farris, H. E., Wells, G. B. & Ricci, A. J. 2006. Steady-state adaptation of mechanotransduction modulates the resting potential of auditory hair cells, providing an assay for endolymph [ca2+]. *The Journal of neuroscience : the official journal of the Society for Neuroscience,* 26**,** 12526-12536.

Faulkner, A., Rosen, S. & Norman, C. 2006. The right information may matter more than frequency-place alignment: Simulations of frequency-aligned and upward shifting cochlear implant processors for a shallow electrode array insertion. *Ear Hear,* 27**,** 139-52.

Fettiplace, R. & Fuchs, P. 1999. Mechanisms of hair cell tuning. *Annual review of physiology,* 61**,** 809.

Fettiplace, R. & Hackney, C. M. 2006. The sensory and motor roles of auditory hair cells. *Nature reviews. Neuroscience,* 7**,** 19-29.

Finley, C. C., Holden, T. A., Holden, L. K., Whiting, B. R., Chole, R. A., Neely, G. J., Hullar, T. E. & Skinner, M. W. 2008. Role of electrode placement as a contributor to variability in cochlear implant outcomes. *Otol Neurotol,* 29**,** 920-8.

Fischer, N., Pinggera, L., Weichbold, V., Dejaco, D., Schmutzhard, J. & Widmann, G. 2015. Radiologic and functional evaluation of electrode dislocation from the scala tympani to the scala vestibuli in patients with cochlear implants. *AJNR Am J Neuroradiol,* 36**,** 372-7.

Forge, A. & Wright, T. 2002. The molecular architecture of the inner ear. *British medical bulletin,* 63**,** 5-24.

Francis, H. W., Buchman, C. A., Visaya, J. M., Wang, N. Y., Zwolan, T. A., Fink, N. E. & Niparko, J. K. 2008. Surgical factors in pediatric cochlear implantation and their early effects on electrode activation and functional outcomes. *Otol Neurotol,* 29**,** 502-8.

Franke-Trieger, A. & Murbe, D. 2015. Estimation of insertion depth angle based on cochlea diameter and linear insertion depth: A prediction tool for the ci422. *Eur Arch Otorhinolaryngol,* 272**,** 3193-9.

Fraysse, B., Macias, A. R., Sterkers, O., Burdo, S., Ramsden, R., Deguine, O., Klenzner, T., Lenarz, T., Rodriguez, M. M., Von Wallenberg, E. & James, C. 2006. Residual hearing conservation and electroacoustic stimulation with the nucleus 24 contour advance cochlear implant. *Otol Neurotol,* 27**,** 624-33.

Friedmann, D. R., Peng, R., Fang, Y., Mcmenomey, S. O., Roland, J. T. & Waltzman, S. B. 2015. Effects of loss of residual hearing on speech performance with the ci422 and the hybrid-l electrode. *Cochlear Implants Int,* 16**,** 277-84.

Fu, Q. J. & Galvin, J. J., 3rd 2007. Perceptual learning and auditory training in cochlear implant recipients. *Trends Amplif,* 11**,** 193-205.

Furness, D. N. & Hackney, C. M. 2008. Form and ultrastructure of the cochlea and its central connections. *Gleeson M. Scott-Brown's Otorhinolaryngology, Head and Neck Surgery,* 3**,** 3126-3146.

Gani, M., Valentini, G., Sigrist, A., Kós, M.-I. & Boëx, C. 2007. Implications of deep electrode insertion on cochlear implant fitting. *Journal of the Association for Research in Otolaryngology : JARO,* 8**,** 69-83.

Gantz, B. J., Hansen, M. R., Turner, C. W., Oleson, J. J., Reiss, L. A. & Parkinson, A. J. 2009. Hybrid 10 clinical trial: Preliminary results. *Audiol Neurootol,* 14 Suppl 1**,** 32-8.

Gantz, B. J., Turner, C., Gfeller, K. E. & Lowder, M. W. 2005. Preservation of hearing in cochlear implant surgery: Advantages of combined electrical and acoustical speech processing. *Laryngoscope,* 115**,** 796-802.

Gantz, B. J. & Turner, C. W. 2003. Combining acoustic and electrical hearing. *Laryngoscope,* 113**,** 1726-30.

Garcia-Ibanez, L., Macias, A. R., Morera, C., Rodriguez, M. M., Szyfter, W., Skarszynski, H., Emamdjomeh, H. & Baumgartner, W. D. 2009. An evaluation of the preservation of residual hearing with the nucleus contour advance electrode. *Acta Otolaryngol,* 129**,** 651-64.

Garcia-Valdecasas, J., Jimenez-Moleon, J. J., Sainz, M., Fornieles, C. & Ballesteros, J. M. 2009. Prophylactic effect of clarithromycin in skin flap complications in cochlear implants surgery. *Laryngoscope,* 119**,** 2032-6.

Gates, G. A. & Mills, J. H. 2005. Presbycusis. *Lancet,* 366**,** 1111-20.

Gaylor, J. M., Raman, G., Chung, M., Lee, J., Rao, M., Lau, J. & Poe, D. S. 2013. Cochlear implantation in adults: A systematic review and meta-analysis. *JAMA otolaryngology--head & neck surgery,* 139**,** 1-8.

Gelfand, S. 2010. Essentials of audiology.

Gfeller, K., Oleson, J., Knutson, J. F., Breheny, P., Driscoll, V. & Olszewski, C. 2008. Multivariate predictors of music perception and appraisal by adult cochlear implant users. *Journal of the American Academy of Audiology,* 19**,** 120-34.

Gfeller, K., Turner, C., Oleson, J., Kliethermes, S. & Driscoll, V. 2012. Accuracy of cochlear implant recipients in speech reception in the presence of background music. *Annals of Otology, Rhinology & Laryngology,* 121**,** 782-91.

Gfeller, K. E., Olszewski, C., Turner, C., Gantz, B. & Oleson, J. 2006. Music perception with cochlear implants and residual hearing. *Audiology & Neuro-Otology,* 11 Suppl 1**,** 12-5.

Giardina, C. K., Brown, K. D., Adunka, O. F., Buchman, C. A., Hutson, K. A., Pillsbury, H. C. & Fitzpatrick, D. C. 2019. Intracochlear electrocochleography: Response patterns during cochlear implantation and hearing preservation. *Ear Hear,* 40**,** 833-848.

