Electrically evoked compound action potentials as a tool for programming cochlear implants in children

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“Everyone carries a room about inside him. This fact can even be proved by means of the sense of hearing. If someone walks fast and one pricks up one’s ears and listens, say in the night, when everything round about is quiet, one hears, for instance, the rattling of a mirror not quite firmly fastened to the wall.”

Franz Kafka, Blue Octavo Notebooks

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ABSTRACT

Cochlear implants are generally the best treatment for young children with a profound hearing loss (or worse) when ordinary hearing aids cannot provide enough auditory stimulation. For these youngest recipients, there must be a valid rationale for deciding the level of stimulation. The aim of this thesis was to investigate aspects that are clinically relevant when programming CIs for young children and choosing implant type for this group, with focus on the electrically evoked compound action potential (ECAP) as a basis for programming stimulation levels. The four studies that constitutes this thesis all regards different properties of the ECAP measurement, though, Study IV were more focused on the impedance related issues for two implant types from Cochlear Ltd. Study I and IV were comprised of both children and adults, Study III only included children, whereas Study II only included adults due to its design and aim. Study I to III were all prospective studies, whereas Study IV was of retrospective design. The results from Study I showed that the ECAP measurement should be re-recorded at least one month after activation of the implant to get a reliable response. For Study II, the result showed that it was possible to apply the profile from the ECAP recording to the subjective thresholds, although, a modification of the ECAP-profile was needed to get an acceptable agreement. In Study III, the result showed that, on group level, the children performed as well with their original ECAP-based setting as with the study implemented subjective setting. However, intra-individual variances between the original ECAP-based and the subjectively based setting was very large, ≥30 current levels, for a few of the subjects. The results from Study III further indicated a possible, small adaptation within the auditory nerve to changes in stimulation levels. Study IV showed that impedance related issues in general was low for both implant types concerned, but that the slim lateral wall (LW) implant for the children was, more likely to get higher impedance levels and electrode failures, compared to the perimodiolar (PM) implant. After five years of usage the probability of still having the default pulse width for the PM implant was 94%, whereas the slim LW implant had dropped to 80% ($p<0.001$) for the children. The overall results show that the ECAP measurement in general can be a valid tool for programming stimulation levels for young children with CIs, and additionally, that care need to be taken when choosing implants for young recipients and acknowledge limitations that might rise after activation.

Keywords: Cochlear implants, ECAP, children, impedance, T-levels, C-levels

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SAMMANFATTNING PÅ SVENSKA

För barn som har en grav eller ännu mer uttalad hörselnedsättning där vanliga hörapparater inte bidrar tillräckligt till hörandet kan ett cochleaimplantat (CI) till viss del återskapa den hörsel som gått förlorad. Barn får oftast CI mycket tidigt i livet, därför måste det finnas bra sätt att bestämma graden av stimulering för dessa yngsta användare. Syftet med denna avhandling är att undersöka aspekter som är kliniskt relevanta vid programmering av stimuleringsnivåerna för barn med CI. Denna avhandling utgår från användning av den elektrofysiologiska mätningen *electrically evoked compound action potential* (ECAP) för att programmera stimuleringsnivåerna. De fyra delstudierna som ingår i denna avhandling behandlar alla olika aspekter gällande ECAP-mätningen, även om delstudie IV är mer inriktad på impedansmätningar. I delstudie I och IV medverkade både barn och vuxna, i delstudie III inkluderades endast barn, medan delstudie II endast inkluderade vuxna på grund av studiens utformning och syfte. Delstudie I, II och III var prospektiva studier, medan delstudie IV var en retrospektiv studie. Resultatet från delstudie I visade att ECAP-mätningen bör utföras minst en månad efter aktivering av implantatet för att ge ett tillförlitligt resultat. För delstudie II visade resultatet att det var möjligt att använda profilen från ECAP-mätningen för att förutsäga profilen för de subjektiva tröskelvärdena, dock krävdes en modifiering av ECAP-resultatet för att få ett godtagbart resultat. I delstudie III fick barn själva medverka till inställning av subjektiva stimuleringsnivåer. Detta för att jämföra resultatet från den inställningen med de ECAP-baserade stimuleringsnivåer de tidigare använt. Den ECAP-baserade inställningen fungerade bra på gruppnivå, dock var den inomindividuella skillnaden mellan den ECAP-baserade inställningen och den subjektivt baserade inställningen mycket stora för några av deltagarna. Resultatet indikerade att en subjektiv inställning bör tillämpas när en sådan är möjlig att uppnå. Resultaten från delstudie III indikerade vidare att det i hörselnerven antagligen skedde en liten anpassning efter stimuleringsnivån. Delstudie IV visade att det tunna raka implantatet från Cochlear Ltd. var mer benäget att drabbas av impedansrelaterade problem, jämfört med det förböjda implantatet från samma tillverkare. Efter fem års användning var sannolikheten att fortfarande använda den förinställda pulsbredden signifikant lägre för den tunna raka elektroden jämfört med den förböjda implantattypen.

Det övergripande resultatet visar att ECAP-mätningen överlag fungerar bra som utgångspunkt för att programmera stimuleringsnivåer för små barn med CI. Dessutom att val av implantat bör göras med omsorg för dessa unga användare med tanke på de förändringar som kan uppkomma efter aktiveringen.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Björsne, A., Magnusson, M. When Can Stable AutoNRT Thresholds be Expected? A Clinical Implication When Fitting Young Children. Journal of the American Academy of Audiology, 2020; 31:69–75.

II. Björsne, A., Magnusson, M. The relationship between AutoNRT thresholds and subjective programming levels revisited.
Submitted for publication

III. Björsne, A., Hällgren, M., Magnusson, M. Validity of ECAP thresholds for predicting cochlear implant settings for young children – Long-term follow-up and comparison with subjectively obtained T- and C-levels.
In manuscript

IV. Björsne, A., Hällgren, M., Johansson, B., Eklöf, M., Magnusson, M. Impedance changes in cochlear implants after activation – A retrospective study of cochlear implants from Cochlear Ltd for children and adults.
In manuscript

CONTENT

ABBREVIATIONS

AGF	Amplitude growth function
CA	Contour advance
CI	Cochlear implant
CL	Current level
C-level	Comfort level
CG	Common ground
dB	Decibel
EABR	Electrically evoked auditory brainstem response
ECAP	Electrically evoked compound action potential
ESRT	Electrically evoked stapedial reflex threshold
HINT-C	Hearing in noise test developed for children
HINT-C-Quiet	HINT-C sentences presented without competing noise
HL	Hearing level
Hz	Hertz
IHC	Inner hair cells
IQR	Interquartile range
kΩ	Kiloohm
MAP	A common term for programming parameters
MP1	Monopolar
MP1+2	Monopolar 1 and 2

MP2	Monopolar 2
OHC	Outer hair cells
RMSE	Root mean square error
SD	Standard deviation
SE	Standard error
SPL	Sound pressure level
SS	SlimStraight
T-level	Threshold level

1 INTRODUCTION

Cochlear implants (CI) are a highly valid treatment for children born with a profound hearing loss or worse. Research has shown that it is beneficial for the child's language development, and related aspects to receive CIs as soon as possible, which in some cases can be as early as around 6 months of age (Naik et al., 2021; Purcell et al., 2021). In the inner ear's cochlea there are sensory cells that activate the neurons within the auditory nerve when exposed to sound vibrations. However, for most children born with a permanent hearing loss these sensory cells are sparse or completely missing. If there are too few sensory cells, acoustic amplification of the sound will not generate enough auditory stimulation. For these children a CI can be helpful since it stimulates the auditory nerve from its place within the cochlea, somewhat comparable to how the sensory cells would have. Although, a CI cannot fully emulate the fine structure or resolution of the natural hearing, it most often creates a perception of sound that facilitate speech and language understanding close to or on the same level as the child's normal hearing peers. How much the implant should stimulate the auditory nerve need to be set individually for each child and implanted ear. This can be problematic for the youngest recipients since they do not have the ability to describe how they perceive the sound through the implant. If stimulation levels are not set properly the implant will generate poor audibility.

The main topic for this thesis is the programming of stimulation levels for CIs implanted in young children and issues that affect audibility with the CI. The aim is to broaden the knowledge of how to use the ECAP measurement as a tool when determining stimulation levels for the youngest recipients, as well as matters that is affected by the choice of implant.

1.1 SOUND AND HEARING

The basic definition of sound is vibration that propagates through a medium, such as a gas like air. Sound is often described according to two qualities, its intensity and its frequency composition. The intensity is expressed in decibels (dB), which is a relative measure on a logarithmic scale, and used because the variance in magnitude between the softest sound that can be perceived and the loudest sound is 1 to 10 million. The logarithmic scale makes this variation manageable. The decibel itself has no dimensions and must relate to a reference value, which often is the sound pressure level (SPL) of 20 micropascal, generally shortened to dB SPL. When performing hearing measurements, decibel hearing level (dB HL) is used, which has reference values adjusted to the normal human hearing. Frequency, on the other hand is how fast the vibration moves back and forth, and is described as how long it takes for the vibration to complete one cycle. The unit for frequency is Hertz (Hz) and is defined as cycles per second. One Hz equals one full cycle with a duration of one second, and 1000 Hz equals 1000 full cycles in one second (Gelfand, 2018). A difference in frequency is perceived as a change of pitch; low frequency sounds are perceived as low pitched and high frequency sound are perceived as high pitched. A young functional human ear has a dynamic range of about 0 to over 120 dB SPL and can perceive sound frequencies between 20 to 20 000 Hz.

The perception of sound is the decoding of these vibrations, vibrations that contain enough information not only to be able to tell that a car is coming from behind without looking over our shoulder, but also provide a good sense of the speed and size of the vehicle. The perception of sound has been exploited through evolution as a mean of communication within species, an ability that humans have refined through the development of spoken language that has made it possible for us to share abstract concepts that cannot be conveyed in other ways than by a common language.[1] Furthermore, the sound information within a spoken sentence extends the words it contains; the meaning can change depending on how we emphasize a certain word and can also reflect the temperament and mood of the talker. All this and much more can be understood by detecting small vibrations that propagates through the air, and all of it is done by the auditory system, which converts these vibrations to electrical signals sent through the central nervous system onward to the brain

[1] Sign language is a fully developed language based solely on visual ques, but is not addressed within the scope of this thesis.

which interprets and assigns the signals to events in the surrounding environment and creating meaning out of them.

1.1.1 ANATOMY AND PHYSIOLOGY OF THE AUDITORY SYSTEM

The ear (Figure 1) is the most peripheral part of our auditory system and is responsible for converting sound vibrations to electrical signals. The external ear consists of the auricle and the external canal, which guides sound vibrations to the ear drum. The eardrum, also known as the tympanic membrane, converts the vibrations from the air to mechanical vibrations. These vibrations are transmitted through the middle ear's ossicular chain, which consists of the three tiny bones: malleus, incus and stapes, where the stapes is placed over the oval window and conducts the sound vibrations to the cochlea within the inner ear (Gelfand, 2018).

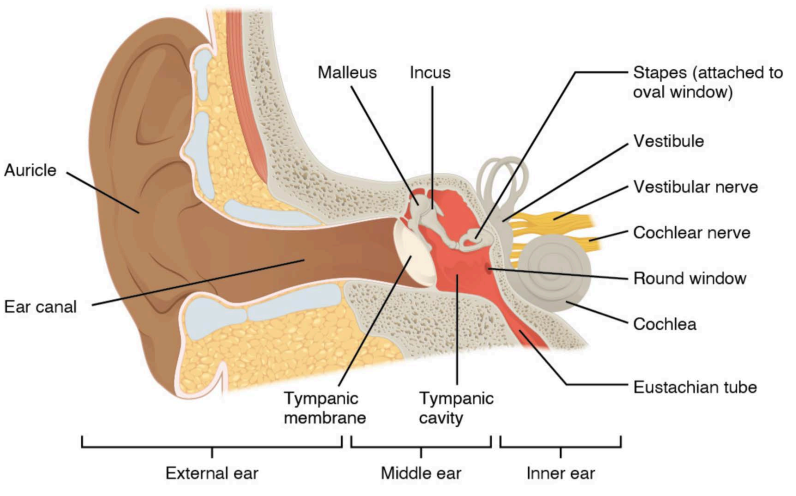

Figure 1. Schematic view of the external ear, middle ear and inner ear. Reprinted from: Betts, J. G., Young, K. A., Wise, J. A., Johnson, E., Poe, B., Kruse, D. H., Korol, O., Johnson, J. E., Womble, M., & DeSaix, P. (2013). Anatomy and Physiology. OpenStax. Access for free at https://openstax.org/books/anatomy-and-physiology/pages/1-introduction. Used under Creative Commons CC-BY license.

