Dual electrode stimulation in cochlear implants: From concept to clinical application

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Dual electrode stimulation in cochlear implants: From concept to clinical application

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Chapter 1

Introduction and outline of the thesis

The Dutch population counts about 12,000 adults and children with severe to profound hearing loss (2012). Hearing aids are a poor solution for this group. A paramount opportunity of rehabilitation is a cochlear implant. Cochlear implant users regain part of their hearing by direct electrical stimulation of the auditory nerve. Experiments with electrical stimulation of the auditory system started several centuries ago with the electrical stimulation by a battery (Volta 1800). Technological improvements and the increasing computing capabilities of computer chips have led to new possibilities and improvements of speech coding strategies. Nowadays, manufacturers develop multi-channel cochlear implants with advanced speech coding strategies.

All current multi-channel cochlear implant systems have the same basic components and functions as the "Chorimac", developed in the mid-Seventies by Bertin for Chouard. A cochlear implant consists of an external and internal part. The

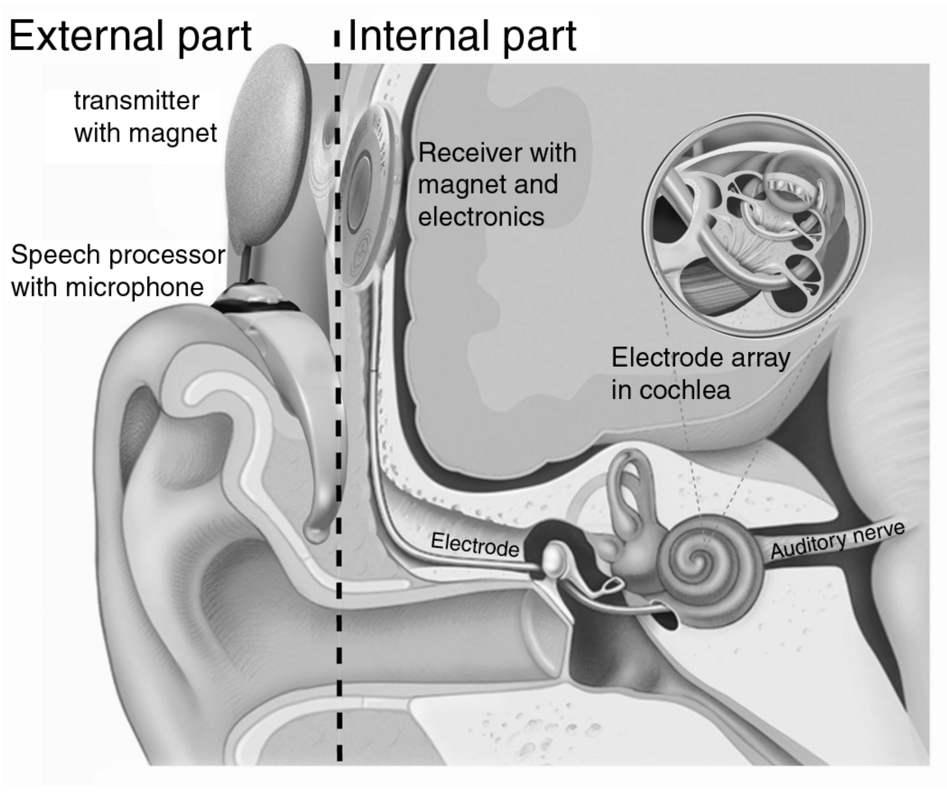

Figure 1. *Graphical representation of the basic components of a cochlear implant system with the internal and external part.*

external part consists of an externally worn speech processor and a microphone (Figure 1). The microphone captures incoming sounds, and the sound signal is processed in a speech processor. The speech processors can be divided into two groups, the body worn and the behind the ear processor. The processors filter the auditory signal into separate frequency bands, corresponding to each active channel of a cochlear implant. With a specific speech coding strategy a digital code is generated. This coded auditory signal is sent from the speech processor via a head piece containing a transmitting coil to the internal part. The transmitter is held in place by a small magnet linked to a similar implanted magnet. Next, the electronics of the internal part are in charge (Figure 1). The signal is decoded into electric current in the implanted processor. Most implants use charge balanced biphasic current pulses with regulated amplitude, which are sent to a specific electrode contact. In present-day devices, the number of contacts varies between 12 -22. These contacts are situated on an electrode array, which usually is placed in the scala tympani and are distributed in this way along the cochlear duct such that each contact can stimulate a separate sub population of nerve fibers. The assumption is that due to the tonotopic order of the nerve fibers the patient experiences in this way a different sound percept. Here the apical part of the cochlea encodes low frequencies while the basal part encodes high frequencies.

Early start of electrical stimulation of the inner ear

Alessandro Volta (Figure 2), the inventor of the battery, was in 1790 the first to describe how electricity can be used to hear sounds (Volta 1800). He used two metal bars connected to a 50 volt battery and placed them in both ear canals. He perceived a "crackling and boiling" sensation, which can be compared with boiling soup. In the next century, Duchenne de Boulogne (1855), a neurologist who did pioneering work on muscular diseases, electro-diagnostics and electrical stimulation, realized that sound is a vibration. He used experiments with alternating current, where the patient perceived a sound comparable with the moving wings of a fly. In the 20th century the first implant was a fact. Andre Djourno and Charles Eyries (Djourno and Eyries 1957) implanted a self-made mono channel implant in a 50 years old patient, who became deaf after several ear surgeries on both sides. The implant had an external coil and an internal electrode, which was placed directly on the auditory nerve. The patient was able to detect noises, but speech recognition was impossible. The patient did, however, improve his lip-reading capabilities with the use of this implant.