Gibbin, K. P., Raine, C. H. & Summerfield, A. Q. 2003. Cochlear implantation--united kingdom and ireland surgical survey. *Cochlear Implants Int,* 4**,** 11-21.

Golub, J. S., Won, J. H., Drennan, W. R., Worman, T. D. & Rubinstein, J. T. 2012. Spectral and temporal measures in hybrid cochlear implant users: On the mechanism of electroacoustic hearing benefits. *Otology & Neurotology,* 33**,** 147-53.

Goycoolea, M. V. & Lundman, L. 1997. Round window membrane. Structure function and permeability: A review. *Microsc Res Tech,* 36**,** 201-11.

Groenwold, R. H., Donders, A. R., Roes, K. C., Harrell, F. E., Jr. & Moons, K. G. 2012. Dealing with missing outcome data in randomized trials and observational studies. *Am J Epidemiol,* 175**,** 210-7.

Gstoettner, W., Helbig, S., Settevendemie, C., Baumann, U., Wagenblast, J. & Arnoldner, C. 2009. A new electrode for residual hearing preservation in cochlear implantation: First clinical results. *Acta Otolaryngol,* 129**,** 372-9.

Gstoettner, W. K., Hamzavi, J., Baumgartner, W. D. & Czerny, C. C. 2000. Fixation of the electrode array with bone pate in cochlear implant surgery. *Acta Otolaryngol,* 120**,** 369-74.

Gstoettner, W. K., Heibig, S., Maier, N., Kiefer, J., Radeloff, A. & Adunka, O. F. 2006. Ipsilateral electric acoustic stimulation of the auditory system: Results of long-term hearing preservation. *Audiology and Neurotology,* 11**,** 49-56.

Guimaraes, A. C., Carvalho, G. M., Duarte, A. S., Bianchini, W. A., Sarasty, A. B., Gregorio, M. F., Zernotti, M. E., Sartorato, E. L. & Castilho, A. M. 2015. Hearing preservation and cochlear implants according to inner ear approach: Multicentric evaluation. *Braz J Otorhinolaryngol,* 81**,** 190-6.

Guldner, C., Wiegand, S., Weiss, R., Bien, S., Sesterhenn, A., Teymoortash, A. & Diogo, I. 2012a. Artifacts of the electrode in cochlea implantation and limits in analysis of deep insertion in cone beam tomography (cbt). *Eur Arch Otorhinolaryngol,* 269**,** 767-72.

Guldner, C., Wiegand, S., Weiss, R., Bien, S., Sesterhenn, A., Teymoortash, A. & Diogo, I. 2012b. Artifacts of the electrode in cochlea implantation and limits in analysis of deep insertion in cone beam tomography (cbt). *European Archives of Oto-Rhino-Laryngology,* 269**,** 767-72.

Hackney, C. M. & Furness, D. N. 1995. Mechanotransduction in vertebrate hair cells: Structure and function of the stereociliary bundle. *American Journal of Physiology - Cell Physiology,* 268**,** 1-13.

Hardy, M. 1938. The length of the organ of corti in man. *American Journal of Anatomy,* 62**,** 291-311.

Hassepass, F., Aschendorff, A., Bulla, S., Arndt, S., Maier, W., Laszig, R. & Beck, R. 2015. Radiologic results and hearing preservation with a straight narrow electrode via round window versus cochleostomy approach at initial activation. *Otol Neurotol,* 36**,** 993-1000.

Hassepass, F., Bulla, S., Maier, W., Laszig, R., Arndt, S., Beck, R., Traser, L. & Aschendorff, A. 2014. The new mid-scala electrode array: A radiologic and histologic study in human temporal bones. *Otol Neurotol,* 35**,** 1415-20.

Havenith, S., Lammers, M. J., Tange, R. A., Trabalzini, F., Della Volpe, A., Van Der Heijden, G. J. & Grolman, W. 2013. Hearing preservation surgery: Cochleostomy or round window approach? A systematic review. *Otol Neurotol,* 34**,** 667-74.

Helbig, S., Adel, Y., Rader, T., Stover, T. & Baumann, U. 2016. Long-term hearing preservation outcomes after cochlear implantation for electric-acoustic stimulation. *Otol Neurotol,* 37**,** e353-9.

Helbig, S., Baumann, U., Hey, C. & Helbig, M. 2011a. Hearing preservation after complete cochlear coverage in cochlear implantation with the free-fitting flexsoft electrode carrier. *Otol Neurotol,* 32**,** 973-9.

Helbig, S., Rader, T., Bahmer, A. & Baumann, U. 2009. A case of bilateral cochlear implantation in single-sided untreated acoustic neurinoma. *Acta Otolaryngol,* 129**,** 694-6.

Helbig, S., Van De Heyning, P., Kiefer, J., Baumann, U., Kleine-Punte, A., Brockmeier, H., Anderson, I. & Gstoettner, W. 2011b. Combined electric acoustic stimulation with the pulsarci(100) implant system using the flex(eas) electrode array. *Acta Otolaryngol,* 131**,** 585-95.

Heutink, F., De Rijk, S. R., Verbist, B. M., Huinck, W. J. & Mylanus, E. a. M. 2019. Angular electrode insertion depth and speech perception in adults with a cochlear implant: A systematic review. *Otol Neurotol,* 40**,** 900-910.

Hirsch, B. E., Blikas, A. & Whitaker, M. 2007. Antibiotic prophylaxis in cochlear implant surgery. *Laryngoscope,* 117**,** 864-7.

Hochmair, I., Arnold, W., Nopp, P., Jolly, C., Müller, J. & Roland, P. 2003. Deep electrode insertion in cochlear implants: Apical morphology, electrodes and speech perception results. *Acta Otolaryngol,* 123**,** 612-7.

Hodez, C., Griffaton-Taillandier, C. & Bensimon, I. 2011. Cone-beam imaging: Applications in ent. *European annals of otorhinolaryngology, head & neck diseases,* 128**,** 65-78.

Hodges, A. V., Schloffman, J. & Balkany, T. 1997. Conservation of residual hearing with cochlear implantation. *American Journal of Otology,* 18**,** 179-83.

Holden, L. K., Finley, C. C., Firszt, J. B., Holden, T. A., Brenner, C., Potts, L. G., Gotter, B. D., Vanderhoof, S. S., Mispagel, K., Heydebrand, G. & Skinner, M. W. 2013. Factors affecting open-set word recognition in adults with cochlear implants. *Ear Hear,* 34**,** 342-60.