The cochlea is located within the temporal bone and is coiled in shape similar to a snail-shell. If stretched out, the cochlea is about 35 mm long. It is a fluid filled cavity with three chambers called scala vestibuli, scala media and scala tympani. Both scala vestibuli and scala tympani, which are connected at the top (apex) of the cochlea, are filled with perilymphatic fluid with a high concentration of sodium and a low concentration of potassium. Scala media, on the other hand, is filled with endolymphatic fluid, which has a high concentration of potassium and low concentration of sodium and is separated from the scala vestibuli by the Reissner's membrane and the scala tympani by the basilar membrane. On the basilar membrane, within scala media, the organ of corti is located, which is our hearing organ. The organ of corti has two different types of sensory cells: the outer hair cells (OHC) and inner hair cells (IHC). There are approximately 12 000 OHCs and approximately 3 500 IHCs. Both the OHCs and IHCs have a hair-like stereocilia bundle at the top of the cell, which are excitatory when bent towards the longest stereocilia and inhibitory when bent in the other direction (Dallos, 1992; Gelfand, 2018). The auditory nerve neurons that innervate the OHC and IHC are called spiral ganglion cells and runs through the Rosenthal's canal, which is located in the center part of the cochlea known as the modiolus. There are about 35 000 spiral ganglion cells, a majority of which are afferent neurons. Between 90–95% of these neurons innervate the IHC, which means that the auditory information sent through the central nervous system mainly originates from the IHC. The spiral ganglion axons enter the brainstem and terminate in the ipsilateral cochlea nuclei. However, when sent through the auditory system, the signal continues in both afferent and efferent pathways on both the ipsilateral and contralateral side up to the temporal lobe of our brain where the auditory cortex is found (Gelfand, 2018; Guild et al., 1931; Spoendlin & Schrott, 1989).

The decoding of sound frequency is mainly done within the cochlea by means of the structure of the basilar membrane. The membrane is stiff and narrow in the base and gets looser and wider towards the apex of the cochlea. This change in stiffness results in different maxima of the standing wave along the membrane, that will change depending on the incoming sound frequency. A high frequency sound will generate a maximum displacement at the stiff basal end of the basilar membrane, and a low frequency sound will cause the most pronounced vibrations closer to the apex. In this way, hair cells near the base are activated by the high frequency sounds, and apical placed hair cells are activated by low frequency sounds. This tonotopic organization is kept within the auditory nerve; for example, spiral ganglions that connect to apical placed hair cells carry low frequency sound information. The frequency-specific information from the spiral ganglion neurons is then maintained throughout the auditory pathway to the auditory cortex (Oxenham & Wojtczak, 2010).

1.1.2 HEARING LOSS

According to the World Health Organization (2021), 1.5 billion people globally experience some degree of hearing loss, and about 60.5 million of these people have hearing loss that is classified as severe or worse in the better ear. The proportion of children, 18 years of age or younger, with mild or worse, bilateral hearing loss is around 2.2% (Wang et al., 2019). With universal newborn hearing screening, it is possible to detect children born with hearing loss, and in developed countries, about 1 child per 1000 is born with bilateral, mild or worse (>25 dB HL), permanent hearing loss (Butcher et al., 2019). In a study based on a Swedish population, the prevalence of severe or worse hearing loss (>60 dB HL) before the age of one was 0.28 per 1000, a number that increased to 1 per 1000 for the 18 year-olds in the same study (Uhlén et al., 2020).

Sensorineural hearing loss is the most common type of permanent hearing loss in children (Parving, 1983), and is mainly a result of damage or loss of OHC and IHC. For half of all children with congenital sensorineural hearing loss, the cause is of genetic origin and includes nonsyndromic causes (e.g. mutations in the GJB2 gene that affect the potassium balance for the hair cells) and hearing loss that is a part of a syndrome with other conditions (e.g. Pendred and Uscher syndromes). About one third of the incidence of congenital sensorineural hearing loss is associated to temporal bone malformations, and between 5 to 30% originates from a congenital cytomegalovirus infection. Postnatally acquired hearing loss in children has different causes. Risks associated with childbirth are premature birth, low birth weight and treatment in a neonatal intensive care units. Later onset can originate from infections (e.g. meningitis and rubella), head trauma, ototoxic medicine, etc. (Lieu et al., 2020).

1.2 COCHLEAR IMPLANTS

1.2.1 COCHLEAR IMPLANTS IN CHILDREN AND EARLY IMPLANTATION

For most children who are born with profound sensorineural hearing loss or deafness, or adults with an acquired profound or total hearing loss, the CI can provide hearing that otherwise cannot be achieved. It has a thin electrode array that is placed within the cochlea with between 12 to 22 individual stimulation electrodes. The electrodes stimulate the auditory nerve's spiral ganglion cells with a weak electric current that causes the sensation of sound. Cochlear implant recipients generally acquire open-set speech recognition without additional visual ques when listening in a quiet setting, but have more difficulties than normal hearing peers when following conversations in competing noise. It is important to note that a CI does not fully correct or cure the effects of the loss of sensory hearing.

The common criteria for unilateral CI candidacy in Sweden for adults are, a pure-tone average[2] >70 dB HL in the better ear and a speech perception <50% for phonemically balanced monosyllabic words without competing noise in the better ear. However, these criteria are not exclusive and other indications exists (Nationella medicinska indikationer, 2011). Cochlear implants for children should generally be considered in cases of a bilateral severe to profound hearing loss with limited benefit from binaural acoustic amplification. Duration of deafness is also critical, and if implantation is suitable, children should preferable receive a CI as soon as possibly due to developmental factors (Purcell et al., 2021). Up until the year 2019 about 736 900 individual CIs were registered around the world (National Institutes of Health, 2021). In Sweden, approximately 100 children, aged 0 to 19 years receive CIs each year, most 4 years or younger (Socialstyrelsen, 2022). According to statistics collected by the Swedish user organization Barnplantorna, a majority of the children receives bilateral implants. The numbers also show that there are three major CI manufacturers active in Sweden: Cochlear Ltd., MED-EL and Advanced Bionics, although, only one child to date has received an Advanced Bionics implant according to the statistics (Barnplantorna, 2021).

In recent years, several studies have shown that early implantation at between 6 and 11 months of age is both safe and beneficial for a child's development (e.g. Colletti et al., 2011; Karltorp et al., 2020; Nicholas & Geers, 2018; O'Connell et al., 2016). Language development has been shown to be highly

2 Pure tone average for frequencies 500, 1000, 2000 and 4000 Hz.

correlated to time of implantation. In a review study by Ruben (2018), it was noted that all studies (n = 8) that had compared implantation before 12 months found better outcomes in both expressive and receptive language compared children who received an implanted later, even at long term follow-ups, up to 10 years after activation. Factors influencing improved hearing outcomes include the plasticity in the infant brain, which is efficient in adopting and interpreting the sound from the CI. Furthermore, if the infant brain is deprived of sound stimulation, other modalities can begin to take up cortical areas that are otherwise used for sound processing (Purcell et al., 2021). Although preferable, early implantation may not always be possible, for example, in cases where other coexisting conditions increase the risks associated with surgery (Naik et al., 2021).

1.2.2 COCHLEAR IMPLANT HISTORY

Early attempts towards treating hearing loss with electrical stimulation were carried out on a few patients in the 1950s and 60s. With a crude electrode stimulation these early implantees were able get a sound sensation but it was not specific enough to generate speech perception. During the late 1970s, an electrode array was developed, which was placed in the scala tympani with multiple stimulation points to take advantage of the tonotopically organization of the cochlea. For the postlingually profound hearing impaired volunteers that first got to test this array design, this electrode array generated a difference in pitch depending on whether stimulation occurred with basal or more apically placed electrodes. It further improved their speech recognition mainly in combination with speech reading, but also to some degree when listening only through the implant. During the early 1980s the stimulation strategies (the stimulation pattern of the electrodes) were developed further, improving audibility to some extent. It was also during the 80s that the first pre- and postlingual children with profound hearing loss received implants within research programs. For these early implantees it was noticed that children that had not developed a langue did not get as good open-set speech recognition compared to those who lost their hearing after developing a language. These poor results were partly depending on the still crude stimulation strategy, that since has been improved more and today these differences does not exist. The documented benefit from the CI encouraged trails on children from two years of age. Cochlear implants were finally approved by the Food and Drug Administration in the USA in 1990 for children over the age of two (Clark, 2003). As of today, implantation is approved from 9 months in the US (U.S. Food and Drug Administration, 2020).

1.2.3 THE COCHLEAR IMPLANT SYSTEM

The CI systems used today consists of an internal and an external component (Figure 2). The external part consists of a sound processor, microphones and a transmitter coil. The sound processor converts the acoustic sound to a digital signal and processes the sound information to create a meaningful stimulation pattern in the auditory nerve. The signal is transmitted transcutaneously by radiofrequency from the external coil to the internal part of the implant. The external coil also supplies the internal part with power through electromagnetic induction. The internal part (the receiver/stimulator) consists of a telemetry coil, magnet and the stimulating intracochlear electrodes. The telemetry coil receives the stimulation pattern and electrical power but can generally also send back information to the sound processor (e.g. the impedance levels of the electrodes). The internal magnet holds the external coil (which also has a magnet but in opposite polarity) in place over the receiver. The number of stimulating electrodes varies between implant makers, and today's implants have between 12 to 22 intracochlear electrodes (Carlson et al., 2012; Clark, 2003). Implants from Cochlear Ltd., which is of primary concern to this thesis, have 22 intracochlear electrodes. The electrodes are numbered 1 to 22, with 1 at the array base, placed near the cochlear base, to 22 near the tip of the array, closer to the apex. This means that when changing stimulation from, for example electrode 3 to electrode 11, the perceived pitch (sound frequency) is lowered, owing to the tonotopic organization within the cochlea when stimulation is changed in apical direction. In visual representations where electrode numbering is placed on the x-axis, numbering commonly goes from 22 to 1 (left to right) analogue to how frequencies are represented on similar scales. Stimulation units for Cochlear Ltd. electrodes are denoted as current level (CL) with a range from 1 to 255 CL, stimulating from 17.5 µA at 1 CL to 1750 µA at 255 CL, this apply to implants from the CI24RE up to the 600-series (Cochlear Limited, 2022, 2023). An increment of 1 CL corresponds to 0.16 dB, and a 6 CL increment is thus nearly a 1 dB change (van Dijk et al., 2007). The implants have two extracochlear reference electrodes, a ball or short pin-shaped electrode, monopolar 1 (MP1), placed under the musculus temporalis and a plate electrode, monopolar 2 (MP2), placed on or built into the receiver/stimulator of the implant. In everyday use, the intracochlear electrodes use both extracochlear electrodes by default as reference, monopolar 1 and 2 (MP1+2), when stimulating (Cochlear Limited, 2023).

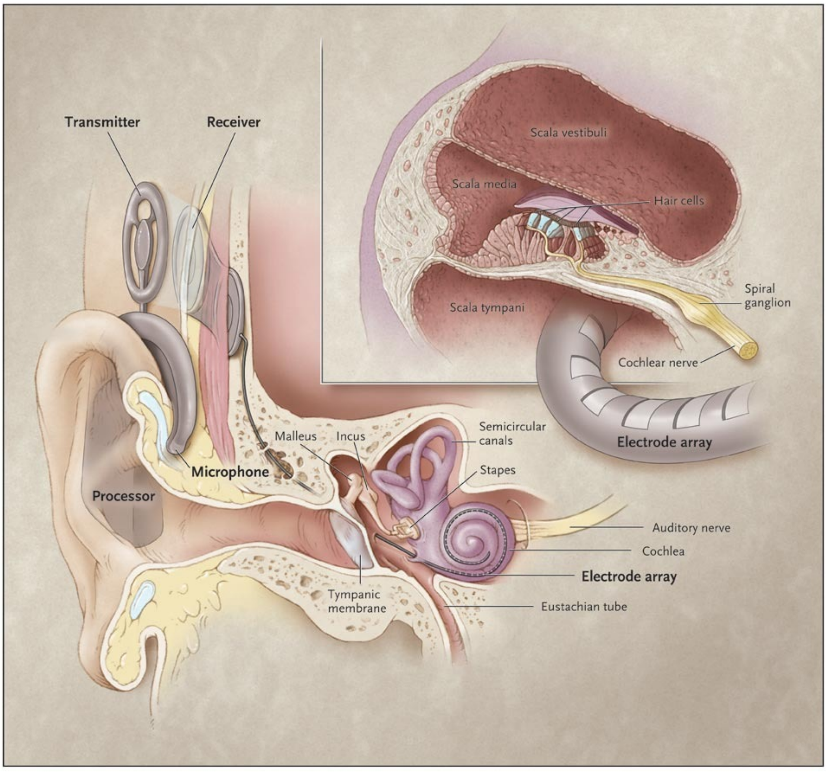

Figure 2. The internal and external components of a cochlear implant system. Reproduced with permission from Papsin, B. C., & Gordon, K. A. (2007). Cochlear Implants for Children with Severe-to-Profound Hearing Loss. New England Journal of Medicine, 357(23), 2380–2387. Copyright Massachusetts Medical Society

Function of the implant can be monitored by measuring impedance levels of the individual intracochlear electrodes. The results will show if there are short or open circuits, and is also used to assess the voltage compliance level for individual electrodes. Impedance measurement are generally performed routinely at clinical visits, and today the programming software perform the impedance check automatically when the sound processor is connected to the computer (Cochlear Limited, 2023). The impedance is the resistance of the current flow between the stimulating electrode and the reference electrode and measured in the SI-unit of Ohm (Ω). Impedance measurements are performed for the common ground (CG), MP1, MP2 and the MP1+2 condition. The CG condition is when one intracochlear electrode is stimulating and the other intracochlear electrodes together act as a single reference electrode. The MP1, MP2 and MP1+2 conditions are described above. Short and open circuits are determined by the results from the CG condition. Short circuit is considered when the impedance levels is lower than 0.565 kΩ, and open circuits for electrodes with impedance levels above 30 kΩ. The compliance limit is also obtained to control the restrictions on maximum stimulation output, based on battery capacity in relation to the impedance level. If the C-levels lies above the compliance limit, the implant cannot stimulate through the entire dynamic range (see section 1.2.6 for more information about compliance levels). This check is generally performed based on the MP1+2 condition since it is the default reference condition for the stimulation electrode (Wolfe & Schafer, 2014).