Figure 2. *Alessandro Volta, 1745-1827*

This work was continued by an American otologist William House, together with a collaborating engineer Doyle in 1961. House implanted a new electrode array into the scala tympani. This array was designed to stimulate at five different places. However, the silicone of the array, which was used in these first implants, contained toxic substances and yielded rejection and explantation (Doyle et al. 1964). In 1968, William House continued his work on the cochlear implant and implanted a 5-channel array, which was changed later into a single electrode array, into several patients. House also produced in mid-1972 the first wearable speech processor with a speech coding strategy. Patients were not able to understand speech yet, but it was an addition to lip reading (House and Urban 1973).

In 1980 House developed the single-electrode 3M/House implant (Figure 3). In this implant the amplitude of an analog sound waveform was compressed and subsequently the amplitude was modulated to a 16-kHz sinusoidal carrier to serve as the effective electric stimulus. Only a few patients were able to obtain open-set speech understanding, which was not surprising given the limited spectral resolution. This single-channel stimulation did not make use of the tonotopic arrangement of the nerve fibers, unlike all modern multi-electrode implants have been developed to do. In 1984 the first multi-channel cochlear implant, developed by Graeme Clark, was launched on the market as the Nucleus Multi-channel Cochlear Implant. A study of 40 users showed significant and substantial improvement in speech reading, and in speech understanding with electrical stimulation alone (Dowell et al. 1986).

Figure 3. *The single-electrode 3M/House implant (1980); measuring 8.6 cm x 5.1 cm x 1.6 cm. This was the first cochlear implant approved by the FDA. It used a transmitter that had been worn just behind the ear, a microphone that had been pinned to the clothing and a body worn single channel speech processor.*

Speech processing strategies

The speech processor plays an important role in a cochlear implant. It is responsible for the extraction of specific acoustic features, after which the processor encodes these features via radio frequency transmission, and finally controls the parameters of electric stimulation.

Although a wide range of different speech processing strategies were developed over the last 30 years, they all make use of an implemented bank of filters to divide speech into different frequency bands. They differ, however, significantly in their processing strategies to extract, encode and transfer the right frequencies. The pathway towards used strategies nowadays is influenced by the processing capabilities of the original speech processors, insights in electrical stimulation and manufacturer's vision and implant design as will be described in the next section.

Spectral cues: Explicit feature extraction

The first multichannel Nucleus implant used a strategy, which was based on speech production and perception. The human ear is able to distinguish vowels from each other, because each vowels has a few fixed formants. A formant is a resonance on a certain frequency. Formants make an important contribution to the timbre of the voice and are also called the spectral peaks of the sound spectrum of the voice. Along this strategy spectral peaks of formants are extracted and delivered to different electrodes. The F0/F2 strategy (Clark et al. 1987; Seligman et al. 1984) was the first available strategy for the Nucleus wearable speech processor (WSP, (1982)) (Figure 4a). By using zero crossing detectors the fundamental frequency

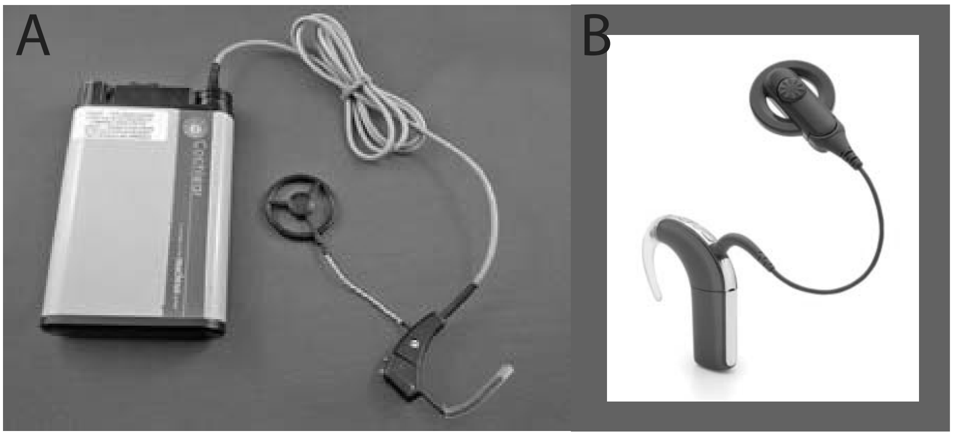

Figure 4. *(A) Wearable Speech Processor (1982); measuring 11.7 cm x 7.6 cm x 2.1 cm and weighing 255 gram with batteries; (B) CP810 (2012); measuring 5.1 cm x 0.9 cm x 1.9 mm and weighing 10.9 gram. Both are Nucleus® speech processors from Cochlear™, where (A) is the first processor, body worn and (B) is the most recent processor, worn behind the ear.*

F0, estimated from the output of a 270 Hz low-pass filter and the second formant (F2) estimated from the output of a 1000-4000 Hz band pass filter, have been extracted from the speech signal. The F0/F2 processor conveys F2 frequency information by stimulating the appropriate electrode in the 22-electrode array. Voicing information is conveyed with F0 by stimulating a selected electrode at a rate of F0 pulses per second. Initial results with the F0/F2 strategy were encouraging, because, as mentioned before, it enabled some patients to obtain open-set speech understanding (Dowell et al. 1986). In 1985 this strategy was modified to include information about the first formant frequency (F1), which resulted in the F0/F1/F2 strategy (Blamey et al. 1987). An additional zero-crossing detector was included to estimate F1 from the output. The processor selects two electrodes for stimulation, one corresponding to the F1 frequency, selected out of the first five apical electrodes, and one corresponding to the F2 frequency, selected out of the remaining 15 electrodes. The speech-recognition performance improved significantly by adding F1 information (Dowell et al. 1987; Tye-Murray et al. 1990). This was self-evident, given the importance of F1-F2 for normal-hearing listeners on speech recognition. However, it did not significantly improve on consonant-recognition scores. This is due to the fact that consonants do not have formants and that the F0/F1/F2 strategy emphasizes low-frequency information, which is required for vowel recognition. By including high-frequency information and spectral information in new hardware, Cochlear Limited improved the F0/F1/F2 strategy to the MPEAK strategy (Patrick and Clark 1991) in 1989 and this way improving the perception of consonants. Next, a new processor, the Miniature Speech Processor (MSP), was introduced, which used a custom integrated circuit for digital signal processing. In spite of large improvements in speech recognition (Dowell et al. 1991; Skinner et al. 1991), there were still several major limitations, including being the extraction of a speech signal embedded in noise.