Hooper, P., Jutai, J. W., Strong, G. & Russell-Minda, E. 2008. Age-related macular degeneration and low-vision rehabilitation: A systematic review. *Can J Ophthalmol,* 43**,** 180-7.

Hoskison, E., Mitchell, S. & Coulson, C. 2017. Systematic review: Radiological and histological evidence of cochlear implant insertion trauma in adult patients. *Cochlear Implants Int,* 18**,** 192-197.

Huang, C. Q., Tykocinski, M., Stathopoulos, D. & Cowan, R. 2007. Effects of steroids and lubricants on electrical impedance and tissue response following cochlear implantation. *Cochlear Implants Int,* 8**,** 123-47.

Hudspeth, A. J. & Jacobs, R. 1979. Stereocilia mediate transduction in vertebrate hair cells. *Proceedings of the National Academy of Sciences - PNAS,* 76**,** 1506-1509.

Iseli, C., Adunka, O. F. & Buchman, C. A. 2014. Scala tympani cochleostomy survey: A follow-up study. *Laryngoscope,* 124**,** 1928-31.

Iso-Mustajarvi, M., Matikka, H., Risi, F., Sipari, S., Koski, T., Willberg, T., Lehtimaki, A., Tervaniemi, J., Lopponen, H. & Dietz, A. 2017. A new slim modiolar electrode array for cochlear implantation: A radiological and histological study. *Otol Neurotol,* 38**,** e327-e334.

James, C. J., Fraysse, B., Deguine, O., Lenarz, T., Mawman, D., Ramos, A., Ramsden, R. & Sterkers, O. 2006. Combined electroacoustic stimulation in conventional candidates for cochlear implantation. *Audiol Neurootol,* 11 Suppl 1**,** 57-62.

Jia, H., Wang, J., Francois, F., Uziel, A., Puel, J. L. & Venail, F. 2013. Molecular and cellular mechanisms of loss of residual hearing after cochlear implantation. *Annals of Otology, Rhinology & Laryngology,* 122**,** 33-9.

Jiang, D. & Fitzgerald O'connor, A. 2007. The assessment of the access to the round window via a posterior tympanotomy: A practical classification.

Jones, G. L., Ho Won, J., Drennan, W. R. & Rubinstein, J. T. 2013. Relationship between channel interaction and spectral-ripple discrimination in cochlear implant users. *Journal of the Acoustical Society of America,* 133**,** 425-433.

Jurawitz, M. C., Buchner, A., Harpel, T., Schussler, M., Majdani, O., Lesinski-Schiedat, A. & Lenarz, T. 2014. Hearing preservation outcomes with different cochlear implant electrodes: Nucleus(r) hybrid-l24 and nucleus freedom ci422. *Audiol Neurootol,* 19**,** 293-309.

Jwair, S., Van Eijden, J. J. M., Blijleven, E. E., Dankbaar, J. W. & Thomeer, H. G. X. M. 2021. Radiological and surgical aspects of round window visibility during cochlear implantation: A retrospective analysis. *European Archives of Oto-Rhino-Laryngology*.

Kamakura, T. & Nadol, J. B., Jr. 2016. Correlation between word recognition score and intracochlear new bone and fibrous tissue after cochlear implantation in the human. *Hearing Research,* 339**,** 132-41.

Kang, B. J. & Kim, A. H. 2013. Comparison of cochlear implant performance after round window electrode insertion compared with traditional cochleostomy. *Otolaryngol Head Neck Surg,* 148**,** 822-6.

Kiefer, J., Gstoettner, W., Baumgartner, W., Pok, S. M., Tillein, J., Ye, Q. & Von Ilberg, C. 2004. Conservation of low-frequency hearing in cochlear implantation. *Acta Otolaryngol,* 124**,** 272-80.

Kisser, U., Wunsch, J., Hempel, J. M., Adderson-Kisser, C., Stelter, K., Krause, E., Muller, J. & Schrotzlmair, F. 2016. Residual hearing outcomes after cochlear implant surgery using ultra-flexible 28-mm electrodes. *Otol Neurotol,* 37**,** 878-81.

Kochhar, A., Hildebrand, M. S. & Smith, R. J. H. 2007. Clinical aspects of hereditary hearing loss. *Genetics in medicine,* 9**,** 393-408.

Kos, M. I., Boex, C., Sigrist, A., Guyot, J. P. & Pelizzone, M. 2005. Measurements of electrode position inside the cochlea for different cochlear implant systems. *Acta Oto-Laryngologica,* 125**,** 474-80.

Krstic, R. V. 1991. *Human microscopic anatomy : An atlas for students of medicine and biology / radivoj v. Krstić,* Berlin ;, Springer-Verlag.

Kuthubutheen, J., Coates, H., Rowsell, C., Nedzelski, J., Chen, J. M. & Lin, V. 2015. The role of extended preoperative steroids in hearing preservation cochlear implantation. *Hear Res,* 327**,** 257-64.

Kuthubutheen, J., Grewal, A., Symons, S., Nedzelski, J., Shipp, D., Lin, V. & Chen, J. 2019. The effect of cochlear size on cochlear implantation outcomes. *Biomed Res Int,* 2019**,** 5849871.

Kuthubutheen, J., Joglekar, S., Smith, L., Friesen, L., Smilsky, K., Millman, T., Ng, A., Shipp, D., Coates, H., Arnoldner, C., Nedzelski, J., Chen, J. & Lin, V. 2018. The role of preoperative steroids for hearing preservation cochlear implantation: Results of a randomized controlled trial. *Audiology and Neurotology,* 22**,** 292-302.

Laszig, R., Ridder, G. J. & Fradis, M. 2002. Intracochlear insertion of electrodes using hyaluronic acid in cochlear implant surgery. *J Laryngol Otol,* 116**,** 371-2.

Lazard, D. S., Vincent, C., Venail, F., Van De Heyning, P., Truy, E., Sterkers, O., Skarzynski, P. H., Skarzynski, H., Schauwers, K., O'leary, S., Mawman, D., Maat, B., Kleine-Punte, A., Huber, A. M., Green, K., Govaerts, P. J., Fraysse, B., Dowell, R., Dillier, N., Burke, E., Beynon, A., Bergeron, F., Baskent, D., Artieres, F. & Blamey, P. J. 2012. Pre-, per- and postoperative factors affecting performance of postlinguistically deaf adults using cochlear implants: A new conceptual model over time. *PLoS One,* 7**,** e48739.