1.2.4 ELECTRODE ARRAY DESIGN

There are two major designs for the intracochlear electrode array: a straight array that is positioned close to the lateral wall (LW) of the cochlea, and a pre-curved, perimodiolar (PM) array that is positioned near the modiolus. The PM electrode arrays were developed so that the stimulating electrodes could be placed as close as possible to the spiral ganglions in the auditory nerve, aiming to reduce cross channel stimulation. The downside, however, has generally been that the PM array causes more damage to the cochlea during implantation. Compared to the LW, the PM array has a higher risk of translocation to the scala vestibuli when inserted, and also damage the structures of scala media. The surgical method of choice for the PM array was initially cochleostomy, but round window insertion has subsequently proven to be effective, and is generally believed to cause less damage. Lateral wall arrays, on the other, hand can offer a relatively atraumatic round window electrode insertion, although, it comes with higher risk of damage to the outer wall of the scala tympani through its insertion angle relative to the wall and through the force applied. The LW implant can reach a more apical part of the cochlea, allowing the implant array to reach more low frequency coding auditory neurons than what is possible with the current PM design (Dhanasingh & Jolly, 2017; Risi, 2018). Furthermore, CI recipients, in some cases, have some residual hearing in the lower frequency region, and if this low frequency hearing can be kept intact it has been shown beneficial for the hearing outcome to perceive both electric and acoustic hearing in the same ear (Gifford et al., 2013; Plant & Babic, 2016; Rader et al., 2013). Thinner LW arrays have therefore been developed to reduce insertion trauma even more, to be used when it is desirable to preserve the recipient's remaining hearing. For Cochlear Ltd.'s implants, the diameter of the LW implant SlimStraight (SS) is 0.3–0.6 mm compared to the company's PM implant Contour Advanced (CA) that is 0.5–0.8 mm (Lenarz et al., 2009; Skarzynski et al., 2012, 2014). It is worth noting that Cochlear Ltd. recently introduced a thinner PM electrode that aims to preserve cochlear structures and residual hearing (Aschendorff et al., 2017; Haber et al., 2021; Ramos-Macías et al., 2017). However, the long-term effects of using slim LW arrays to promote hearing preservation are not clear, and studies comparing 12-month post-operative hearing results between LW and PM arrays have shown conflicting results that do not entirely support the use of slim LW arrays is preferable for hearing preservation (Mady et al., 2017; Perkins et al., 2022; Thompson et al., 2020; Wanna et al., 2018). A downside of a thinner implant array is that the surface area of the stimulation electrodes is reduced, which can lead to problems associated with higher impedance levels in theses electrodes (Saunders et al., 2002; Zarowski et al., 2020). High impedances increases the charge needed for the stimulation electrodes, which increases power consumption and the risk of voltage compliance problems that reduce the dynamic range of stimulation and reduce the audibility with the CI (Saoji et al., 2021).

1.2.5 ELECTRICALLY EVOKED COMPOUND ACTION POTENTIAL

The electrically evoked compound action potential (ECAP) is a measurement of neural activity initiated by an electrical stimulation. The communication from our sensory organ to our brain is done through changes in electrical properties. Through neurons within our central nervous system, information is sent through electrical transients called action potentials. For the auditory system the action potential is generated by incoming sound vibrations which causes displacement of the stereocilia of the hair cells within the cochlea and an inflow of potassium from the endolymph in the scala media into the cell. The potassium flow depolarizes the cell and in turn will initiate an inflow of sodium at the base of the cell, leading to the release of neurotransmitters within the synaptic cleft of the hair cell and the spiral ganglion neuron of the auditory nerve. The release of neurotransmitters depolarizes the neuron and generates an action potential through the nerve (Henkel, 2018). When stimuli reach the threshold level, the action potential of individual neurons will always have the same magnitude which make the action potential binary. After the activation of the action potential, there is a refractory period when no new action potential can occur within the specific neuron. Measurements of neural activity are often done at some distance, at a site outside the neuron; therefore the measurement does not represent a single neuron’s action potential, but simultaneous activity from a group, or compound of neurons (Dwyer, 2018). For CI recipients, the compound action potential of the auditory nerve can be measured by using the implant to stimulate the nerve, but also to record the response from the nerve, which places the recording electrode in close proximity to the activated neurons. The ECAP measurement with a CI can be done relatively effortlessly, using the same equipment used for sound processor programming and the CI manufactures provided computer software to carry out the recording. Commercial ECAP recording was first introduced by Cochlear Ltd. in 1998 under the name Neural Response Telemetry (NRT). Advanced Bionics released the Neural Response Imaging (NRI) system in 2001 for ECAP recordings, and MED-EL's ECAP system, Auditory Response Telemetry (ART) was introduced in 2007 (He et al., 2017).

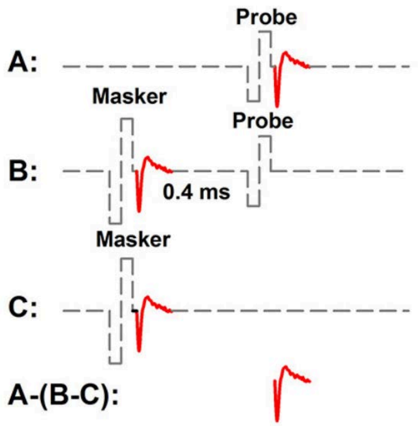

Figure 3. Illustration of forward masking paradigm. Probe indicate the response activating stimulating and masker the nerve saturating stimulation. The dashed gray line indicates the biphasic stimulation and the red solid line the elicited response. Reprinted excerpt from: He, S., Teagle, H. F. B., & Buchman, C. A. (2017). The Electrically Evoked Compound Action Potential: From Laboratory to Clinic. Front Neurosci, 11, 339. Used under Creative Commons CC-BY license.

The technique of recording ECAP from the auditory nerve using the CI intracochlear electrodes in humans was first described in the beginning of the 1990s (Brown et al., 1990). The time from the electrical stimulation to activate a response from the auditory nerve is very short (~0.5 ms). This short time is problematic when recording the nerve response, as the stimulating signal has not fully subsided when the response starts, therefore a large stimuli artefact needs to be removed before being able to record a response from the nerve alone. The problem with the stimuli artifact contaminating the response was solved by Brown et al. (1990) by applying a forward masking method that takes advantage of the refractory period after stimulation to remove the artifact and was based on the assumption that the same stimulation produces identical stimuli artefacts. To achieve forward masking, recording was done by stimulating in three steps, as shown in Figure 3. First, a recording is made that contains both the stimuli artifact and nerve activity, (*A* in Figure 3) by stimulating with a biphasic pulse, *probe*. In the second recording, the probe is preceded by a *masker* stimuli (*B*). The biphasic masker elicits a response, leaving the nerve neurons in a refractory state. When the probe is presented, no response is evoked, thus creating a recording with only the masker and stimuli artefact. The third recording is done with the masker alone to record lingering stimuli artefacts and nerve activity originating from the masker. These three recording are then used to form a single results; by subtracting the second (*B*) recording from the third (*C*) the remaining effects from the masker stimulation are removed, yielding a result that contains only the stimuli artifact. That result is then subtracted from the recording that was done with the probe only (*A*), thus removing the stimuli artefact and keeping only the nerve response. To ensure that neurons are put in a refractory state, the masker is presented at a higher stimulation level than used for the probe stimulation; if this is not done, it is possible that neurons will be activated during the probe stimulation in the masker-probe condition (*B*) this will degrade the final results (Brown et al., 1990; He et al., 2017). To further reduce unwanted electrical background noise, an additional averaging technique is also used, which combines multiple measurements (one measurement being the *A-(B-C)* result in Figure 3) to reduce the level of background noise in the recording. The averaging is generally done across 35 to 200 measurements, where a higher number of measurement may be needed at lower stimulation levels (Abbas et al., 1999; Botros et al., 2007; Dillier et al., 2002).

The characteristics of the ECAP when recorded as described above can be seen in Figure 4. The first part of the response is a large negative peak (N1) at about 0.2–0.4 ms after the stimulation followed by a positive peak (P2) appearing around 0.6–0.8 ms after the stimulation. This single positive peak pattern is the most prevalent, occurring approximately in 80% of the time. However, in about, in about 20% of the time there is an additional positive peak (P1) appearing before P2. If the P1 is present, it generally occurs around 0.4–0.5 ms after stimulation. Both peak patterns are shown in Figure 4. The peripheral response of the ECAP is not affected by the maturation process within the central auditory system. Consequently, there is no difference in the response characteristics between children and adults. The amplitude of the ECAP increases with the stimulation level and can be up to 1–2 mV before it is saturated; higher amplitudes have been observed at apical electrodes compared to basal electrodes when presented at an equal loudness level (He et al., 2017). The ECAP recording is not affected by anesthesia because it records a peripheral response and can accordingly be performed during surgery. The measurement can thus be used intraoperatively to estimate the functionality of the implant but, as well as whether the auditory nerve is activated by the stimulation, which is crucial for the CI (Abbas, 2007). Although, the measurement can be recorded intraoperatively, studies have shown that there is large variation between thresholds measured during the insertion of the implant and at postoperative measurements (Gordin et al., 2009; Spivak et al., 2011). The use of the ECAP measurement when programming stimulation levels is of importance for this thesis; this application is described in section 1.2.7.

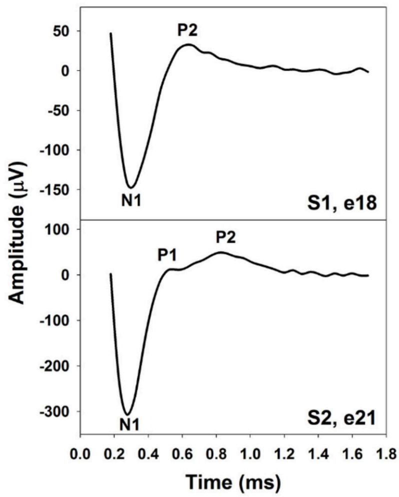

Figure 4. Two electrically evoked action potential responses from two different pediatric Cochlear Nucleus implant users with prelingual deafness and different intracochlear position. The upper recording contains one positive peaks (P2) and the lower two positive peaks (P1 and P2). Reprinted from: He, S., Teagle, H. F. B., & Buchman, C. A. (2017). The Electrically Evoked Compound Action Potential: From Laboratory to Clinic. Front Neurosci, 11, 339. Used under Creative Commons CC-BY license.

The most common use for ECAP recordings is to measure threshold responses from individual intracochlear electrodes, often described as the lowest stimulation that will elicit response. The ECAP threshold is generally either visually determined or extrapolated from the amplitude growth function (AGF). The visually determined threshold is the lowest level where the clinician can observe an ECAP response. An extrapolated threshold, on the other hand, is based on the linear change in amplitude between N1 and P2 (or P1 if present) as stimulation level increases. The change in amplitude with stimulation level, for a group of supra threshold measurements is then used to extrapolate the level of the ECAP threshold (Cafarelli Dees et al., 2005; Franck & Norton, 2001).

In the mid-2000s Cochlear Ltd. improved their integrated amplifier with the introduction of the CI24RE implant, which lowered the noise floor for ECAP recordings and made it possible to record thresholds at lower levels (Battmer et al., 2010; Lai et al., 2009). After the introduction of the CI24RE, an automated version of the NRT system was introduced (AutoNRT). The system has been shown to yield similar accuracy in judgment compared to clinical observers, further it reduces variability identified between different observers and can be managed by clinicians with a limited experience performing ECAP recordings. Measurement time is also reduced significantly compared to manually recorded ECAP thresholds (Gärtner et al., 2010; van Dijk et al., 2007).

The automatic procedure is designed to identify the ECAP morphology waveform in the recording mimicking the visual determination of the ECAP threshold. The use of visually determination rather than an extrapolated threshold based on AGF was mainly used for two reasons: the need for more suprathreshold measurements at higher stimulation levels for the AGF method that would prolong the recording, and a high risk of discomfort associated with the loud sound sensation for the recipient at higher stimulation levels. Further, the CI24RE implant recording showed non-linear AGF when comparing higher suprathreshold stimulation levels to near-threshold levels; this had not been the case for previous implant generations due to a higher noise floor, making the preceding implants less sensitive for low amplitude responses. The nonlinearity was problematic, since the extrapolation process is highly dependent on the number of suprathreshold measurements, and results may vary substantially depending on how much of the AGF that is recorded. The peak picking algorithm for finding N1 and P1/P2 was achieved through a machine learning process based on a large dataset of ECAP measurements. The data set contained measurements with both recognized peaks (positive responses) and without peaks (negative responses), and a few hard-to-judge measurements containing artefacts. The peak picking was then applied to two subsequent systems: an initial ascending system and a second descending system. The ascending system increases stimulation levels in steps of 6 CL and is designed to identify ECAP responses when increasing from a level where no response is recorded to a level where a response is obtained with high sensitivity, adding margin by measuring two consecutive steps above the first recognized peaks. When the ascending system has identified an ECAP response, the second system starts a descending series that decreases in steps of 3 CL to find the threshold with high overall all confidence for both positive and negative judgments. The threshold is then calculated as the mean of the lowest level with an ECAP response and the highest level without a response. The response recording is done with a resolution of 32 samples sampled at

20 kHz. The measurement has an intraoperative and a postoperative setting. What signifies the intraoperative measurement is a higher stimulation rate, 250 Hz, compared to the postoperative measurement, which stimulates at 80 Hz. The faster stimulation rate is mainly applied to speed up the recording processes during surgery. Furthermore, the intraoperative setting uses a high current conditioning pulse to reduce the impedance on the selected electrode before beginning the recording. The intraoperative measurement has a default starting level of 170 CL and the postoperative default is 100 CL. Both of the preset levels can be changed by the clinician. The subsequent parameters are the same for both settings and cannot be altered; each stimulation level is performed with 35 averages and a biphasic pulse is mostly used for stimulation in combination with forward masking to minimize stimuli artefact. A pulse width of 25 µs is employed and a masker probe interval of 400 µs. The recording electrode is one electrode apart from the stimulating electrode in the apical direction (i.e. electrode 3 is recording ECAP generated by electrode 1). For electrodes 21 and 22 this cannot not apply, and the recordings are accordingly performed by electrodes 19 and 20 respectively. The extra cochlear electrodes serve as reference electrodes during the recording. When stimulating, the MP1 is the reference electrode, and when recording it is the MP2 electrode. During recordings there can be a remaining stimulus artifact saturating the amplifier. When this occurs, the AutoNRT system tries to reduce the artefacts in the following steps: first by trying to add a third negative phase (i.e. using a triphasic pulse), in the probe recording for the masker-probe-condition (*B* in Figure 3), in an attempt to neutralize the artefact. If that is not successful, the system goes back to a biphasic pulse and reduces the gain from 50 dB to 40 dB and increases the number of averages with a factor of 1.5 to maintain the signal to noise ratio during recording at the lower gain. If the artefact still remains, both the triphasic pulse and lower gain is applied, and if the amplifier still saturates, the measurement is canceled for that electrode (Botros et al., 2007; Gärtner et al., 2010; van Dijk et al., 2007).