Currently these speech specific feature extractions are not used any more in speech coding strategies.

Temporal cues

Compressed analog

Another line of strategy is the waveform strategy, which tries to present some type of waveform derived by filtering the speech signal into different frequency bands. An example of a waveform strategy is the compressed analog (CA) approach, which was first introduced in 1988 (Eddington 1980) and originally used in the Ineraid device. The Ineraid device used 6 active electrode contacts including two ground electrodes, which can be used as a reference electrode in monopolar stimulation. The device made use of monopolar stimulation and of percutaneous transmission. The CA approach is shown in Figure 5 in a block diagram. The acoustic signal is first compressed using an analog automatic gain control, because the amplitude levels or dynamic output range of the microphone do not match the dynamic input range

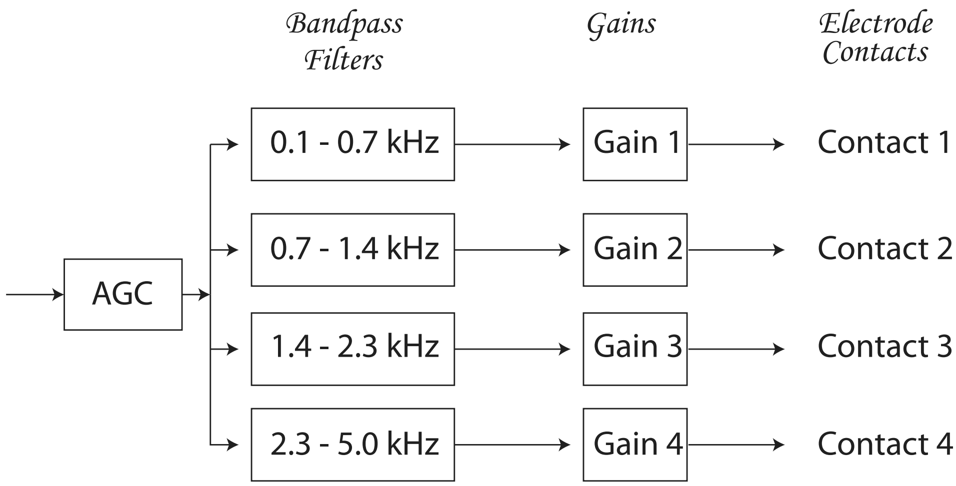

Figure 5. *Block diagram of the compressed analog (CA) approach used in the Ineraid device. The signal is first compressed using an automatic gain control. The compressed signal is then filtered into four frequency bands (with the indicated frequencies), amplified using adjustable gain controls, and then sent directly to four intra cochlear electrodes.*

of the processor. The compressed signal is then filtered into four consecutive frequency bands. In the next step the signal passes through adjustable gain controls and is sent directly to four intra cochlear electrode contacts. These waveforms are delivered simultaneously in an analog form. The electrodes operate in a monopolar configuration with the return electrode located outside the cochlea in the temporalis muscle.

The Clarion device (Advanced Bionics) (Schindler and Kessler 1992) made use of the compressed-analog processing in the Simultaneous-Analog-Strategy (SAS), which came on the market in 1996. One of the differences between CA and SAS is, is that CA is completely analog and SAS makes also use of digital signals. In the SAS mode, the acoustic signal is processed through eight filters, compressed and transferred simultaneously to eight electrode pairs. It makes use of bipolar electrode coupling in which each electrode is paired with another electrode that is proximate; the return electrode is in this case situated intra-cochlear.

Continuous interleaved sampling

The simultaneous stimulation appeared to be a problem for the CA approach due to a high interaction between channels caused by summation of electrical field from individual electrodes. With a Continuous Interleaved Sampling (CIS) approach, introduced in 1991 (Wilson et al. 1991), the channel interaction issue was addressed by using non-simultaneous interleaved pulses. Only one electrode has been stimulated at a time with this approach. The preprocessing is similar to the preprocessing of the CA processor, where the signal is first pre-emphasized, i.e. low-frequencies are attenuated and high frequencies amplified. Next, signals pass through a bank of band pass filters (Figure 6). The envelopes of the filtered waveforms are then extracted by full-wave rectification followed by low-pass filtering, i.e. low-frequencies pass through and higher frequencies are attenuated. Next the envelope outputs are compressed and used to modulate biphasic pulses.