Lee, A., Jiang, D., Mclaren, S., Nunn, T., Demler, J. M., Tysome, J. R., Connor, S. & Fitzgerald O'connor, A. 2010a. Electric acoustic stimulation of the auditory system: Experience and results of ten patients using med-el's m and flexeas electrodes. *Clin Otolaryngol,* 35**,** 190-7.

Lee, J., Nadol, J. B., Jr. & Eddington, D. K. 2010b. Depth of electrode insertion and postoperative performance in humans with cochlear implants: A histopathologic study. *Audiol Neurootol,* 15**,** 323-31.

Lehnhardt, E. 1993a. Intracochlear electrode placement facilitated by healon. *Adv Otorhinolaryngol,* 48**,** 62-4.

Lehnhardt, E. 1993b. [intracochlear placement of cochlear implant electrodes in soft surgery technique]. *Hno,* 41**,** 356-9.

Li, P. M., Somdas, M. A., Eddington, D. K. & Nadol, J. B., Jr. 2007. Analysis of intracochlear new bone and fibrous tissue formation in human subjects with cochlear implants. *Ann Otol Rhinol Laryngol,* 116**,** 731-8.

Liu, W., Atturo, F., Aldaya, R., Santi, P., Cureoglu, S., Obwegeser, S., Glueckert, R., Pfaller, K., Schrott-Fischer, A. & Rask-Andersen, H. 2015a. Macromolecular organization and fine structure of the human basilar membrane - relevance for cochlear implantation. *Cell Tissue Res,* 360**,** 245-62.

Liu, Y., Jolly, C., Braun, S., Janssen, T., Scherer, E., Steinhoff, J., Ebenhoch, H., Lohner, A., Stark, T. & Kiefer, J. 2015b. Effects of a dexamethasone-releasing implant on cochleae: A functional, morphological and pharmacokinetic study. *Hearing Research,* 327**,** 89-101.

Mahmoud, A. F., Massa, S. T., Douberly, S. L., Montes, M. L. & Ruckenstein, M. J. 2014. Safety, efficacy, and hearing preservation using an integrated electro-acoustic stimulation hearing system. *Otology & Neurotology,* 35**,** 1421-5.

Manrique, M., Picciafuoco, S., Manrique, R., Sanhueza, I., Dominguez, P., Perez, N., Zubieta, J. L. & De Abajo, J. 2014. Atraumaticity study of 2 cochlear implant electrode arrays. *Otology & Neurotology,* 35**,** 619-28.

Marx, M., Risi, F., Escude, B., Durmo, I., James, C., Lauwers, F., Deguine, O. & Fraysse, B. 2014. Reliability of cone beam computed tomography in scalar localization of the electrode array: A radio histological study. *Eur Arch Otorhinolaryngol,* 271**,** 673-9.

Mclean, T., Clamp, P., Campbell, L., Hampson, A., Chambers, S., Collins, A., Bester, C. & O'leary, S. 2021. The effect of different round window sealants on cochlear mechanics over time. *Otol Neurotol,* 42**,** 1253-1260.

Menardo, J., Tang, Y., Ladrech, S., Lenoir, M., Casas, F., Michel, C., Bourien, J., Ruel, J., Rebillard, G., Maurice, T., Puel, J. L. & Wang, J. 2012. Oxidative stress, inflammation, and autophagic stress as the key mechanisms of premature age-related hearing loss in samp8 mouse cochlea. *Antioxid Redox Signal,* 16**,** 263-74.

Mick, P., Amoodi, H., Shipp, D., Friesen, L., Symons, S., Lin, V., Nedzelski, J. & Chen, J. 2014. Hearing preservation with full insertion of the flexsoft electrode. *Otology & Neurotology,* 35**,** e40-4.

Moons, K. G., Donders, R. A., Stijnen, T. & Harrell, F. E., Jr. 2006. Using the outcome for imputation of missing predictor values was preferred. *J Clin Epidemiol,* 59**,** 1092-101.

Morrel, W. G., Holder, J. T., Dawant, B. M., Noble, J. H. & Labadie, R. F. 2020. Effect of scala tympani height on insertion depth of straight cochlear implant electrodes. *Otolaryngol Head Neck Surg,* 162**,** 718-724.

Mosnier, I., Sterkers, O., Bebear, J.-P., Godey, B., Robier, A., Deguine, O., Fraysse, B., Bordure, P., Mondain, M., Bouccara, D., Bozorg-Grayeli, A., Borel, S., Ambert-Dahan, E. & Ferrary, E. 2009. Speech performance and sound localization in a complex noisy environment in bilaterally implanted adult patients. *Audiology & neurotology,* 14**,** 106-114.

Moteki, H., Nishio, S. Y., Miyagawa, M., Tsukada, K., Iwasaki, S. & Usami, S. I. 2016. Long-term results of hearing preservation cochlear implant surgery in patients with residual low frequency hearing. *Acta Oto-Laryngologica***,** 1-6.

Mowry, S. E., Woodson, E. & Gantz, B. J. 2012. New frontiers in cochlear implantation: Acoustic plus electric hearing, hearing preservation, and more. *Otolaryngologic Clinics of North America,* 45**,** 187-203.

Naderpour, M., Aminzadeh, Z., Jabbari Moghaddam, Y., Pourshiri, B., Ariafar, A. & Akhondi, A. 2020. Comparison of the pediatric cochlear implantation using round window and cochleostomy. *Iran J Otorhinolaryngol,* 32**,** 3-10.

Nadol, J. B., Jr. 1997. Patterns of neural degeneration in the human cochlea and auditory nerve: Implications for cochlear implantation. *Otolaryngol Head Neck Surg,* 117**,** 220-8.

Nadol, J. B., Jr. & Eddington, D. K. 2004. Histologic evaluation of the tissue seal and biologic response around cochlear implant electrodes in the human. *Otol Neurotol,* 25**,** 257-62.

Nadol, J. B., Jr. & Eddington, D. K. 2006. Histopathology of the inner ear relevant to cochlear implantation. *Adv Otorhinolaryngol,* 64**,** 31-49.

National Institute on Deafness and Other Communication Disorders. 2019. *Cochlear implants* [Online]. Available: https://www.nidcd.nih.gov/health/cochlear-implants [Accessed 25th March 2022].