1.2.6 PROGRAMMING STIMULATION LEVELS

The programming of the CI sound processor is the processes of determining optimal stimulation of the electrodes for the recipient. There is a plethora of settings that can be adjusted regarding the stimulation; however, it is mainly the stimulation levels that primarily needs to be adjusted. The process described here is mainly based on the Cochlear Ltd.'s implant system. There are other rationales for other implant systems, although the underlying principles are universally applicable.

Activation of the CI is often done between 2–6 weeks after implantation surgery (Vaerenberg et al., 2014; Wathour et al., 2021). At the activation visit, the sound processor is programmed with an initial preliminary setting for the stimulation levels, which is done by establishing the threshold levels (T-levels), which is the lowest amount of stimulation that an individual electrode will generate. T-levels are often set at or near the threshold response of the stimulating electrode. The highest level of stimulation is set to a comfort level (C-level) that is loud but not uncomfortably loud (here Cochlear Ltd.'s terminology is used, MED-EL and Advanced Bionics calls the highest stimulation M-level, short for *maximum comfortable threshold* and *most comfortable level* respectively). During the first days or weeks, the sound processor is reprogrammed with new T- and C-levels, since these levels can change during the early stages of adapting to electrical hearing. In general, there are about four programming visits over the first few weeks after the activation visits, but this also varies from clinic to clinic. The T- and C-levels need to be set accurately. If T-levels are set too low, soft sounds may become inaudible, and if they are set too high the recipient may experience unwanted noise. Additionally, if C-levels are set too low, the dynamic range will decrease the amplitude resolution and reduce audibility, and if set too high, it may cause discomfort for the user. The T- and C-levels are generally set based on behavioral measurements, T-levels are often set with an ascending-descending method and C-levels with an ascending method, where a visual analogue loudness chart can be used to aid the recipient to indicate perceived loudness from the stimulation (Browning et al., 2020; Clark, 2003; Craddock, 2007). It is only necessary to measure T- and C-levels on a subset of electrodes spread across the array and then using the software to interpolate values for the electrodes that are not measured (Cochlear Limited, 2023). A loudness balancing step across electrodes is also generally performed at or near the C-level to ensure equal loudness between electrodes. Correct loudness balancing is important for the audibility, and it has been suggested that proper loudness balance has a higher impact on hearing perception than correctly set T-levels (Dawson et al., 1997; Sainz et al., 2003). MAP is an overarching term widely used, incorporating all parameters used when programming including the T- and C-levels (although this term is not an abbreviation or acronym, it is often stylized with capital letters).

An additional factor when programming stimulation levels is the voltage compliance of the electrode. In order to stimulate across the full dynamic range, the implant must generate enough voltage for the stimulation at each time point. If the impedance level increases for the electrode in relation to its reference electrode, e.g. because of more tissue growth in the area surrounding the electrode, more of the discharge energy will be needed for generating enough voltage and leaving less to the actual stimulation. Therefore, if impedance level rises the maximum stimulation level will be lowered, since there is a limited amount of energy that the system can accumulate for every single discharge. If impedances get to high the default setting of the system will not be able to generate enough energy discharge to stimulate the upper part of the dynamic range, which will reduce the loudness sensation for that electrode and, consequently, cause reduced audibility. An electrodes maximum compliance level should therefore always lay above the dynamic range of the stimulation, if it drops to a level within the dynamic range it is generally referred to of being out-of-compliance (Newbold et al., 2004; Saoji et al., 2021; Wilk et al., 2016). Since there is no more energy to accumulate to stimulate enough neurons and generate a sensation level for louder sounds, a compensation of the momentous loss of stimulation level can be achieved by increasing the duration of the pulse width, e.g. increasing from 25 to 37 µs. For the short time spans concerned here pulse duration and not just amplitude will affect the perception of loudness (Wolfe & Schafer, 2014). The use of a wider pulse width, though, has the disadvantage of increasing the forward masking effect which possibly can decrease audibility (Shannon, 1985; Zhou et al., 2020).

1.2.7 PROGRAMMING STIMULATION LEVELS FOR YOUNG CHILDREN WITH ELECTRICALLY EVOKED ACTION POTENTIALS

As described above, programming highly depends on the active participation of the recipient. This is usually not a problem when creating a new MAP for older recipients, but CIs are also implanted in very young children that cannot participate in such an elaborate task. For the youngest recipients, but also for others who cannot actively participate in the programming process, the clinician needs to use psychophysical measurements for guidance when setting the T- and C-levels. The ECAP thresholds can be used for programming the stimulation levels and have certain advantages over other methods, such as electrically evoked auditory brainstem response (EABR) and the electrically evoked stapedial reflex threshold (ESRT) measurements. The EABR response is a very weak signal that requires more averaging than the ECAP, which prolongs the measurement. It also generally requires a visually determination of the response by an experienced clinician. Whereas the ESRT generally provides a good estimation of the C-levels when recorded postoperatively, it has been reported that it is not measurable in as many as 25–35% of recipients. If recorded intraoperatively, the ESRT is elevated and cannot be used with reliability. While recording, the recipient must remain quiet and still, which can be problematic when ESRT is measured in children (Abbas, 2007). The

ECAP has the advantage of being a fast and reliable method to record a response from the auditory nerve with the aid of AutoNRT. A child can be asleep or awake, and the child does not need to remain still to get an accurate recording. However, the ECAP response does not directly correspond to either T- or C-levels. Instead, it has been reported that the ECAP response tends to lie in the upper part of the dynamic range (Cafarelli Dees et al., 2005; Holstad et al., 2009; Lai et al., 2009; Smoorenburg et al., 2002). The efficacy of using ECAP as a base for programming has been called into question to a certain extent, and the correlation between subjectively measured thresholds and ECAP thresholds has varied substantially between studies. In a review on the subject by de Vos et al. (2018), the pooled correlation across studies was considered too low for the purpose. For the T-levels and ECAP thresholds, the correlation was $r = 0.58$, and for the C-levels it was $r = 0.61$ (de Vos et al., 2018). However, it has long been suggested that the intra-electrode profile can be used for programming in combination with one or a few subjective discreet electrode measurements (Brown et al., 2000). Botros and Psarros (2010) took this notion a step further and suggested that the ECAP profile should be scaled when adapted to programming levels. Based on the observation that the C-level profile is generally flatter compared to the T-level profile, a scaling model was developed for use in combination with a single electrode measurement and ECAP thresholds. The profile flattens as the stimulation level increases, and at very low T-levels, ≤89 CL, the ECAP profile is unaltered. The results presented in the study showed that the scaled profile yielded a better correlation to subjectively set T- and C-levels than the unscaled ECAP profile (Botros & Psarros, 2010). The use of the profile facilitates loudness balancing across electrodes, which has been pointed out as a critical step when programming the MAP (Dawson et al., 1997; Sainz et al., 2003), but very hard to perform when patients are children.

Although disputed, ECAP is often used as a tool for programming in pediatric CI recipients. In a recent survey study by Browning et al. (2020), it was reported that 62% of respondents (41 clinically active audiologist in the United States) *always or almost always* performed ECAP recording to assist them when programming the MAP or keeping track of implant functionality. In comparison, the routine use of ESRT was only 14% in this group in the same study. According to the study, the respondents did not use the ECAP to generate absolute T- and C-levels, but instead used the profile and shape of the ECAP recording. However, the study by Browning et al. (2020) did not specify exactly how the profile was implemented.

1.2.8 INTRODUCTION SUMMARY AND RATIONALE

Cochlear implants offer a unique opportunity for people with congenital or acquired, profound hearing loss or deafness that cannot be remedied by acoustic amplification to gain or regain the sense of hearing. Since the first electrodes were implanted, CI has gone from simply delivering sound sensations to creating a complex signal that can offer the opportunity to understand speech without additional visual ques. For children born without functional hearing, CI offers the opportunity to understand and express themselves through spoken language. It is clear, however, that it is important to be exposed to sounds and spoken language early in life when the brain is most plastic and receptive to developing language. Therefore, children born without hearing need to receive an implant as early as possible in order to develop hearing-related capacities as well as possible. Furthermore, for a child to benefit from early implantation, it is extremely important that stimulation is set to levels that make the dimensions of spoken language as accessible and perceivable as can be achieved. This thesis will take an in-depth look at aspects of ECAP recordings performed with AutoNRT and how the measurement can be applied by clinicians when programming stimulation levels for young children. It will also look at the implications of impedance measurement, which can assist clinicians when deciding implant type.

2 AIM

The aims of this thesis are to aid clinicians in the programming of CIs for young children using AutoNRT recordings and to address related issues that can be of assistance when choosing between implant types. Below are the primary aims for each study.

Study I

- To determine when AutoNRT thresholds remain stable over time in order to use these when programming stimulation level.

Study II

- To explore the relationship between AutoNRT thresholds and subjectively measured T- and C-levels for using AutoNRT as a basis for the stimulation levels.

Study III

- To evaluate the benefit of a subjectively based MAP for children old enough to participate in a programming session similar to that performed for adults compared to an initial ECAP-based MAP. Additionally, the study aimed to evaluate whether the reprogramming of stimulation levels caused a changed in ECAP thresholds.

Study IV

- To examine implications of programing parameters and implant function in relation to impedance levels for two common implant types, and further examine the risk of not being able to record AutoNRT due to high impedance.

3 MATERIALS AND METHODS

3.1 STUDY POPULATION

A compilation of the number of participants divided by age group can be seen below in Table 1.

Table 1. Number of participants divided by age group, and included year range by group.

Study	Age group	Range years	Number
I	Children	0 – 3	53
	Adults	20 – 80	80
II	Adults	18 – 80	41
III	Children	7 – 12	14
IV	Children	0 – 17	208
	Adults	18 – 92	296

Study I

The data in Study I was collected from 13 centers in Italy, Israel, Spain and Sweden. Inclusion criteria for Study I were: bilateral severe to profound hearing loss with a duration no longer than 15 years, no cochlear malformation or ossification that could affect electrode insertion negatively, and no signs of retrocochlear or central hearing loss. For the purpose of the study, participants were divided into two groups: children aged 0–3 years and adults 20 years or older. This resulted in 80 adults, with a mean age of 56.9 years, and 53 children, with a mean age of 1.8 years. Only CI24RE implants were included in the study and only one implant per participant.

Study II

Forty-one adult subjects, with a mean age of 52 years, were included in Study II. Participants for this study were pooled from the same original multicenter study as Study I, but results only included adults over 18 years of age. Data were collected from 10 centers located in Italy, Israel, Spain and Sweden (some centers only included the pediatric group, which is why there are fewer centers in Study II compared to Study I). The demographic differences for Study II compared to Study I were due to the aim of comparing subjectively measured stimulation levels and AutoNRT, which could not be achieved for the young children from Study I. Study II therefore only included adults. Apart from the inclusion criteria from Study I, the following additional criteria was used: participants had to concurrently perform both AutoNRT and undergo subjective measures of T- and C-levels at 6 month follow-up and/or 12 month follow-up and had to use a pulse width of 25 µs. As for Study I, only CI24RE implants were included and one implant per participant.

Study III

Study III was a single center study with inclusion criteria as follows: children aged 7–14 years who received their first CI before 3 years of age and had no cochlear malformation. All children had to have Cochlear Ltd. implant CI24RE or newer and had recorded sound field measurements results from pure tone and speech audiometry, indicating that they were able to participate in the test intended for the study. All children at the concerned clinic had a MAP based on ECAP thresholds. Thirteen of the included children had CI bilaterally and one child was bimodally fitted (CI in one ear and hearing aid on the opposite side). The mean age for participants in this study was 9.1 years.

Study IV

Study IV was a retrospective study of recipients implanted with either the CA or the SS implant. All subjects were included through the database used when programming Cochlear Ltd. implants. Inclusion criteria were implants of either CA or SS implant type and had impedance levels recorded for a year or more after activation. Participants were grouped by children, participants implanted before the age of 18, and adults, implanted at the age of 18 or older. The study included 208 children and 296 adults. The median age for children was 2.55 years and 60.8 years for adults.