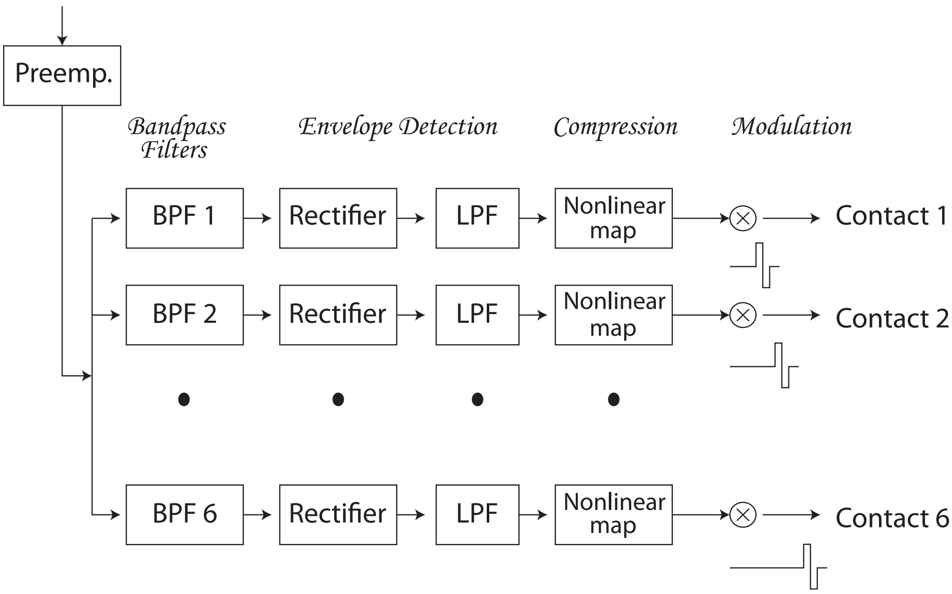

Figure 6. *Block diagram of the Continues Interleaved Sampling (CIS) strategy. The signal is first pre-emphasized and filtered into six frequency bands. The envelopes of the filtered waveforms are then extracted by full-wave rectification and low-pass filtering. The envelope outputs are compressed to fit the patient's dynamic range and then modulated with biphasic pulses. The biphasic pulses are transmitted to the electrodes in an interleaved fashion.*

A compression function is used to ensure that the envelope outputs fit the patient's dynamic range of electrically evoked hearing. In a typical CIS implementation, the number of band-pass filters is identical to the number of electrodes, ranging from 8 in the original Clarion CI device of Advanced Bionics (Figure 7a), to 12 in the Med El devices (Combi and Tempo) (Figure 8a) and 22 in the Nucleus devices. The HiRes strategy of Advanced Bionics is a close variation of CIS that uses relatively high rates of stimulation, relatively high cut-off frequencies for the envelope detectors, and up to 16 processing channels and corresponding stimulus sites.

With the development of CIS all the other strategies became superfluous, because of the large improvement in speech perception scores. Except for SAS, which still remained in use by Advanced Bionics next to CIS for several years, as some cochlear implant users performed better with SAS than with CIS (Battmer et al. 1999; Osberger and Fisher 1999; Stollwerck et al. 2001; Zwolan et al. 2005).

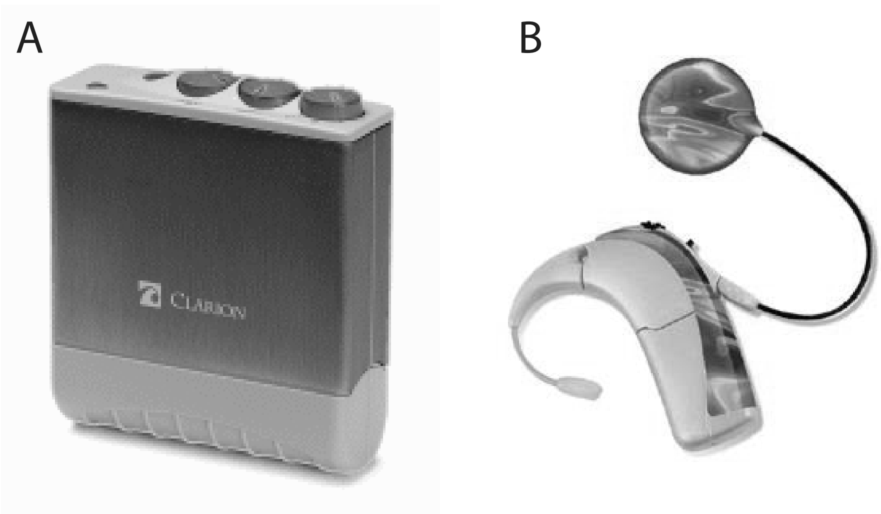

Figure 7. *(A) Clarion CI device (1996); (B) Harmony processor (2010). Both are processors from Advanced Bionics®, where (A) is their first processor, body worn and (B) is the most recent processor, worn behind the ear.*

"n-of-m"

Another variation on CIS is the "n-of-m" strategy (Wilson et al. 1988) were the number of physical contacts and filters (m) can be greater than the number of stimulating electrodes (n). In this strategy the envelopes of the n sub bands with the highest energy are selected to stimulate the corresponding electrodes. This strategy has been used in the Nucleus SPEAK (Spectra 22 (1995)) and ACE processor (Freedom (2005), behind the ear). The pre-processing is similar to the pre-processing of the CIS strategy, including the band pass filters and the envelope extraction blocks. A difference can be found in that the “n-of-m” strategy is based on temporal frames, whereas the CIS strategy does not have any explicit processing frames. Also, only the corresponding “n” electrodes out of the “m” electrodes are stimulated in a particular frame. The SPEAK strategy selects 6-8 largest peaks and has a fixed 250 Hz per channel rate. The ACE strategy has a larger range of peak selection and higher rate than the SPEAK strategy. If n=m, then SPEAK and ACE strategies are essentially the same as the CIS strategy.

A newer method is MP3000, which is a modification of the ACE strategy. This method uses a psychophysical masking model to select the amplitude components that are not masked by higher amplitude components and should be included in the signal. The other components are omitted from the transmission. This approach could improve spectral resolution. Four channels of this algorithm gave indeed a better performance with sentence-in-noise test (Buchner et al. 2008). The test with eight channels gave, however, comparable results.