Nguyen, S., Cloutier, F., Philippon, D., Cote, M., Bussieres, R. & Backous, D. D. 2016. Outcomes review of modern hearing preservation technique in cochlear implant. *Auris Nasus Larynx,* 43**,** 485-8.

Nice 2019. Cochlear implants for children and adults with severe to profound deafness.

Nordfalk, K. F., Rasmussen, K., Hopp, E., Bunne, M., Silvola, J. T. & Jablonski, G. E. 2016. Insertion depth in cochlear implantation and outcome in residual hearing and vestibular function. *Ear Hear,* 37**,** e129-37.

O'connell, B. P., Cakir, A., Hunter, J. B., Francis, D. O., Noble, J. H., Labadie, R. F., Zuniga, G., Dawant, B. M., Rivas, A. & Wanna, G. B. 2016a. Electrode location and angular insertion depth are predictors of audiologic outcomes in cochlear implantation. *Otol Neurotol,* 37**,** 1016-23.

O'connell, B. P., Hunter, J. B., Gifford, R. H., Rivas, A., Haynes, D. S., Noble, J. H. & Wanna, G. B. 2016b. Electrode location and audiologic performance after cochlear implantation: A comparative study between nucleus ci422 and ci512 electrode arrays. *Otol Neurotol,* 37**,** 1032-5.

O'connell, B. P., Hunter, J. B., Haynes, D. S., Holder, J. T., Dedmon, M. M., Noble, J. H., Dawant, B. M. & Wanna, G. B. 2016c. Insertion depth impacts speech perception and hearing preservation for lateral wall electrodes. *Laryngoscope,* 17**,** 17.

O'connell, B. P., Hunter, J. B. & Wanna, G. B. 2016d. The importance of electrode location in cochlear implantation. *Laryngoscope Investig Otolaryngol,* 1**,** 169-174.

O'leary, S. J., Choi, J., Brady, K., Matthews, S., Ozdowska, K. B., Payne, M., Mclean, T., Rousset, A., Lo, J., Creber, N., Tari, S., Dowell, R. & Briggs, R. 2021. Systemic methylprednisolone for hearing preservation during cochlear implant surgery: A double blinded placebo-controlled trial. *Hear Res,* 404**,** 108224.

O'leary, S. J., Monksfield, P., Kel, G., Connolly, T., Souter, M. A., Chang, A., Marovic, P., O'leary, J. S., Richardson, R. & Eastwood, H. 2013. Relations between cochlear histopathology and hearing loss in experimental cochlear implantation. *Hear Res,* 298**,** 27-35.

Papsin, B. C. 2005. Cochlear implantation in children with anomalous cochleovestibular anatomy. *Laryngoscope,* 115**,** 1-26.

Pau, H. W., Just, T., Bornitz, M., Lasurashvilli, N. & Zahnert, T. 2007. Noise exposure of the inner ear during drilling a cochleostomy for cochlear implantation. *Laryngoscope,* 117**,** 535-40.

Perenyi, A., Bella, Z., Barath, Z., Magyar, P., Nagy, K. & Rovo, L. 2016. [role of cone-beam computed tomography in diagnostic otorhinolaryngological imaging]. *Orvosi Hetilap,* 157**,** 52-8.

Pringle, M. B. & Konieczny, K. M. 2021. Anatomy of the round window region with relation to selection of entry site into the scala tympani. *Laryngoscope,* 131**,** E598-e604.

Quesnel, S., Nguyen, Y., Elmaleh, M., Grayeli, A. B., Ferrary, E., Sterkers, O. & Couloigner, V. 2011. Effects of systemic administration of methylprednisolone on residual hearing in an animal model of cochlear implantation. *Acta Otolaryngol,* 131**,** 579-84.

Radeloff, A., Shehata-Dieler, W., Scherzed, A., Rak, K., Harnisch, W., Hagen, R. & Mlynski, R. 2012. Intraoperative monitoring using cochlear microphonics in cochlear implant patients with residual hearing. *Otol Neurotol,* 33**,** 348-54.

Rader, T., Adel, Y., Fastl, H. & Baumann, U. 2015. Speech perception with combined electric-acoustic stimulation: A simulation and model comparison. *Ear & Hearing,* 36**,** e314-25.

Rader, T., Fastl, H. & Baumann, U. 2013. Speech perception with combined electric-acoustic stimulation and bilateral cochlear implants in a multisource noise field. *Ear Hear,* 34**,** 324-32.

Rajan, G. P., Kontorinis, G. & Kuthubutheen, J. 2013. The effects of insertion speed on inner ear function during cochlear implantation: A comparison study. *Audiol Neurootol,* 18**,** 17-22.

Rajan, G. P., Kuthubutheen, J., Hedne, N. & Krishnaswamy, J. 2012. The role of preoperative, intratympanic glucocorticoids for hearing preservation in cochlear implantation: A prospective clinical study. *Laryngoscope,* 122**,** 190-5.

Rajput, M. & Nilakantan, A. 2019. Functional outcomes in cochleostomy and round window insertion technique: Difference or no difference? *Indian J Otolaryngol Head Neck Surg,* 71**,** 1615-1620.

Ramos, B. F., Tsuji, R. K., Bento, R. F., Goffi-Gomez, M. V., Ramos, H. F., Samuel, P. A. & Brito, R. 2015. Hearing preservation using topical dexamethasone alone and associated with hyaluronic acid in cochlear implantation. *Acta Oto-Laryngologica,* 135**,** 473-7.

Raphael, Y. & Altschuler, R. A. 2003. Structure and innervation of the cochlea. *Brain Res Bull,* 60**,** 397-422.

Rauch, S. D., Halpin, C. F., Antonelli, P. J., Babu, S., Carey, J. P., Gantz, B. J., Goebel, J. A., Hammerschlag, P. E., Harris, J. P., Isaacson, B., Lee, D., Linstrom, C. J., Parnes, L. S., Shi, H., Slattery, W. H., Telian, S. A., Vrabec, J. T. & Reda, D. J. 2011. Oral vs intratympanic corticosteroid therapy for idiopathic sudden sensorineural hearing loss: A randomized trial. *JAMA,* 305**,** 2071-2079.

Rebscher, S. J., Hetherington, A., Bonham, B., Wardrop, P., Whinney, D. & Leake, P. A. 2008. Considerations for design of future cochlear implant electrode arrays: Electrode array

stiffness, size, and depth of insertion. *Journal of Rehabilitation Research & Development,* 45**,** 731-47.