3.2 MATERIALS

3.2.1 AUTONRT MEASUREMENT (STUDY I, II AND III)

The AutoNRT measurement performed in Study I, II and III has two measurement protocols that cannot be altered other ways than changing initial stimulation levels. The intraoperative protocol, which used an initial high level conditioning pulse and a stimulation rate of 250 Hz, was only used in Study I since no other study contained intraoperative recordings. The postoperative protocol, which used a stimulation rate of 80 Hz and no conditioning pulse, was employed for all other studies and the postoperative recordings of Study I. In Study I AutoNRT recordings from all intracochlear electrodes were used. For Study II and III a subset of electrodes where considered, for Study II electrodes 3, 5, 9, 14, 18 and 22 and electrodes 2, 4, 6, 10, 14, 18 and 22 for Study III.

3.2.2 MEASUREMENT OF T- AND C-LEVELS (STUDY II AND III)

The measurement of T-levels was performed in similar ways for both Study II and Study III using the ascending-descending method for individual electrodes. The C-levels were applied somewhat differently between the studies. In Study II, it was the actual discreet electrode measurement that was reported, setting the C-levels to the point where an individual electrode was rated as loud without causing discomfort. For Study III, the rationale was different since the actual MAPs were to be compared, not only the measured C-levels, which may alter somewhat when applied to a MAP due to the summation effects when multiple electrodes stimulate together. Therefore, to achieve an acceptable MAP for these experienced CI users, the C-levels were programmed in two steps for Study III. Initially, the same rating was used on individual electrodes as in Study II. In addition, a loudness comparison was also performed with the previous MAP, where participants listened to the clinician's voice to ensure that the overall loudness was the same as their initial MAP. For Study II, electrodes 3, 5, 9, 14, 18 and 22 were measured, and for Study III, electrodes 2, 4, 6, 10, 14, 18 and 22 were measured. In Study III, a deactivated electrode was replaced by an adjacent activated electrode if possible.

3.2.3 IMPEDANCE MEASUREMENTS (STUDY III AND IV)

Impedance measurements were performed using the programming software's default stimulus duration of 25 μs, which is presented at a rate of 250 Hz and measured in four different conditions: CG, MP1, MP2 and MP1+2. For Study IV, the analysis of open and short circuits was based on the following values: short circuit was considered present if the impedance of the CG measurement was <0.565 kΩ, and open circuit was considered present if the CG impedance was >30 kΩ. The analysis of open and short circuits also excluded electrode 1 since it is more likely to be placed outside the cochlea. In Study III impedance measurement was used to analyze non-recordable AutoNRT. Based on the result in Study III a logistic-regression model for 50% risk of non-recordable AutoNRT was calculated from the MP1 condition impedance results and applied in Study IV. The MP1 condition was chosen since it is the reference to the stimulating electrode for the AutoNRT recording. The accuracy of the model was considered good with an accuracy estimated to 83% and consequently a misclassification rate of 17%. The cut-of value employed in Study IV, according to the model, was 15.34 kΩ for MP1, above which there was >50% risk of not recording AutoNRT.

3.2.4 SOUND FIELD MEASUREMENTS (STUDY III)

All sound field measurements were performed in a soundproof both using a single speaker placed at a distance of approximately 1 meter in front of the subject (0° azimuth). All measurements were performed with one implant at the time; no measurements were made with bilateral stimulation.

Pure tone audiometry

Measurements were performed with a warble tone for the following frequencies: 0.25, 0.5, 1, 2, 3, 4 and 6 kHz according to the ascending-descending method, with tone increments of 5 dB at no response and decreasing in steps of 10 dB at response during the threshold-finding phase. A threshold was considered to be the lowest level where two consecutive responses were given at the same level, or where three out of five responses were given at the same level.

Speech audiometry

The speech reception test was carried out using the sentences from the Swedish version of the Hearing in Noise Test developed for Children (HINT-C) (Hjertman et al., 2021) and used with and without competing noise. During both measurements, the participants were asked to report the entire sentence back correctly, and in both conditions, the speech level was kept constant at 65 dB SPL. Before starting the test, a practice round consisting of 10 sentences was performed. The HINT-C measurement performed without competing noise, hereafter shortened to HINT-C-Quiet, was reported as a percentage; each measurement consisted of one list, with one list consisting of 20 sentences. Only participants that received a score ≥50% were tested with the HINT-C, using competing noise as originally intended for the test. The sentences were presented with an adaptive noise level starting with a noise level 8 dB below the presentation level of the sentences then increasing the noise by 2 dB for every sentence reported back correctly and decreasing the noise level if the sentence was reported back incorrectly. The results were presented as average signal-to-noise ratio for the presented list, excluding the first four sentences and including the value for the sentence 21, which was not presented.

3.2.5 INFORMAL LISTENING TEST (STUDY III)

At the final visit, participants in Study III were asked to express their preference between the initial ECAP-based MAP and the subjectively set MAP. This was done by comparing the two MAPs blinded, while listening to the clinician and the parent's voice, and stating which sounded best.

Table 2. Overview of included tests for each study, I-IV.

Test	Study I	Study II	Study III	Study IV
AutoNRT	X	X	X	
T- and C-levels		X	X	
Sound field measurements (pure tone and speech audiometry)			X	
Impedance measurements			X	X
Informal listening test			X	
Pulse width increment				X

3.3 STUDY DESIGN AND DATA COLLECTION

Study I

Study I was a prospective multi center intervention study where participants received a CI unilaterally and were followed for the first year after implantation. Data collection for adult participants (i.e. AutoNRT recordings) in Study I was done at four time points: intraoperatively, at the initial activation, and 6 and 12 months after activation. Data for children were collected at six time points: intraoperatively, at the initial activation, and 1, 3, 6 and 12 months after initial activation.

Study II

Study II has the same study design as Study I. Data for Study II were collected at 6 and 12 months. At both time points, AutoNRT and subjective T- and C-levels were measured.

Study III

Study III was a single center prospective intervention study in which enrolled participants received a new MAP based on subjectively measured T- and C-levels, the study outline is presented in Table 3. At the initial visit, baseline AutoNRT recordings and sound field measurements of pure tone audiometry, HINT-C-Quiet and HINT-C, were performed. At the second visit, 4 months after the first visit, the reprogramming of the MAP was done along with an AutoNRT measurement. At the last visit, 8 months after the first visit, AutoNRT and sound field measurements were performed along with the informal listening test for MAP preference. The purpose of the first visit 4 months before intervention was to record the AutoNRT threshold variation before any changes in stimulation levels were made (i.e. the variation between first and second visit) to be able to compare the variations after changes in stimulation (i.e. the variation between the second and third visit). In order to avoid participant fatigue during the second visit and the need for additional visits for participants who travelled long distances to the clinic, the baseline measurements were also performed at the first visit.

Table 3. Outline for Study III, months indicating time after first visit.

	First visit *0 month*	**Second visit** *4 months*	**Third visit** *8 months*
AutoNRT measurement	X	X	X
Pure tone audiometry	X		X
HINT-C-Quiet	X		X
HINT-C	X		X
Reprogramming of the MAP based on subjective T- and C-levels		X	
Informal listening test: MAP preference			X

Study IV

Study IV was a single center retrospective study of impedance data. Data were collected from all patients in the database used for programming Cochlear Ltd. Implants who matched the inclusion criteria. At the respective clinics, impedance is generally checked at routine visits to verify implant function. Currently, the software performs impedance measures automatically when connecting the sound processor. Electrode impedance was generally checked routinely, every year or every other year, until the age of 20. Recipients that received implants aged 20 years or older were routinely checked for two years after activation. Impedance was also measured at return visits initiated by the recipients. Impedance measurements were sometimes recorded several times during the same visit on the same implant. In those cases, the last measurement was included for that specific date and implant. Otherwise, all measurements were included for this study.

3.4 STATISTICAL ANALYSIS

Due to the aim of the study and data collection procedure, different analyses were performed for the studies. An alpha level of 0.05 and two-sided *p*-values were applied for all studies. To compare difference between two groups, the t-test was used if data were normally distributed and the Mann-Whitney (also known as Wilcoxon signed-rank test) if data were not normally distributed. The pairwise implementation of the Wilcoxon signed-rank test was used in Study III. To reduce the probability of type I error (incorrectly rejecting the null hypothesis) when performing multiple comparisons in Study II, the Holm method was applied to adjust the *p* -value. The main method used to evaluate normal distribution was the Shapiro-Wilk test in addition to histograms.

In Study I, the main analysis was done with the Pearson correlation coefficient. Data were considered to be normally distributed in order to compare measurements over time. Although the method has been employed in previous studies (e.g. Lai et al., 2009; Tavartkiladze et al., 2015), it became clear that correlation was not ideal for this type of analysis (Altman & Bland, 1983; Westgard & Hunt, 1973). Although the results in the original study were also interpreted in light of the mean absolute difference between measurements and the overall mean change, additional Bland-Altman plots have been included in the analysis for the presentation in this thesis. This analysis is better suited since the correlation is not designed to evaluate agreement and has certain drawbacks (e.g. a wider data range will generally produce a higher coefficient than a smaller range even with similar variances) (Bland & Altman, 1986).

In studies II and III, a Spearman rank correlation was used since data were not normally distributed. The linear mixed model in Study II was used as the main analysis method for the relationship between the T- and C-levels and AutoNRT because of its ability to capture variation between individuals in the analysis that ordinary correlation or regression cannot; however, the Spearman correlation analysis was included for comparison purposes. The linear mixed model used for this study incorporated AutoNRT threshold, model slope, electrodes and intercept offset as fixed effects, and subjects were included as random intercepts. The advantage of the linear mixed model is that it can estimate general variation between individuals and how well the tests correspond to each other if all subjects were to have the same baseline (i.e. the same intercept). The results from the linear mixed model motivated the use of a linear regression for calculating the intra-electrode profile based on AutoNRT. In Study IV, the Kaplan-Meier survival analysis was used to calculate the probability of keeping the preset pulse width, and the log-rank test was used to calculate differences in survival. A logistic regression was also employed to calculate the risk of not being able to perform AutoNRT, based on the results from Study II. The Fishers' exact test was applied for comparison of categorical, binary outcomes in Study IV.

3.5 ETHICAL CONSIDERATIONS

All studies received ethical approval before commencing. Studies I and II were performed at multiple centers in Europe and in Israel; approvals were granted according to regulations applicable at each center. The validity of the documents has also been verified by translating them from their original language (Italian, Spanish and Hebrew) into Swedish. The intervention in studies I and II was similar to the routine generally applied for CI recipients but with extended postoperative testing. Study III offered participating children reprogramming of the stimulation levels outside the clinical routine to investigate whether such reprogramming would be advantageous. It was expected that the participants would experience some difference after intervention, but care was taken to ensure that the difference was not too large, since all children in the study were highly dependent on functional hearing. Parents were also informed that they should contact the clinic if the new settings were problematic. Studies I, II and III all included participants prospectively after participants provided informed consent. Study IV, on the other hand, was a retrospective study concerning registry data in a database used for programming CIs. For this study no information was given to the participants and no informed consent was obtained. This type of study does of course also require considerations of ethical consequences even though the potential data were already collected, as all handling of this type of sensitive personal data. The database data were already pseudonymized, and in addition to implant parameters, only birth date and sex was extracted. Even though name and birth date are listed in the database, no contact information is stored, and the collection of such information would involve an additional source and a higher degree of handling of sensitive information than what was needed for the study. The collection of informed consent in this case could therefore be viewed as an unjustified intrusion of personal privacy.

4 RESULTS

4.1 STUDY I

The research question for Study I was to determine when the results from AutoNRT remain stable over time between measurements. The analysis was performed on change of individual electrodes, not subjects averages. The relationship between the measurements was originally analyzed with a Pearson correlation (results are presented in Table 4), but since correlation analysis was not suitable for this kind of analysis, a more appropriate Bland-Altman plot has been added. However, the Bland-Altman plot is a more visually driven analysis and does not yield a value to relate to as the correlation coefficient, instead the 95% confidence interval was used to estimate the variance between measurements.

Table 4. Pearson correlation coefficient calculated between AutoNRT, from the intraoperative measurement to 12 months after activation. All intracochlear electrodes were measured.

Children		Adults	
Compared time points	*r*	*Compared time points*	*r*
Intraoperative and Initial activation	0.58	Intraoperative and Initial activation	0.72
Initial activation and 1 month	0.79	Initial activation and 6 months	0.82
1 month and 3 months	0.89	6 month and 12 months	0.93
3 months and 6 months	0.91		
6 months and 12 months	0.91		

Figure 5 shows the Bland-Altman plot for children. As indicated by the Pearson correlation in Table 4, the agreement between measurements becomes better over time, with the main change occurring for the first three comparisons. The mean differences on all postoperative comparisons are close to 0 CL, and the 95% confidence interval were clearly reduced for the first three comparisons from an interval of -33.9–54.7 (mean difference = 10.4 CL) for the *Intraoperative – Initial activation* comparison to -20.6–19.0 (mean difference = -0.78 CL) for the *1 month – 3 months* comparison. The subsequent reduction was not as large and ends up with a 95% confidence interval of -16.0–15.3 for the *6 months – 12 months* comparison (mean difference = -0.37 CL). Further, the amount of measurements with a difference ±10 CL or less, which can be considered an acceptable variance, was 66% for the *Initial activation – 1 month comparison* but 79% for the *1 month – 3 months* comparison, and only increased somewhat more at the last comparison to 87%. For the adults, the same trend can be seen as for the children as shown in Figure 6. The 95% confidence interval reduces from -25.4–47.6 (mean difference = 11.1 CL) for the *Intraoperative – Initial activation* comparison to -13.9 – 12.0 (mean difference = -0.93 CL) for the *6 months – 12 months* comparison. For the adults, 41.2% of the measurements was within ±10 CL for the first comparison, 70.7% for the second comparison and 90.2% for the last comparison.