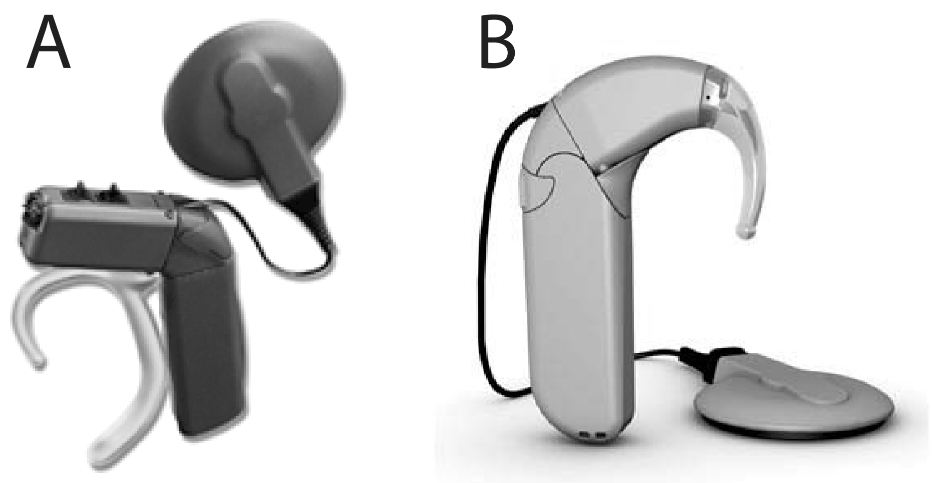

Figure 8. *(A) Combi (1996); (B) OPUS 2XS (2007). Both are processors from Med El and worn behind the ear.*

Fine features

The latest developments on speech processor strategies focus on how to encode spectral and temporal fine structure cues in cochlear implants, so speech recognition in noise and listening to music can be improved. In basic CIS like strategies, the fine timing or fine-structure of the sound waves are largely lost in the process from acoustic input to a fixed-rate sequence of biphasic electrical pulses. These implant users must rely on perceiving temporal envelopes (not temporal fine-structure) at specific places in the cochlea. Another problem is that with monopolar stimulation, which is used in these strategies, the place of excitation has not the desirable precision due to low spatial selectivity. For high levels of melody recognition, at least 64 individual channels are needed (Smith et al. 2002).

One way to encode the temporal fine structure is to increase the electric stimulation carrier rate so that the temporal fine structure cue can be represented in the waveform domain (e.g. Med El's FSP processor) (Figure 8b). Another approach is to represent the fine frequency information within bands using multiple sites of stimulation for each band and associated channel rather than the single site for each band and channel used in CIS and other strategies. This approach is a variation of HiRes (Advanced Bionics) and is called the HiRes with the Fidelity 120 option (HiRes 120) (Harmony processor) (Figure 7b). By stimulating two electrodes simultaneously, the number of discriminable sites is increased beyond the number of physical electrodes. This concept is called simultaneous dual electrode stimulation, current steering or virtual channels. In HiRes 120, 16 physical electrode contacts generate 8 intermediate pitches per electrode contact pair, giving a total of 120 different precepts. Unfortunately, no large improvements in speech perception are found with these fine feature speech processor strategies (Brendel et al. 2008; Buechner et al. 2008; Buechner et al. 2010; Donaldson et al. 2011; Firszt et al. 2009).

Another solution can be found in "conditioning" (Rubinstein et al. 1999). This processing is based on a physiological model. The auditory nerve in a normal-hearing ear has spontaneous activity effectively keeping the nerve ready to fire when an acoustic event activates it. The auditory nerve of a deaf ear lies dormant if it receives no input. Electrical stimulation of this last nerve leads to a high degree of synchrony firing across the spectrum, causing an extremely limited electrical dynamic range of about 10 to 30 dB. By using a "conditioner", a low-level, constant amplitude high-rate pulsatile stimulation, a pseudo spontaneous activity can be created and the dynamic range can be increased. This has been tried in a Conditioned CIS (CCIS) processing strategy, where a low-level conditioning stimulus at about 10 percent of the dynamic range has been combined with traditional CIS processing. The initial results of 30 subjects suggested better speech perception in noise for halve of the users and many implantees reported that music sounded better, but melody recognition showed no significant difference with CIS (Drennan and Rubinstein 2008). The implementation of CCIS is, however, limited because it can only be implemented on Advanced Bionics devices. This strategy has not made the transition from the academic trial to the clinic up till now.

Old methods brought into practice

Several methods to the improvement of speech perception with cochlear implants are under investigation at the moment. Of interest is that some of these methods were already known for several years, but due to technical limitations could not aptly be put into clinical practice.

Current steering, as mentioned in the previous paragraph, was first introduced by Townshend et al. (Townshend et al. 1987) in the late eighties to increase the number of distinct pitches a subject can discriminate. They showed that the perception of pitch can be varied between two adjacent electrodes by delivering the current simultaneously to both contacts. Recipients systematically reported a single-sound percept with a pitch that was between the base pitches of the individually stimulated contacts. This method was, however, not ready to be used in a speech coding strategy until recently (Brendel et al. 2008) in the Fidelity 120.

Another way to enhance the number of pitches is with phantom stimulation. This method had first been introduced by Wilson et al. (Wilson et al. 1993) in the early nineties to generate a pitch sensation lower than that produced by monopolar stimulation of the most apical electrode contact or higher than the most basal electrode contact. A phantom channel is a form of partial bipolar stimulation, with non-equal amplitudes out of phase on two adjacent stimulating electrode contacts, which results in that the excitation area is being pushed away from the stimulated contacts. This way the number of pitches can be enhanced beyond the electrode array. Saoji and Litvak (Saoji and Litvak 2010) showed in 2010 that it is possible to push the percept from 0.5 to 2 contact spacings away. After more fundamental research, one of the next steps is implementing this method in a speech coding strategy.