Reiss, L. A., Turner, C. W., Erenberg, S. R. & Gantz, B. J. 2007. Changes in pitch with a cochlear implant over time. *J Assoc Res Otolaryngol,* 8**,** 241-57.

Renauld, J. M. & Basch, M. L. 2021. Congenital deafness and recent advances towards restoring hearing loss. *Current protocols,* 1**,** e76-e76.

Richardson, W. S., Wilson, M. C., Nishikawa, J. & Hayward, R. S. 1995. The well-built clinical question: A key to evidence-based decisions. *ACP J Club,* 123**,** A12-3.

Rivas, A., Cakir, A., Hunter, J. B., Labadie, R. F., Zuniga, M. G., Wanna, G. B., Dawant, B. M. & Noble, J. H. 2017. Automatic cochlear duct length estimation for selection of cochlear implant electrode arrays. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology,* 38**,** 339-346.

Roland, J. T., Jr. 2005. A model for cochlear implant electrode insertion and force evaluation: Results with a new electrode design and insertion technique. *Laryngoscope,* 115**,** 1325-39.

Roland, P. S. & Wright, C. G. 2006. Surgical aspects of cochlear implantation: Mechanisms of insertional trauma. *Advances in Oto-Rhino-Laryngology,* 64**,** 11-30.

Roland, P. S., Wright, C. G. & Isaacson, B. 2007. Cochlear implant electrode insertion: The round window revisited. *Laryngoscope,* 117**,** 1397-402.

Rowe, D., Chambers, S., Hampson, A., Eastwood, H., Campbell, L. & O'leary, S. 2016a. Delayed low frequency hearing loss caused by cochlear implantation interventions via the round window but not cochleostomy. *Hear Res,* 333**,** 49-57.

Rowe, D., Chambers, S., Hampson, A., Eastwood, H. & O'leary, S. 2016b. The effect of round window sealants on delayed hearing loss in a guinea pig model of cochlear implantation. *Otol Neurotol,* 37**,** 1024-31.

Rubin, D. B. 1987. Multiple imputation for survey nonresponse. New York: Wiley.

Ruivo, J., Mermuys, K., Bacher, K., Kuhweide, R., Offeciers, E. & Casselman, J. W. 2009. Cone beam computed tomography, a low-dose imaging technique in the postoperative assessment of cochlear implantation. *Otol Neurotol,* 30**,** 299-303.

Saeed, S. R., Selvadurai, D., Beale, T., Biggs, N., Murray, B., Gibson, P., Risi, F. & Boyd, P. 2014. The use of cone-beam computed tomography to determine cochlear implant electrode position in human temporal bones. *Otology & Neurotology,* 35**,** 1338-44.

Saenz, M. & Langers, D. R. 2014. Tonotopic mapping of human auditory cortex. *Hear Res,* 307**,** 42-52.

Saleh, S. 2013. *The efficacy of fitting cochlear implants based on pitch perception.* PhD thesis, University College London.

Santa Maria, P. L., Domville-Lewis, C., Sucher, C. M., Chester-Browne, R. & Atlas, M. D. 2013. Hearing preservation surgery for cochlear implantation--hearing and quality of life after 2 years. *Otol Neurotol,* 34**,** 526-31.

Santa Maria, P. L., Gluth, M. B., Yuan, Y., Atlas, M. D. & Blevins, N. H. 2014. Hearing preservation surgery for cochlear implantation: A meta-analysis. *Otol Neurotol,* 35**,** e256-69.

Seyyedi, M. & Nadol Jr, J. B. 2013. Does residual spiral ganglion cell count predict performance in patients with bilateral multichannel cochlear implants? *Otolaryngology - Head and Neck Surgery (United States),* 1)**,** P97.

Shaddock, L. C., Wright, C. G. & Hamernik, R. P. 1985. A morphometric study of microvascular pathology following experimental rupture of reissner's membrane. *Hear Res,* 20**,** 119-29.

Shishodia, S. & Saurav, D. 2021. Round window versus conventional bony cochleostomy technique in pediatric cochlear implantation; a randomized controlled double blinded trial. *International Journal of Otorhinolaryngology and Head and Neck Surgery,* 7**,** 1297.

Skarzynski, H., Lorens, A., Matusiak, M., Porowski, M., Skarzynski, P. H. & James, C. J. 2012. Partial deafness treatment with the nucleus straight research array cochlear implant. *Audiology & Neuro-Otology,* 17**,** 82-91.

Skarzynski, H., Lorens, A., Matusiak, M., Porowski, M., Skarzynski, P. H. & James, C. J. 2014. Cochlear implantation with the nucleus slim straight electrode in subjects with residual low-frequency hearing. *Ear & Hearing,* 16**,** 16.

Skarzynski, H., Lorens, A. & Piotrowska, A. 2003. A new method of partial deafness treatment. *Med Sci Monit,* 9**,** Cs20-4.

Skarzynski, H., Lorens, A., Piotrowska, A. & Anderson, I. 2007. Preservation of low frequency hearing in partial deafness cochlear implantation (pdci) using the round window surgical approach. *Acta Otolaryngol,* 127**,** 41-8.

Skarzynski, H., Lorens, A., Piotrowska, A. & Podskarbi-Fayette, R. 2009. Results of partial deafness cochlear implantation using various electrode designs. *Audiology & Neuro-Otology,* 14 Suppl 1**,** 39-45.

Skarzynski, H., Matusiak, M., Lorens, A., Furmanek, M., Pilka, A. & Skarzynski, P. H. 2016. Preservation of cochlear structures and hearing when using the nucleus slim straight (ci422) electrode in children. *Journal of Laryngology & Otology,* 130**,** 332-9.

Skarzynski, H., Van De Heyning, P., Agrawal, S., Arauz, S. L., Atlas, M., Baumgartner, W., Caversaccio, M., De Bodt, M., Gavilan, J., Godey, B., Green, K., Gstoettner, W., Hagen, R., Han, D. M., Kameswaran, M., Karltorp, E., Kompis, M., Kuzovkov, V., Lassaletta, L., Levevre, F., Li, Y., Manikoth, M., Martin, J., Mlynski, R., Mueller, J., O'driscoll, M., Parnes, L., Prentiss, S., Pulibalathingal, S., Raine, C. H., Rajan, G., Rajeswaran, R., Rivas, J. A., Rivas, A., Skarzynski, P. H., Sprinzl, G., Staecker, H., Stephan, K., Usami, S., Yanov, Y., Zernotti, M. E., Zimmermann, K., Lorens, A. & Mertens, G. 2013. Towards a consensus on a hearing preservation classification system. *Acta Otolaryngol Suppl***,** 3-13.