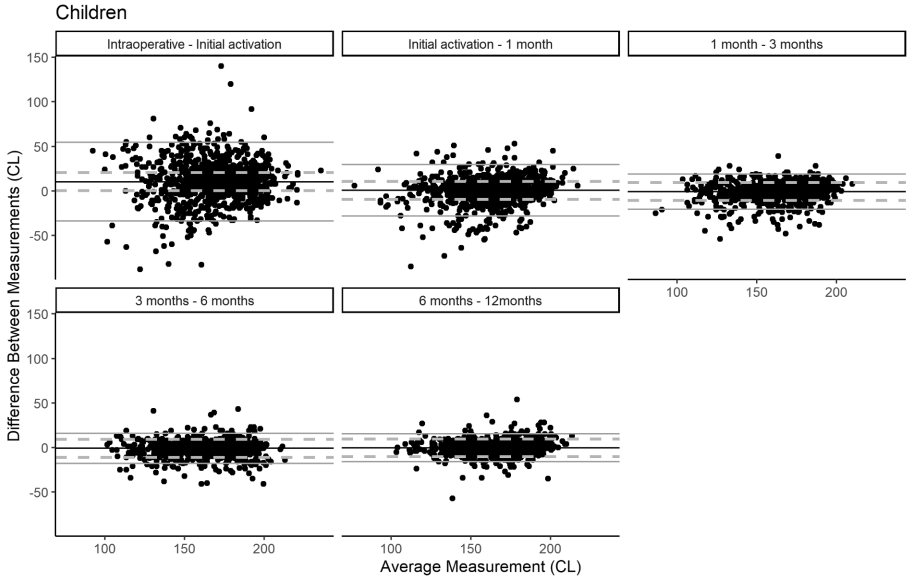

Figure 5. Bland-Altman plot over variance between subsequent AutoNRT measurements performed on all intracochlear electrodes in children. The y-axis indicates the difference in current level (CL) between to measurement on the same electrode, and the x-axis the mean value of the same two electrodes. The black horizontal line shows the overall mean difference, the gray solid line shows the 95% confidence interval, and the dashed gray line shows where the ±10 CL difference is.

In the original data analysis, an analysis was performed on individual electrodes that included mean absolute differences. This can be used to demonstrate that it is difficult to conclude that any electrode is more stable than others or that any part of the array is more stable. Electrodes 19, 20 and 21 from the children's measurements can be taken as an example. For the *Intraoperative – Initial activation* comparison, electrode 20 had the lowest mean absolute difference of 13 CL, however, flanked by electrodes 21 and 19 both with a higher difference of 18 CL. At the *Initial activation – 1 month* comparison, the mean absolute difference changed only slightly to 12 CL for electrode 20, but for electrodes 21 and 19, the difference dropped to 9 CL. At the *1 month – 3 month* comparison, electrode 21 had a mean absolute difference of 8 CL, electrode 20 a difference of 6 CL and electrode 19 a difference of 5 CL. Similar irregularities in variation can be seen across the array. Notably, electrode 1 seems to stand out, as it consistently showed a relatively high variation and repeatedly had the highest mean absolute difference, varying from 24 CL at the first comparison to 9 CL at last. That can be compared to the overall mean of the absolute difference across all electrodes, which was 19 CL at the first comparison to 5 CL at the last. The results for the adults show a similar trend, with the exception that electrode 1 does not stand out as being more disposed to variation than the other electrodes.

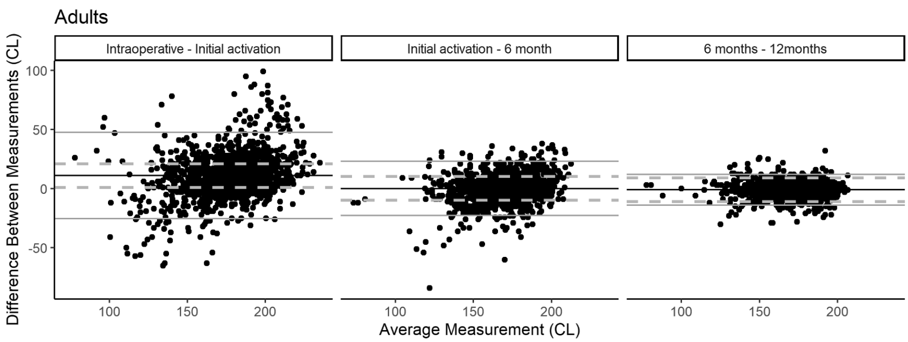

Figure 6. Bland-Altman plot of variance between subsequent AutoNRT measurements performed on all intracochlear electrodes in adults. The y-axis indicates the difference in current level (CL) between two measurements on the same electrode, and the x-axis the mean value of the same two electrodes. The black horizontal line shows the overall mean difference, the gray solid line shows the 95% confidence interval, and the dashed gray line shows where the ±10 CL difference is.

4.2 STUDY II

AutoNRT and T- and C-levels measurements performed on electrodes 3, 5, 9, 14, 18 and 22 at both 6 and 12 months were compared in order to examine the relationship between AutoNRT and the subjective thresholds. The linear mixed-effects model showed a large difference when relating AutoNRT thresholds to T- and C-levels. For the T-levels, the total variation for the 6 and 12 months comparison was 25.81 CL and 27.34 CL, respectively, and for the C-levels, 22.45 CL and 23.50 CL, respectively. Most of the variation (a little more than two thirds) could be explained by individual variances in intercept, whereas the rest of the variance was unexplained by the model. The variation in intercept between subjects indicated that the relationship between subjective thresholds and AutoNRT was highly individual when it came to predicting actual T- and C-levels. However, according to the intraclass correlation coefficient (that were between 0.8 to 0.9) the within subject variation was low, and if the difference in intercept were to be disregarded, it would likely yield a better result. For this purpose, the intra-electrode profile was calculated for each measurement and participant, then used in a linear regression model to calculate the relationship between the AutoNRT profile and the profile for the T- and C-levels. The results indicate that the variance between electrodes needs to be reduced by a factor of 0.41 to 0.52 for both the T- and C-levels, but also that the predictability was better for C-levels than for T-levels. According to the models' adjusted R^2, the C-level model explained about 50% of the variation, but only about 25% for the T-levels. No improvement of the model could be seen if stimulation levels were added as a factor, as was indicated by Botros and Psarros (2010). The results from the regression models (hereinafter *model fit*) were then compared to other rationales to estimate intra-electrode profiles: a *scaled fit* in accordance to Botros and Psarros (2010), an *unaltered fit* keeping AutoNRT variation unadjusted and a *flat fit* equal to zero intra electrode variation. The scaled fit resulted in a mean scaling factor for the T-levels of 0.86 and 0.85 for the two timepoints, and the C-level scaling factor was on average 0.63 and 0.62 at each of the two time points. As the scaling increased with the stimulation level, the T-levels are less affected by the scaling fit than the C-levels. Variation between rationales was quantified through a calculation of the root mean square error (RMSE). The RMSE values can be seen in Table 5. In line with the adjusted R^2, the results showed that it was more difficult to predict the T-level profile compared to the C-levels. The model calculated for this study indicated the best agreement across comparisons with the least amount of variation. For the T-levels, the model fit was significantly lower than the three other fits at 12 months ($p<0.05$), but at 6 months, no significant difference was observed between the model fit and the flat fit, although, it was significantly lower than the scaled and unaltered fit ($p<0.01$). For the C-levels, there was no significant difference between the model fit and the scaled fit at either 6 or 12 months. The model fit had significantly lower variation compared to both the unaltered and the flat fit ($p<0.01$).

Table 5. The root mean square error (RMSE) and standard error (se) for four different rationales for predicting T- and C-level intra electrode variance based on AutoNRT. The model fit was based on a regression model, the scaled fit was calculated according to Botros and Psarros (2010), an unaltered fit that kept the AutoNRT variance as is and a flat fit that with a variance at zero for all electrodes.

	T-levels				**C-levels**			
	6 months		*12 month*		*6 months*		*12 months*	
	RMSE	(se)	RMSE	(se)	RMSE	(se)	RMSE	(se)
Model fit	7.52	(0.48)	6.81	(0.56)	5.70	(0.47)	5.27	(0.30)
Scaled fit	9.67	(0.74)	9.31	(0.62)	6.20	(0.56)	6.13	(0.47)
Flat fit	8.67	(0.69)	7.96	(0.66)	8.37	(0.64)	7.08	(0.51)
Unaltered	10.48	(0.78)	10.27	(0.66)	8.15	(0.67)	8.44	(0.67)

4.3 STUDY III

4.3.1 CHANGE OF T- AND C-LEVELS

Reprogramming the original ECAP-based MAP with subjectively set stimulation levels resulted in a significant lowering of the T-levels, from a median value of 129 CL (interquartile range (IQR) =119–135) to 125 CL (IQR=111–131) ($p=0.016$). For the C-levels, no significant change could be observed, with an ECAP-based C-levels having a median of 173 CL (IQR=166–184) and a subjective MAP median of 175 CL (IQR=159–180) ($p=0.84$). The results further showed that there were substantial differences between the ECAP and the subjective based MAP on individual electrodes for some participants, especially for the T-levels, which resulted in a lowering of the threshold of 30 CL or more, for seven electrodes in four participants. For the C-levels, no comparably large changes were observed. The change in stimulation levels for the subjective MAP resulted in a significantly larger dynamic range with a median of 53 CL (IQR=43–60), whereas the ECAP-based MAP had a median of 47 CL (IQR=44–51) ($p=0.041$). Looking across the seven measured electrodes, however, there was only a significant difference in dynamic range for electrodes 2 and 22 ($p=0.041$ and $p=0.026$ respectively).

4.3.2 HEARING OUTCOMES

The pure-tone measurement resulted in no significant difference, with an overall median of 21 dB HL for both MAPs (IQR for the ECAP-based MAP was 19–25; IQR for the subjective MAP was 19–23, $p=0.17$). For the speech recognition test HINT-C-Quiet, the results for the subjective MAP were significantly higher compared to the ECAP-based MAP, although the difference was small. The median result for the subjective MAP was 95% (IQR=85–100) and for the ECAP-based MAP, it was 90% (IQR=75–95) , ($p=0.009$). Two children did not have a passing result of 50% for either ear or MAP and consequently did not continue with HINT-C. Regarding HINT-C, no significant difference between MAPs were observed. The results showed a median for the ECAP-based MAP of 4.71 dB SNR (IQR=3.41–6.24), and for the subjective MAP, the median was 4.00 dB SNR (IQR=3.26–5.47). Regarding the informal listening test for MAP preference at the final visit, 21 ears had a preference towards the subjective MAP, and the ECAP-based MAP was preferred in seven ears. Only one subject chose the ECAP-based MAP as a preference for both ears.

4.3.3 RELATIONSHIP BETWEEN STIMULATION LEVELS AND ECAP-THRESHOLDS

If there was a relationship between change in stimulation levels and a change in ECAP thresholds, the change between the ECAP-based MAP and the subjective MAP would induce a similar change for the ECAP thresholds recorded at the second and third visit (i.e. outcome change). A comparison was also performed between the change in ECAP thresholds between the first and second visit as a baseline comparison. The results showed that there was less difference in change between both the T- and C-levels when they were compared to the outcome change, than what could be seen for the baseline change ($p=0.004$ for both the T- and C-level comparison). That is, if stimulation level was increased for an individual electrode when reprogrammed with the subjective MAP the ECAP threshold between the second and third visit was more likely to increase for that electrode, compared to what was seen for the ECAP comparison between the first and second visit. A Spearman rank correlation analysis was performed to analyze the relationship between the change of stimulation levels and change in ECAP thresholds and showed an $r=0.49$ ($p<0.001$) for the T-levels and $r=0.39$ ($p<0.001$) for the C-levels. Although there seems to be a moderate relationship between the stimulation levels and the ECAP thresholds, the results also showed that a 1 CL change of the T-levels on average causes a 0.33 CL change in ECAP thresholds, and that 1 CL change in C-levels only causes an average change of 0.28 CL for the ECAP thresholds.

On a side note, for this comparison, it was observed that it was not possible to record AutoNRT in 36% of the tested electrodes due to voltage compliance issues. Impedance analysis showed significantly higher results ($p<0.001$) for these non-response electrodes for the MP1 condition (MP1 acting as reference electrode to the stimulating intracochlear electrode during the AutoNRT measurement), with a median of 19.14 kΩ compared to electrodes where thresholds could be recorded, which had a median of 10.58 kΩ. Seventy percent of the non-measurable electrodes belonged to CI422 implants, 25% belonged to CI24REs and 5% to CI512s. In total, 10 CI24REs, 9 CI422s and 8 CI512 implants were included in the study.