Large current spreads can impose limitations in cochlear implants and possibly degraded speech perception scores. Next to (partial) bipolar and (partial) tripolar stimulation, where two flanking electrode contacts are stimulated with non-equal amplitudes out of phase to reduce the region of excitation, Van Compernolle (van Compernolle 1985) suggested using all electrode contacts simultaneously (multipole stimulation) to reduce these effects of monopolar stimulation in the mid-eighties. This so-called phased array algorithm was validated by Van den Honert et al. (van den Honert and Kelsall 2007) in patients with respect to the electrode potentials in 2007 and the effect on neural excitation was investigated by Frijns et al. (2011) in a computational model of the cochlea in 2011. Before phased array channels can be implemented in a speech coding strategy, several issues remain to be addressed. For example, due to the focusing penalty, impractically high currents may be required to achieve sufficient loudness.

Overview of the present study

This thesis describes a translational study of dual electrode stimulation (DES), the stimulation type underlying Fidelity 120 and phantom stimulation as described above. The mechanisms of DES will be investigated both psychophysically and in a computational model of the cochlea, followed by a clinical implementation of DES to correct for defective electrode contacts.

There are different ways of stimulation. If the most apical electrode on an array is stimulated alone, we speak of Single Electrode Stimulation (SES) and subjects perceive a low pitch (Figure 9A). If the next electrode in the array is stimulated alone (SES), a higher pitch is perceived (Figure 9B). If these two electrodes are stimulated simultaneously with identical in-phase pulses, we speak of simultaneous Dual Electrode Stimulation (DES) or current steering; in this case the subject can perceive a pitch intermediate to the stimulated electrodes (Figure 9C). The current ratio divided over these two electrodes can change, expressed in percentages and each different percentage can give a different percept. Several studies showed that patients are able to discriminate different percepts with DES. However, not every patient is able to discriminate extra pitches, which suggest that these users may potentially not benefit from DES. Our objective is to establish how DES can be optimized and whether it has the same qualities as SES, enabling its use in a CIS like strategy. **Chapter 2** describes the comparison of DES with SES with respect to the site of stimulation in the cochlea, the spread of excitation (SOE) and sequential

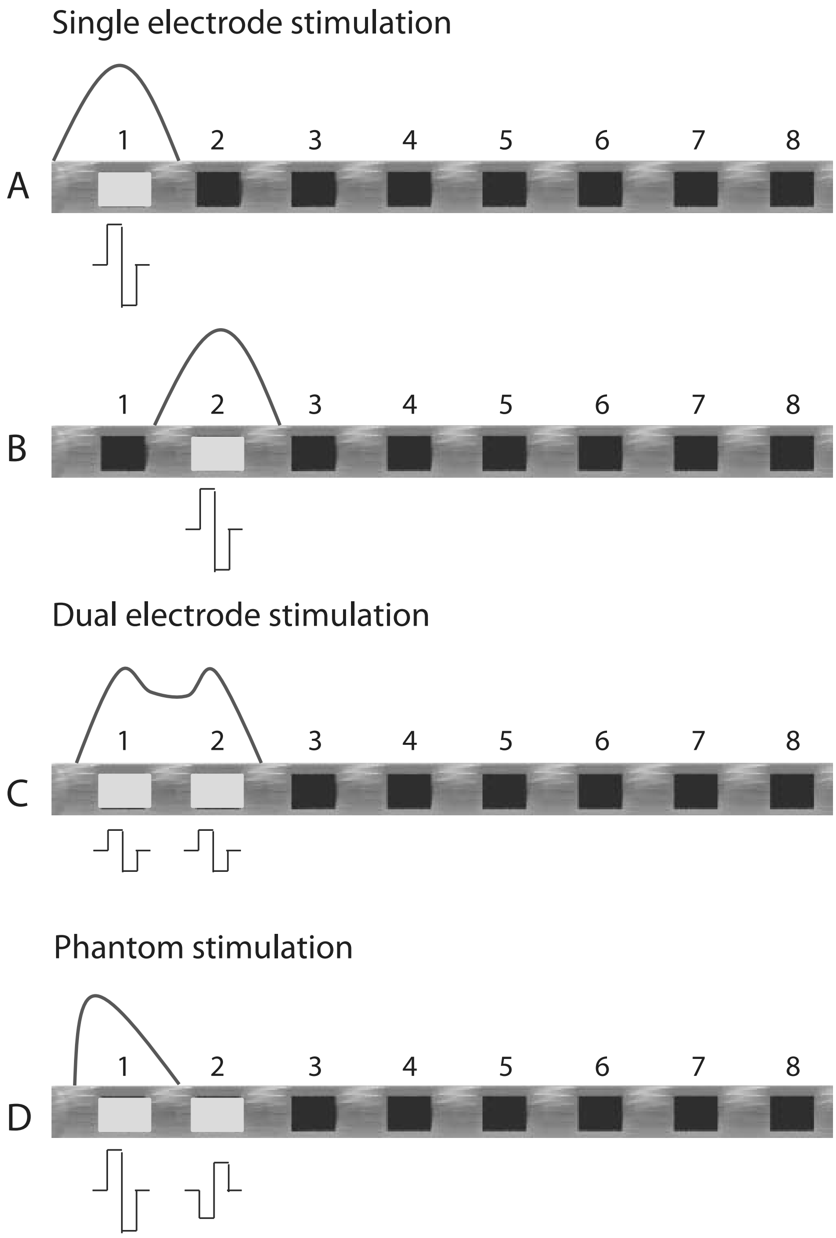

Figure 9. *Schematic illustration of single electrode stimulation on electrode contact 1 (A) and contact 2 (B), dual electrode stimulation (C) and phantom stimulation (D). The light gray electrode contacts are the stimulated contacts. The curve in each panel is hypothetical sketch of the place neural response. Condition is indicated by pulse waveform(s) beneath the stimulated contacts on the electrode array.*

channel interactions. It is of importance to be able to determine in advance whether a patient is able to discriminate extra pitches created with DES. It is investigated whether the number of intermediate pitches created with DES can be predicted from SOE, channel interaction measures, current distribution in the cochlea, or distance of the electrode to the medial wall.