Skinner, M. W., Holden, T. A., Whiting, B. R., Voie, A. H., Brunsden, B., Neely, J. G., Saxon, E. A., Hullar, T. E. & Finley, C. C. 2007. In vivo estimates of the position of advanced bionics electrode arrays in the human cochlea. *Ann Otol Rhinol Laryngol Suppl,* 197**,** 2-24.

Snels, C., Inthout, J., Mylanus, E., Huinck, W. & Dhooge, I. 2019. Hearing preservation in cochlear implant surgery: A meta-analysis. *Otol Neurotol,* 40**,** 145-153.

Soda-Merhy, A., Gonzalez-Valenzuela, L. & Tirado-Gutierrez, C. 2008. Residual hearing preservation after cochlear implantation: Comparison between straight and perimodiolar implants. *Otolaryngology - Head & Neck Surgery,* 139**,** 399-404.

Souter, M., Eastwood, H., Marovic, P., Kel, G., Wongprasartsuk, S., Ryan, A. F. & O'leary, S. J. 2012. Systemic immunity influences hearing preservation in cochlear implantation. *Otology & Neurotology,* 33**,** 532-8.

Spoendlin, H. 1984. Factors inducing retrograde degeneration of the cochlear nerve. *Ann Otol Rhinol Laryngol Suppl,* 112**,** 76-82.

Sterkers, O., Ferrary, E. & Amiel, C. 1988. Production of inner ear fluids. *Physiological reviews,* 68**,** 1083-1128.

Stuermer, K., Winter, T., Nachtsheim, L., Klussmann, J. P. & Luers, J. C. 2021. Round window accessibility during cochlear implantation. *European Archives of Oto-Rhino-Laryngology,* 278**,** 363-370.

Sugawara, M., Corfas, G. & Liberman, M. C. 2005. Influence of supporting cells on neuronal degeneration after hair cell loss. *J Assoc Res Otolaryngol,* 6**,** 136-47.

Suhling, M. C., Lesinski-Schiedat, A., Lenarz, T., Salcher, R., Schussler, M. & Bardt, M. 2019. Hearing preservation potential after cochlear-implantation: Comparison of 6 lateral-wall electrode arrays. *Laryngo- Rhino- Otologie,* 98 (Supplement 2)**,** S273.

Suhling, M. C., Majdani, O., Salcher, R., Leifholz, M., Buchner, A., Lesinski-Schiedat, A. & Lenarz, T. 2016. The impact of electrode array length on hearing preservation in cochlear implantation. *Otol Neurotol,* 37**,** 1006-15.

Sun, C. H., Hsu, C. J., Chen, P. R. & Wu, H. P. 2015. Residual hearing preservation after cochlear implantation via round window or cochleostomy approach. *Laryngoscope,* 125**,** 1715-9.

Suresh, K. 2011. An overview of randomization techniques: An unbiased assessment of outcome in clinical research. *Journal of human reproductive sciences,* 4**,** 8-11.

Svrakic, M., Roland, J. T., Jr., Mcmenomey, S. O. & Svirsky, M. A. 2016. Initial operative experience and short-term hearing preservation results with a mid-scala cochlear implant electrode array. *Otology & Neurotology,* 37**,** 1549-1554.

Sweeney, A. D., Carlson, M. L., Zuniga, M. G., Bennett, M. L., Wanna, G. B., Haynes, D. S. & Rivas, A. 2015. Impact of perioperative oral steroid use on low-frequency hearing preservation after cochlear implantation. *Otology & Neurotology,* 36**,** 1480-5.

Tamir, S., Ferrary, E., Borel, S., Sterkers, O. & Bozorg Grayeli, A. 2012. Hearing preservation after cochlear implantation using deeply inserted flex atraumatic electrode arrays. *Audiol Neurootol,* 17**,** 331-7.

Tan, L., Holland, S. K., Deshpande, A. K., Chen, Y., Choo, D. I. & Lu, L. J. 2015. A semi-supervised support vector machine model for predicting the language outcomes following cochlear implantation based on pre-implant brain fmri imaging. *Brain Behav,* 5**,** e00391.

Trotter, M. I. & Briggs, R. J. 2010. Cochlear implantation in neurofibromatosis type 2 after radiation therapy. *Otol Neurotol,* 31**,** 216-9.

Turner, C., Gantz, B. J. & Reiss, L. 2008. Integration of acoustic and electrical hearing. *Journal of Rehabilitation Research & Development,* 45**,** 769-78.

Usami, S., Moteki, H., Suzuki, N., Fukuoka, H., Miyagawa, M., Nishio, S. Y., Takumi, Y., Iwasaki, S. & Jolly, C. 2011. Achievement of hearing preservation in the presence of an electrode covering the residual hearing region. *Acta Otolaryngol,* 131**,** 405-12.

Usami, S., Moteki, H., Tsukada, K., Miyagawa, M., Nishio, S. Y., Takumi, Y., Iwasaki, S., Kumakawa, K., Naito, Y., Takahashi, H., Kanda, Y. & Tono, T. 2014a. Hearing preservation and clinical outcome of 32 consecutive electric acoustic stimulation (eas) surgeries. *Acta Otolaryngol,* 134**,** 717-27.

Usami, S. I., Moteki, H., Tsukada, K., Miyagawa, M., Nishio, S. Y., Takumi, Y., Iwasaki, S., Kumakawa, K., Naito, Y., Takahashi, H., Kanda, Y. & Tono, T. 2014b. Hearing preservation and clinical outcome of 32 consecutive electric acoustic stimulation (eas) surgeries. *Acta Oto-Laryngologica,* 134**,** 717-727.

Van De Water, T. R., Abi Hachem, R. N., Dinh, C. T., Bas, E., Haake, S. M., Hoosien, G., Vivero, R., Chan, S., He, J., Eshraghi, A. A., Angeli, S. I., Telischi, F. F. & Balkany, T. J. 2010a. Conservation of hearing and protection of auditory hair cells against trauma-induced losses by local dexamethasone therapy: Molecular and genetic mechanisms. *Cochlear Implants Int,* 11 Suppl 1**,** 42-55.