4.4 STUDY IV

4.4.1 IMPEDANCE DIFFERENCES

Results were collected and compiled for the different implant types (CA and SS) and analyzed for children and adults. For the SS implant, measurements were collected up until 11 years after activation for children, and 12 years for adults; for the CA implant, measurements were collected for 18 years for children and 17 years for adults. The difference in time between implant types was due to the fact that the SS implant is a newer type of implant than the CA implant. Overall , the CA implant had a significantly lower impedance compared to the SS implant for both children and adults ($p<0.001$) for both groups. For the children, the CG mean for the CA implant was 8.23 kΩ (SD=1.52) compared 9.98 kΩ for the SS implant (SD=1.76), and for the adults the mean was 7.49 kΩ (SD=1.62) for the CA implant and 8.31 kΩ for the SS implant (SD=1.77). Further, the children had significantly higher mean impedance than adults for both implant types ($p<0.001$). The MP1 measurement also stood out for the children, especially for the SS implant, where the impedance levels seem to slowly rise over the years independent of the other impedance conditions. For the adults this was not seen at all, were all impedance conditions followed each other with a similar offset over time.

4.4.2 INCIDENCE OF SHORT AND OPEN CIRCUITS

The incidence of short and open circuits electrodes was established for electrodes 2–22 and for the first ten years after implantation(the cumulative incidence can be seen in Table 6). In general, there were few incidences (<1%) of both short and open circuits for both implants, but despite this low proportion, significant differences were observed. For the adults, there were significantly more short circuits for the CA implant than for the SS implant ($p=0.015$). Interestingly, the relationship was reversed for the open circuit, for which the SS implant had a significantly higher incidence compared to the CA implant ($p=0.014$). For the children, there was no difference in the incidence of short circuits between the CA and SS implant ($p=0.64$). On the other hand, the higher incidence of open circuit seen in for the SS implant was highly significant ($p<0.001$). Comparing the sum of incidences of either short or open circuits across implants, there was no significant differences for the adults ($p=0.147$). For the children, the SS implant had a significantly higher incidence rate compared to the CA implant ($p=0.043$). The incidence of both open and short circuits was higher for children than adults (short circuits $p=0.002$, open circuits $p=0.014$).

Table 6. Cumulative incidence of short and open circuits for ten-year period. P-values from Fishers' exact test.

	Short circuits					**Open circuits**				
	Contour Advance		SlimStraight			Contour Advance		SlimStraight		
	%	(n)	%	(n)	*p*	%	(n)	%	(n)	*p*
Adults	0.41	(16)	0.08	(2)	0.015	0.03	(1)	0.56	(14)	0.014
Children	0.69	(30)	0.57	(14)	0.64	0.25	(11)	0.94	(23)	<0.001

4.4.3 INCIDENCE OF PULSE WIDTH INCREAMENTS

The increment of the pulse width was calculated based on the present default pulse width. Consequently, >25 µs was regarded as a pulse width increment for the CA implants and for the SS implant pulse widths >37 µs was considered. Each implant could only contribute with one increment. If additional changes were performed after that first included incidence, it did not contribute to the result. During the first year of usage for the children, the survival analysis showed a similar probability of keeping the default pulse width for both implant types, for the CA implant the probability was 0.95 (95% confidence interval = 0.92–0.98) and for the SS implant it was 0.91 (95% confidence interval = 0.86–0.97). After the second year, however, the probability continues to drop for the SS implant to 0.84 (95% confidence interval 0.78–0.91), whereas the CA implant remained at the same probability as after one year (0.95). Due to the implications an increased pulse width may have in children a statistical analysis was performed after five years of usage, mainly because children implanted early in life will likely be able to report changes at the age of 5 or 6. The analysis showed that the CA implant had a probability of 0.94 (95% confidence interval = 0.91–0.97), and the SS implant had a probability of 0.80 (95% confidence interval = 0.73–0.88) after five years of usage, which was significantly lower ($p<0.001$). For the adults the same trend was seen, although with a discernible drop during the first two years of usage for both implant types to 0.77 (95% confidence interval = 0.66–0.79) for the CA implant and down to a probability of 0.65 for the SS implant (95% confidence interval = 0.57–0.74). For the adults, as for the children, the results for the CA implant remained fairly stable after five years of usage with a probability of 0.74 (95% confidence interval=0.67–0.80), while the probability dropped additionally for the SS implant to 0.56 (95% confidence interval = 0.47–0.66) and also showed a significant difference ($p = 0.002$).

4.4.4 ANALYSIS OF RISK OF NOT BEING ABLE TO PERFORM AUTONRT

The risk of not being able to perform AutoNRT was analyzed during the first year of usage and was based on a cut of value of 15.34 kΩ or higher for the MP1 electrode, which serves as reference to the recording electrode. The cut of value was an estimate of a 50% risk of not being able to record AutoNRT. For the children, there was a significantly higher risk of not being able record AutoNRT for the SS implant than for the CA implant ($p<0.001$). For the SS implant, 5.33% of the electrodes had an elevated risk, and for the CA implant, 0.5% of the electrodes were at risk. The adults presented similar results where 4.26% of the SS implants electrodes indicated an elevated risk and 1.5% of the CA implant's electrodes ($p<0.001$). For the children, electrodes with an elevated risk could be seen across the array for the SS implant, but with a predominance towards the apical end from electrode 17 and above. For the adults the SS implant's spread of electrodes at risk across was more uniform across the array.

5 DISCUSSION

The studies within this thesis have considered aspects of programming CI stimulation levels for children and the implications depending on implant type.

The results showed that if ECAP, and specifically AutoNRT, are to be used as a basis for programming, the measurement should preferably be performed, or repeated, at least one month after the activation visits. Before this time, there was substantial variation between measurements. Furthermore, it was evident that actual T- and C-levels could not be derived with enough accuracy from AutoNRT for use in programming as is. Instead, as other studies have shown, the intra electrode variation could be used to get the electrode profiles of the T- and C-levels with an adjusted AutoNRT result that reduces the variance from the measurement to some degree.

Although the ECAP as a base for programming has been questioned, the long term follow-up for children showed a similar result for the ECAP-based MAP as the subjective based MAP. Reprogramming, however, was supported because of the discrepancies seen between the ECAP-based and the subjectively based MAPs, which indicate risk of over- or understimulation at individual electrodes.

Regarding the impedance results, the SS implant was more associated with impedance related issues that can affect audibility and the possibility of recording AutoNRT, than the CA implant.

5.1 STUDY I

The results for Study I were re-analyzed for the presentation in this thesis. The original analysis was performed mainly based on the Pearson correlation coefficient and indicated stable AutoNRT for young children from one month after activation. The current analysis was done with a Bland-Altman plot and shows the same trend as the correlation, but also reveals quite a large spread between the *1 month – 3 months* comparison for which the confidence interval was about ±20 CL around a mean variation of -0.78 CL, but the additional reduction at later time points was not that pronounced. Regarding the number of measurements within ±10 CL no substantial improvement was seen after the *1 month – 3 month* comparison. Therefore, even with the new analysis the variation seems to be stable after one month, however it may be a bit higher than the results of the previous analysis. Since recordings were done at fewer time points for the adults, the same conclusion cannot be drawn; however, the presented results show the same development over time as can be seen for the children. Regarding the variation from the intraoperative measurement to the initial activation, the results presented here demonstrate the same large variation seen in previous studies (Gordin et al., 2009; Hughes et al., 2001; Spivak et al., 2011; Telmesani & Said, 2015). The intraoperative measurement is performed just after a foreign object has been placed inside the cochlea, which in itself can disturb the sensitive environment of the cochlea and has the potential to cause trauma to the cochlear walls and even translocate to the scala media, which will affect the composition of fluids surrounding the implant. With time, the intracochlear environment will stabilize, which can be the change that was reflected in the postoperative measurements. These measurements were all performed with a PM implant. It is therefore possible to hypothesize that a slim LW implant would produce less variance due to reduced trauma; however, in a study by Telmesani and Said (2015) where PM and slim LW implants were compared, the LW implant presented more variance than the PM implant. Spivak et al. (2011) suggested that electrodes 11 and 16 were more stable from the intraoperative measurement than other electrodes. This result was not been reproduced here. The results analyzed across all electrodes demonstrated that this assumption can arise when only a subset of electrodes are measured, as in the study by Spivak et al. (2011), which included five electrodes spread across the array. When all electrodes were measured, as in this study, the results show that there can be large variances from one electrode to the next. However, if an electrode produces truly stable results it would be more likely that a directly adjacent electrode would produce similar response since they activate an overlapping portion of neurons. The results regarding the children, though indicate that electrode 1 is more inclined to vary between time points than other electrodes; the same variance for electrode 1 was not observed in adults. It has been suggested that a cover of fibrous tissue develops gradually around the array after insertion, affecting the flow of electrical current. If this is the case, the structural change may be more pronounced close to the insertion point and will affect electrode 1 more than other electrodes (Spivak et al., 2011; Tykocinski et al., 2005). An additional contributing factor could be that tissue growth is more pronounced within the cochlea for children than for adults (Hughes et al., 2001).

Many clinics perform ECAP measurements routinely during surgery. If these intraoperative thresholds are to be used to program stimulation levels they should to be considered preliminary. The results presented here indicate that if AutoNRT, or ECAP thresholds in general, are to be used for programming T- and C-levels for young children, the measurements should be re-recorded at least one month after activation. Still, it is debated whether ECAP thresholds are a valid basis for programming CI in young children. The question of how

AutoNRT and ECAP measurements should be applied when programming stimulation levels is addressed further in Study II.

5.2 STUDY II

It has previously been stated that it is difficult to predict T- and C-levels directly from ECAP measurements (e.g. de Vos et al., 2018) as was the case for this study, although the extended analysis shows that the intra-electrode variance can be predicted for the stimulation levels with moderate accuracy.

The use of AutoNRT did not generate better agreement, although judgement bias, which can be associated with human observers, was removed. When comparing the current results to previous studies, it does not seem that AutoNRT improves how well T- and C-levels are predicted. It is likely that the variation, as indicated by the linear mixed model, originates from subjective differences in loudness perception. As presented in the review by de Vos et al. (2018), previous studies mainly have used correlation to evaluate agreement between the ECAP threshold relate to the T- and C-levels, however, as for the objection of the analysis in Study I, the same applies here. A linear mixed-model was chosen in this case instead of a Bland-Altman plot since the linear mixed-model can estimate individual variation that is useful for the purpose of the study, but also the within subject variation. The results from the analysis showed that there was a large variation between subjects in intercept, but slope and electrode offset were comparable between subjects according to the intraclass correlation coefficient (0.8–0.9), indicating that intra-electrode variance can be predicted. Based on the results from an additional linear regression analysis of intra-electrode variance alone, which in effect removes the individual difference intercept, a model was reapplied to calculate T- and C-level profiles based on the AutoNRT results. The results from this model fit proved to generate better results than the unadjusted fit and the overall lowest RMSE (see Table 5). The additional comparisons that were made with the scaled fit (as proposed by Botros and Psarros (2010) and a flat fit, showed interesting results. The scaled fit seemed to perform on a similar level as the model fit for the C-levels as the scaling factor increased with stimulation level, but as the results in Table 5 show, it has a higher RMSE than the flat fit. While Botros and Psarros (2010) proposed less scaling for T-levels, the model fit introduced here did not. The model fit presented a very similar scaling for both T- and C-levels. The theory behind lower scaling comes from the fact that the variation between stimulation levels is generally higher between electrodes for T-levels than for C-levels. A similar difference can be seen for acoustic hearing at threshold levels compared to levels in the middle of the dynamic range for individuals with no hearing loss (Botros & Psarros, 2010). The model used here, however, did not corroborate this theory. If stimulation levels were essential, it is likely that adding these would improve the model, but this was not the case. Furthermore, rather than just being a matter of difference in scaling, the results instead signal that it is more difficult to predict T-level profiles from AutoNRT in general than it is to predict C-levels. These discrepancies between T-levels and AutoNRT (and likely ECAP thresholds overall),could originate from other factors. For example, both C-levels and AutoNRT stimulate the auditory nerve at comparable levels and therefore probably activate more or less the same neurons, with a more equal spread of excitation, whereas the lower stimulation of the T-levels could be more affected by smaller intracochlear changes that are evened out at higher levels, adding factors that cannot be adjusted for. The random aspects of the T-levels visible here can be one reason for the comparably low REMSE for the flat fit concerning these levels.

The results indicate that intra-electrode variance for the stimulation levels can be predicted with moderate accuracy from AutoNRT when the current model was applied, but that a prediction of actual T- or C-levels was not achievable. For young children, it is suggested that the model presented here is employed (or at least a general profile with a scaling factor between 0.52 to 0.41) for both the T- and C-levels, adjusting the overall stimulation carefully by using a live voice. Although the results here indicate that ECAP measurements may be valid for programming CI, the study was performed in adults and measured only T- and C-levels, not the functional MAP used. Study III concerns a long-term follow-up in children receiving ECAP-based MAPs (though it was not based on the model suggested here), and compares that to a subjectively based MAP.

5.3 STUDY III

The results from Study III showed that there was a difference in the ECAP-based MAP and the subjective MAP, especially for the T-levels, which were significantly lower for the subjective MAP compared to the ECAP-based MAP, although the average difference was just 4 CL. No significant difference was seen for the C-levels between the two MAPs. The most important finding regarding the MAPs, however, was the large discrepancy seen for individual electrodes regarding the T-levels. In four subjects' ears and for seven electrodes the T-level was more lowered with 30 CL or more when reprogrammed with the subjective MAP, which indicate that the ECAP based MAP overestimated the thresholds. It is possible that the discrepancies in T-levels between the two MAPs can be a manifestation of the lower predictability of the T-level profile from the ECAP thresholds seen in Study II. Regarding hearing outcomes, a significant difference was seen only for the HINT-C-Quiet measurement, although both MAPs produced a high average result of 90 and 95% for the ECAP-based and the subjective MAP, respectively. The HINT-C, or the pure-tone measurement, produced no significant differences. In the informal listening test for judging preferences, a considerable majority of the children chose the subjectively based MAP, and only one participant chose to go back to the ECAP-based MAP on both ears. Although this judgement seems to advocate the use of the subjective MAP, the result may reflect acclimatization more than a real advantage, that is, that the participants were more inclined to choose what they were accustomed to listening to. However, the overall results from the study indicate that the subjective MAP is favorable if it is achievable. On the other hand, the results indicate that an ECAP-based MAP may very well generate a valid MAP for young children.