DES can also be used to create a pitch beyond the electrode array in the apical region by using a pulse with opposite-polarity on the basal electrode contact of the pair (Figure 9D). It is called Phantom stimulation throughout this thesis. The pitch is than shifted away from the apical electrode and is lower in pitch than the pitch of the apical electrode contact with SES. The possibility for each patient to perceive a lower pitch with phantom stimulation is described in **chapter 3**. This phantom stimulation was further explored by using psychophysical experiments and computational modeling of the cochlea. It is investigated whether a current correction was necessary to maintain equal loudness effect and the place of stimulation was determined.

The last three chapters will further explore the possibilities and qualities of simultaneous DES. In **chapter 4** the possibility is explored to bridge defective electrode contacts with DES applied on non-adjacent electrode contacts. This type of DES is called spanning throughout this thesis. With psychophysical experiments spanning was compared with DES on adjacent electrode contacts in terms of the number of intermediate pitches, loudness effects and linearity of the current weighting coefficient with respect to the perceived pitch.

The experiments in all former chapters were performed on Most Comfortable Loudness (MCL) level. When DES will be used in a speech coding strategy, it is also of interest to know what happens at Threshold Level (TL), because of the clinical fitting procedure. TL is the level where the patient is asked to indicate when the signal was just heard. **Chapter 5** investigates the efficiency of DES at lower levels, with the focus on the requirements to correct for threshold variations. TLs were determined both psychophysically and with computational modeling, where the computational model utilized three different neural morphologies with different stages of degeneration.

After fundamental experiments with DES, the challenge remained if implementation of spanning in a speech coding strategy would be possible and would not decrease the performance and the quality of sound. In **chapter 6** three different speech coding strategies are designed, with 1, 2 or 3 defective electrode contacts next to each other. Each of the programs pretended to have a total of 6 defective electrodes. Patients were asked to use and evaluate these different strategies in home situation. Further, speech perception scores were measured in silence and with background noise.

An overall discussion of the major results and conclusions are presented in **chapter 7,** followed by some clinical implications and future perspectives.

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Chapter 2

Spread of excitation and channel interaction in single and dual electrode cochlear implant stimulation

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Abstract

Objectives: To determine how simultaneous Dual-Electrode Stimulation (DES) can be optimized for the individual patient to deliver better sound quality and speech recognition. DES was compared with Single-Electrode Stimulation (SES) with respect to the site of stimulation (X) in the cochlea, the Spread of Excitation (SOE), and channel interaction. Second, it was investigated whether the number of intermediate pitches created with DES can be predicted from SOE, channel interaction measures, current distribution in the cochlea, or distance of the electrode to the medial wall.

Design: Twelve users of the HiRes90K cochlear implant with HiFocus1J electrode were randomly selected to participate in this study. Electrode contacts were selected based on their location in the cochlea as determined by multi slice computed tomography, viz. 120 degrees (basal), 240 degrees (middle), and 360 degrees (apical) from the round window. The number of intermediate pitches with simultaneous DES was assessed with a three-alternative forced choice pitch discrimination experiment. The channel interactions between two single-electrode contacts and two DES pairs were determined with a threshold detection experiment (three-alternative forced choice). The eCAP-based SOE method with fixed probe and variable masker was used to determine the location of the neurons responding to a single-electrode contact or dual-electrode contact stimulus. Furthermore, the intracochlear electrical fields were determined with the Electrical Field Imaging tool kit.

Results: DES was not different from SES in terms of channel interaction and SOE. The X of DES was 0.54 electrode contacts more basal compared with SES stimulation, which was not different from the predicted shift of 0.5. SOE and current distribution were significantly different for the three locations in the cochlea but showed no correlation with the number of perceivable pitches. A correlation was found between channel interaction and the number of intermediate pitches along the array within a patient, not between patients.

Conclusion: SES and DES are equivalent with regard to SOE and channel interaction. The excitation site of DES has the predicted displacement compared with the excitation region induced by the neighboring single-electrode contact. Unfortunately, no predictor for the number of intermediate pitches was found.

Introduction

In the majority of cochlear implant users, the number of electrode contacts required for optimal speech perception is often smaller than the total number of available contacts. Several studies have shown that speech perception in quiet does not improve above about seven electrode contacts (Baskent 2006; Fishman et al. 1997; Friesen et al. 2001; Fu et al. 1998), although a greater number is generally considered beneficial for listening in noise (Frijns et al. 2003; Nie et al. 2006). This asymptote of performance with increasing electrode contact number is thought to be due to channel interactions and limited spatial selectivity of stimulation, which act to limit the degree of spectral discrimination (Fu and Nogaki 2005).

These channel interactions can be divided into two categories, namely electrical and neural interaction. Sequential (non-simultaneous) pulsatile stimulation was initially introduced largely to avoid the electrical interaction that is inevitable with simultaneous stimulation of more than one electrode contact. Nevertheless, even with fast sequential stimulation, interaction still occurs by charge summation on the neural membrane. Because of the wide current spread, the stimuli on several electrode contacts affect an individual neuron. The interaction is somewhat uncontrolled, as it depends on the current spread, influenced for example by electrode location and local tissue conductivity, and the refractory properties of the neuron and the timing between pulses. With simultaneous stimulation, however, current fields can interact by electrical field summation before neural stimulation occurs (de Balthasar et al. 2003; Skinner et al. 1994).