Van De Water, T. R., Dinh, C. T., Vivero, R., Hoosien, G., Eshraghi, A. A. & Balkany, T. J. 2010b. Mechanisms of hearing loss from trauma and inflammation: Otoprotective therapies from the laboratory to the clinic. *Acta Oto-Laryngologica,* 130**,** 308-11.

Van Der Marel, K. S., Briaire, J. J., Verbist, B. M., Muurling, T. J. & Frijns, J. H. M. 2015. The influence of cochlear implant electrode position on performance. *Audiology and Neurotology,* 20**,** 202-211.

Verschuur, C., Causon, A., Green, K., Bruce, I., Agyemang-Prempeh, A. & Newman, T. 2015. The role of the immune system in hearing preservation after cochlear implantation. *Cochlear Implants International,* 16 Suppl 1**,** S40-2.

Verschuur, H. P., De Wever, W. W. & Van Benthem, P. P. 2004. Antibiotic prophylaxis in clean and clean-contaminated ear surgery. *Cochrane Database Syst Rev***,** Cd003996.

Vickers, D., De Raeve, L. & Graham, J. 2016. International survey of cochlear implant candidacy. *Cochlear Implants Int,* 17 Suppl 1**,** 36-41.

Voldrich, L. 1978. Mechanical properties of basilar membrane. *Acta Otolaryngol,* 86**,** 331-5.

Von Ilberg, C., Kiefer, J., Tillein, J., Pfenningdorff, T., Hartmann, R., Sturzebecher, E. & Klinke, R. 1999. Electric-acoustic stimulation of the auditory system. New technology for severe hearing loss. *ORL J Otorhinolaryngol Relat Spec,* 61**,** 334-40.

Voss, S. E., Rosowski, J. J. & Peake, W. T. 1996. Is the pressure difference between the oval and round windows the effective acoustic stimulus for the cochlea? *The Journal of the Acoustical Society of America,* 100**,** 1602-1616.

Vynnycky, E., Adams, E. J., Cutts, F. T., Reef, S. E., Navar, A. M., Simons, E., Yoshida, L. M., Brown, D. W., Jackson, C., Strebel, P. M. & Dabbagh, A. J. 2016. Using seroprevalence and immunisation coverage data to estimate the global burden of congenital rubella syndrome, 1996-2010: A systematic review. *PLoS One,* 11**,** e0149160.

Wanna, G. B., Noble, J. H., Carlson, M. L., Gifford, R. H., Dietrich, M. S., Haynes, D. S., Dawant, B. M. & Labadie, R. F. 2014. Impact of electrode design and surgical approach on scalar location and cochlear implant outcomes. *Laryngoscope,* 124 Suppl 6**,** S1-7.

Wanna, G. B., Noble, J. H., Gifford, R. H., Dietrich, M. S., Sweeney, A. D., Zhang, D., Dawant, B. M., Rivas, A. & Labadie, R. F. 2015. Impact of intrascalar electrode location, electrode type, and angular insertion depth on residual hearing in cochlear implant patients: Preliminary results. *Otol Neurotol,* 36**,** 1343-8.

Wardrop, P., Whinney, D., Rebscher, S. J., Luxford, W. & Leake, P. 2005. A temporal bone study of insertion trauma and intracochlear position of cochlear implant electrodes. Ii: Comparison of spiral clarion and hifocus ii electrodes. *Hear Res,* 203**,** 68-79.

Wever, E. G., Mccormick, J. G., Palin, J. & Ridgway, S. H. 1971. Cochlea of the dolphin, tursiops truncatus: The basilar membrane. *Proceedings of the National Academy of Sciences - PNAS,* 68**,** 2708-2711.

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Wikimedia Commons Contributors 2022b. Earanatomy synchrony dlcoil rw. Wikimedia Commons, the free media repository.

Wilson, B. S. & Dorman, M. 2009. The design of cochlear implants. *Cochlear implants: Principles and practices.* 2nd ed.: Wolters Kluwer Health.

Wilson, B. S. & Dorman, M. F. 2008. Cochlear implants: A remarkable past and a brilliant future. *Hear Res,* 242**,** 3-21.

Wolfe, J. & Schafer, E. C. 2015. *Programming cochlear implants / jace wolfe, phd, erin c. Schafer, phd,* San Diego, CA, Plural Publishing.

Wright, A. 1983. Scanning electron microscopy of the human organ of corti. *Journal of the Royal Society of Medicine,* 76**,** 269-278.

Wright, T. & Valentine, P. 2008. The anatomy and embryology of the external and middle ear. *Gleeson M. Scott-Brown's Otorhinolaryngology, Head and Neck Surgery,* 3**,** 3105-3125.

Wurfel, W., Lanfermann, H., Lenarz, T. & Majdani, O. 2014a. Cochlear length determination using cone beam computed tomography in a clinical setting. *Hear Res,* 316**,** 65-72.

Wurfel, W., Lanfermann, H., Lenarz, T. & Majdani, O. 2014b. Cochlear length determination using cone beam computed tomography in a clinical setting. *Hearing Research,* 316**,** 65-72.

Xu, J., Xu, S. A., Cohen, L. T. & Clark, G. M. 2000. Cochlear view: Postoperative radiography for cochlear implantation. *Am J Otol,* 21**,** 49-56.

Yang, G. S., Song, H. T., Keithley, E. M. & Harris, J. P. 2000. Intratympanic immunosuppressives for prevention of immune-mediated sensorineural hearing loss. *Am J Otol,* 21**,** 499-504.

Ye, Q., Tillein, J., Hartmann, R., Gstoettner, W. & Kiefer, J. 2007. Application of a corticosteroid (triamcinolon) protects inner ear function after surgical intervention. *Ear Hear,* 28**,** 361-9.

Yost, W. A. 2001. Fundamentals of hearing: An introduction. Acoustical Society of America.

Yukawa, K., Cohen, L., Blamey, P., Pyman, B., Tungvachirakul, V. & O'leary, S. 2004. Effects of insertion depth of cochlear implant electrodes upon speech perception. *Audiology and Neurotology,* 9**,** 163-172.

Zhou, L., Friedmann, D. R., Treaba, C., Peng, R. & Roland, J. T. 2014. Does cochleostomy location influence electrode trajectory and intracochlear trauma? *Cochlear Implants Int,* 15 Suppl 1**,** S8-s10.