An additional purpose of this study was to evaluate whether a change in stimulation levels would induce a change in ECAP thresholds as recorded with AutoNRT. The results indicated that there was a moderate correlation between a change in stimulation levels and a change in ECAP-thresholds for the T-levels ($r = 0.49$), while a weaker association was found for the C-levels ($r = 0.39$). This implies that adaptation to stimulation levels within the auditory nerve could partially explain why the ECAP-based MAP generally generates good outcomes, however, the average change to 1 CL in T-level stimulation would only generate an average change of 0.33 CL in ECAP thresholds. However, here the average change to 1 CL in T-level stimulation would only generate an average change of 0.33 CL in ECAP thresholds. Further, the results presented above showed that a possible adaptation cannot adjust for large variations. Since differences of 30 CL and more for the T-levels were registered between the two MAPs in four participants and clearly not fully adapted to the stimulation. Although the participants were relatively young, it is possible that the effect of changes would be even more pronounced at younger ages, as cortical plasticity is believed to peak at about 2 to 4 years of age (Purcell et al., 2021); however, peripheral structures are involved, and this assumption may not apply here. To our knowledge, the results presented here, which indicate an adaptation to stimulation levels within the auditory nerve, have not been presented in any previous research. However, until these results have been replicated in additional studies, they should be interpreted with caution.

An interesting finding from the AutoNRT measurement was that more than a third of the electrodes could not be recorded due to high impedance in the MP1 condition. High impedance for MP1 alone does not generally affect audibility with a CI since stimulation in everyday use relies on the MP1+2 condition, and to effectively stimulate against the electrode with the lowest impedance, it uses either MP1 or MP2. Consequently, if MP2 still has lower impedance, high impedance at MP1 is of little concern. What can be problematic is if there is a rise in impedance for the MP1 condition soon after implantation when programming is to be based on ECAP thresholds from AutoNRT, since the measurements do not allow for a change of reference electrode for the stimulating intracochlear electrode. As pointed out in Study I, measurements should preferably be re-recorded at least 1 month after activation. The risk of not being able to record AutoNRT during the first year and other impedance-related issues were taken into consideration in Study IV.

5.4 STUDY IV

The results from Study III indicate that there can be differences between implant types regarding impedance changes over time. Although the results from that study only concern the MP1 condition, it could indicate that impedance levels develop differently over time depending on implant type. In study III the CI422, an SS implant, had significantly higher impedance levels for the MP1, compared to the CI24RE and CI512, that are CA implants. Besides presenting problems for recording AutoNRT, impedance levels for other conditions than MP1 can be indicative of issues concerning audibility. Study IV therefore aimed to explore differences regarding impedances and related issues for the CA and SS implants from Cochlear Ltd.

The results for impedance differences over time showed that the SS implants, on average, had higher impedance levels and that these differences were significantly higher for the CG condition for both children and adults. Saunders et al. (2002) have shown that electrode area is one of the main factors influencing the impedance level, which makes the smaller electrode surface area of the SS implant the most plausible explanation for the higher impedance compared to the CA implant. The results also showed discrepancies between adults and children regarding the development of impedance for MP1. For the children the MP1 condition showed a slow increase of impedance in relation to the other two conditions (CG and MP2) for both implant types, whereas all condition's impedance levels for adults run parallel for throughout the time series. The reason for this increase in the children's MP1 result is unclear, but it could depend on the previous mentioned differences in healing patterns between children and adults, affecting the growth of tissue or bone surrounding the extracochlear ball or pin electrode and contributes to elevated electrical resistance (Hughes et al., 2001).

The analysis of short and open circuits showed a low incidence (<1%) for both implant types and in both children and adults. For both children and adults, the SS implant showed significantly more open circuits. For short circuits, on the other hand, adults with a CA implant had a significantly higher incidence. For children, the incidence of short circuits was somewhat higher for the CA implant than for the SS implant, though not significantly different. Harris et al. (2021) investigated a pediatric population and demonstrated similar contrasting outcomes for short and open circuits seen for the two implant types in the results here for adults, that short circuit was more common in CA implants and open circuits was more common in SS implants. Further, the results generally showed that children had a significantly higher incidence of both open and short circuits than adults. Different factors may have contributed to this, for example, children may be exposed to more trauma through activities in daily life (e.g. on the playground or through sports). Additionally, children had a higher incidence of open and short circuits for the SS implant type than with the CA implant, as the thinner array may be more sensitive when exposed to external forces either during implantation or postoperatively.

The results from the survival analysis for change of pulse width showed that the SS implant generally has a lower probability of keeping the preset pulse width over time then the CA implant. This result was in line with the higher increase of impedance levels seen for the SS implant compared to the CA implant. Although the probability was quite similar for the two implant types during the first year for the children, it increased to a significant difference after 5 years of usage. The CA implant had a 95% probability of still having the preset pulse width, whereas the SS implant had an 80% probability. The implication for children with SS implants is that in cases where a pulse width increment is preceded by compliance issues, there may have been periods of reduced audibility with the CI. For the youngest children who have difficulty communicating or even acknowledging the reduction, there may be periods when learning is affected and social interactions obstructed. Regarding the probability of change in adults, both implant types showed a more pronounced change than they did in children, since the adults generally had lower impedance levels for both implant types one or several additional factors to the impedance level need to be considered . One possible explanation could be that adults have been reported to have higher C-levels (mainly owing to high stimulation levels towards the apical part of the cochlea) compared to children (Greisiger et al., 2015), which would generate a higher probability of voltage compliance problems and affect both implant types, since C-levels have been reported to be equal for both SS and CA implants (Park et al., 2017). Voltage compliance issues are, however, not as problematic for adults as for children, since adults are likely to notice a reduction in audibility and contact the clinic to correct this. However, this will always be associated with an increase in power consumption, which may be problematic for both children and adults. Lastly, pulse width increments could depend on other factors than voltage compliance limitations, such as facial nerve stimulation (Van Horn et al., 2020), which most likely account for some of the increments in the material presented here. However, facial nerve stimulation is often managed in other ways as well (Bigelow et al., 1998; Pires et al., 2018; Polak et al., 2006). At the current clinic, this is usually done either by reducing the C-level for the electrode causing the stimulation to a maxima without observed facial nerve stimulation or by deactivating the affected electrode.

As indicated in Study III, the SS implant had a significantly higher risk of not being able to record AutoNRT when used in children than the CA implant. Although significantly higher, only 5.33% of the SS implant electrodes had an elevated risk, which is quite low and it would not be problematic if a few electrodes are at risk if they are spread equally across the array. However, the results show that electrodes at risk for the SS implant tended to cluster in the apical end of the array. If the AutoNRT result is to be used for programming stimulation levels and electrodes 17–22 remain unrecorded, thresholds have to be extrapolated from more basal electrodes that may lead to an inferior estimate of the T- and C-levels in this section of the array.

The results from Study IV showed that the SS implant was more inclined to have impedance related issues. Although the frequency of issues was generally low, this increased risk should be considered when choosing implants, particularly for children. In general, if durability is concerned and there is questionable benefit of preserved residual hearing the CA implant should be the preferred choice, although other factors may be influencing the choice as well. Further, it may be advisable to perform more frequent technical checks for young children who receive these implants.

5.5 LIMITATIONS

Studies I and II only concerned the CI24RE implant, an implant with a CA array. The CI24RE has now been replaced by newer CA models with a different housing and extracochlear electrode, however, the electrode array remains similar for all CA models, as well for the ECAP recording amplifier. While the stability of ECAP thresholds may not be affected between the SS and CA implant types in Study I, different results may have been achieved if an SS implant was used instead. The difference in distance to the spiral ganglions for LW and PM arrays may have showed a different relationship between ECAP thresholds and stimulation level and resulted in a different model for the T- and C-level profile calculation in Study II. Another limitation in Study I was the use of fewer time points for measurements in adults than for children, which makes it hard to evaluate variation with the same precision as for children. The fact that Study II only contained results from adults is not ideal. The cause of deafness in children may be different than the cause in adults. Furthermore, the survival of spiral ganglion neurons may affect the relationship between stimulation levels. However, it is likely that the use of the ECAP threshold solely to calculate the profile of the T- and C-levels would yield similar results in adults and children. Study III was initiated with the above in mind as a way to compare how children who received an ECAP-based MAP at a very young age performed compared to a subjective based MAP.

Study III was carried out as a single center study, which implies that other results may have been obtained if it had been carried out elsewhere. There is currently no standard definition for ECAP thresholds when programming stimulation, which is why differences between individual clinics always have to be considered. However, the large intra-individual differences seen for some subjects can appear whenever ECAP thresholds are used for programming. The number of participants in Study III was also too low to analyze the results by implant types; therefore, it is not known if there are any differences worth considering in relation to the ECAP-based MAP. To analyze whether there was an induced change in the ECAP threshold after change in stimulation levels in Study III, only the recorded differences between the ECAP and subjective-based MAP were used. This approach comes with certain limitations, for example, ECAP thresholds may be more disposed to change in the direction of the subjective thresholds than in the other direction, and the limit of a potential adaption is hard to derive from such material. For this purpose, it would have been better to assign change randomly to each subject and to each electrode; however, this would not be an ethical approach since it would cause discomfort to the user.

The use of retrospective data as in Study IV has certain drawbacks. Since participants were not enrolled prospectively the number of impedance measurements vary between subjects. This effect was most pronounced for adults, who had only regular follow-up visits for the first two years. The number of measurements declined drastically between the second and third year for this part of the sample. The children, who were followed regularly for an extended period, did not have the same drop off in the number of measurements at any time point. The effect may be that among adults, selection bias becomes a factor, if after two years mainly adults experiencing some kind of problem with their CI where measured. While this could skew the overall results of the impedance levels, it is not likely to affect the analysis in relation to differences between implant types, since recipients are most likely to visit the clinic if problems occur regardless of implant type. In terms of pulse widths, the nature of the analysis prevents that assertion of true causality between higher impedance levels and the increment of pulse widths. For this to be done, each change in pulse width would need to be assessed if depending on out-of-compliance or not, which cannot be done retrospectively since this data are not stored in the database and is not always documented in the medical journal.

This thesis only concerned implants from Cochlear Ltd, while all implant brands may be used in young children. Studies regarding programming aspects, impedance-related issues and long-term follow-up for young implantees are certainly of relevance in order to provide the best care for the youngest recipients.

6 CONCLUSION

- AutoNRT threshold, or ECAP measurements in general, should be re-recorded at least 1 month after activation if they are to be used as a basis for programming stimulation levels.
- The ECAP thresholds can be used to predict the intra-electrode variance of the T- and C-levels if scaling of the ECAP thresholds is performed.
- Comparing the results with previous studies, there were no indications that AutoNRT would improve the accuracy of the predictions for the T- and C-levels compared to the clinician determined ECAP measurement.
- The ECAP threshold produced a valid MAP on average, but large intra-individual differences indicate that a subjective MAP should be considered when this can be achieved.
- The results indicate that there is a small, peripheral adaptation within the auditory nerve derived from the stimulating levels.
- The SS implant was more likely to gain higher impedance levels for children and adults over time compared to the CA implant.
- The results regarding electrode failures were few (<1%) but these were significantly higher for the SS implant in children. The children also had an overall higher incidence rate compared to adults. No overall difference could be seen for adults.
- The SS implant had a significantly lower probability of retaining the default pulse width after 5 years for both children and adults.
- The SS implant had a significantly higher risk of not being able to record AutoNRT during the first year of usage than the CA implant.

7 FUTURE PERSPECTIVES

The most puzzling and interesting result within this thesis is the possible neural adaptation seen in Study III. Based on the results from only one study it is difficult to conclude anything with certainty and to know if it has any true implications for the CI recipients. If this is the case, this may have an impact on how we approach the programming of stimulation levels for the youngest CI recipients. Additional studies regarding this aspect should be carried out to determine whether the results can be replicated.

The results presented in Study II differed from what was observed in a previous study in terms of predicting the T-level profile from ECAP thresholds. This difference should be explored further in a third population to create a more accurate picture of the relationship between the ECAP thresholds and T-levels. An additional aspect is that Study II only concerned the CI24RE implant; therefore, we do not know how well stimulation levels for the SS implant can be predicted from the ECAP thresholds. It is possible that the LW type of array changes the circumstances in terms of the relationship, which may have implications for programming implants based on ECAP thresholds. Further research is needed to evaluate this.

According to the results presented here, the SS implant type showed higher impedance levels than the CA implant and was more prone to pulse width increments. It would therefore be of interest to evaluate long term impedance results for the Slim modiolar electrode, the CI532 and CI632 implant, with a slim PM array , which is inserted with a different technique than is used with CA implants in order to reduce trauma. If the Slim modiolar electrode produces lower average impedance and lower pulse width increments, it could be a viable alternative to the SS implant for recipients with residual hearing.

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