Simultaneous Dual Electrode Stimulation (DES), also known as “current steering”, makes positive use of electrical interaction to enhance the number of spectral channels. DES involves simultaneous stimulation of two adjacent or non-adjacent (spanning) electrode contacts to stimulate intermediate neural populations and thus generate pitch sensations intermediate to those induced by the individual physical electrode contacts (Donaldson et al. 2005; Firszt et al. 2007; Koch et al. 2007; Snel-Bongers et al. 2011; Townshend et al. 1987). The proportion of current delivered to the two stimulated electrode contacts can be varied, potentially leading to several different pitch sensations for any given electrode contact pair.

Simultaneous DES can only be implemented in cochlear implants with at least two independent current sources. At the present time, the principle of DES is implemented commercially in the Advanced Bionics Harmony system, using the HiRes 120 speech coding strategy (Eklöf, reference note 1). Instead of 16 spectral channels generated using the 16 physical electrode contacts, 8 intermediate or “virtual” channels are available per electrode contact pair, giving a total of 120 spectral channels (from 15 available pairs). The expectation is that more spectral channels will result in a more natural sound percept and higher speech perception scores. Although initial results are promising, they vary among different studies (Brendel et al. 2008; Buechner et al. 2008; Firszt et al. 2009) (Boermans, reference note 2).

It is, however, important to note that benefit from DES is likely to be obtained only when the available spectral channels can be discriminated. Firszt et al. (2007) reported that users of the CII and HiRes 90K implants (using the PSP processor) were able to discriminate between 8 and 451 pitch percepts over the entire electrode array, with an average of 63, which suggests that many, although not all, users of these devices may potentially benefit from DES. The use of 120 channels for all patients might be an overestimation of the discrimination potential in the subject group. In approximately 30% of the subjects, the number of discriminable spectral channels is lower than the number of physical electrode contacts on the array (Firszt et al. 2007; Koch et al. 2007). For this group the use of virtual channels will probably not be beneficial and potentially even detrimental. Therefore it would be important to be able to determine in advance whether a patient is able to discriminate between physical contacts and, if so, how many intermediate pitches can be created, so that individual adjustments can be made.

Therefore, there is considerable interest in how current steering in speech coding strategies may be optimized to deliver better sound quality and speech recognition, but to understand what happens with DES, closer investigation is necessary. On the basis of earlier computational modelling of the cochlea (Frijns et al. 2009), it is predicted that low selectivity, high interaction, or a lateral position of the electrode contacts is beneficial to smooth current steering and therefore might correspond with a high number of intermediate pitches. In the present study, we investigated whether the ability of a patient to discriminate intermediate pitches can be predicted by physiological (Spread of Excitation (SOE) and Electrical Field Imaging (EFI)), psychophysical (channel interaction) or radiological (electrode location and distance to the nerve fibers) measurements. In addition to psychoacoustic evaluations, we also investigate objective measures of shifting neural excitation from Single-Electrode Stimulation (SES) to DES (Busby et al. 2008; Hughes and Goulson 2011; Saoji et al. 2009). Of interest are the site of stimulation (X) and SOE of a current steered signal, and the interaction between two current-steered signals.

Unlike previous studies, the selection of the electrode contacts in the present study was based on location in the cochlea rather than electrode contact number. There are important differences among subjects regarding insertion angle, size of the cochlea and electrode position, which will likely influence data (Kos et al. 2005; Skinner et al. 2007). Consequently, for standardized comparison between patients in the same study, data of electrode contacts at the same position in the cochlea are preferred. We therefore selected the electrode contacts on the basis of their location in the cochlea, using a computed tomography (CT) scan to determine the exact electrode position (Lane et al. 2007; Skinner et al. 1994; Verbist et al. 2005; Verbist et al. 2010a; Verbist et al. 2010b).

To summarize, the main aims of our study were to investigate to what extent SES is comparable with DES in terms of the SOE, sequential interaction index, and site of stimulation and whether the number of intermediate pitches created with DES can be predicted from the sequential interaction index, SOE, EFI or electrode distance to the medial wall. Furthermore, we investigated whether there is any correlation between these parameters and speech perception measured with SES.

Methods

Subjects

The subjects who participated in this study were 11 postlingually and 1 prelingually (S6) deafened adults who had been implanted with a HiRes 90K device with HiFocus1J electrode (Advanced Bionics, Sylmar, CA) at the Leiden University Medical Centre in 2007. No complications were reported during surgery or the rehabilitation program in any of the subjects. Subject information is provided in Table 1. Written consent was obtained from each subject, and the study was approved by the Medical Ethical Committee of the Leiden University Medical Centre (ref. P02.106.I).

The standard Dutch speech test of the Dutch Society of Audiology, consisting of phonetically balanced monosyllabic (consonant –vowel-consonant) word lists, was used(Bosman and Smoorenburg 1995). The phoneme recognition scores measured during normal clinical follow-up at 6 months were used in this study.

Table 1. *Subject demographics.*

	Gender	Age (years)	Aetiology	Duration of deafness (years)	CI usage (months)	CVC Ph%	Electrodes tested		
							120°	240°	360°
S1	Female	55	Rubella intra uterine	50	18	66	14	9	5
S2	Female	43	Congenital hearing loss	36	15	86	14	9	5
S3	Male	60	Congenital hearing loss	47	18	69	14	9	5
S4	Male	64	Otosclerosis	23	18	89	14	8	5
S5	Male	61	Congenital hearing loss	55	15	54	13	6	2
S6	Male	62	Meningitis	57	20	38	13	8	4
S7	Female	62	TBC meningitis	44	11	9	14	9	5
S8	Female	55	Congenital hearing loss	46	13	85	14	10	6
S9	Male	49	Meningitis	42	10	68	14	8	4
S10	Female	44	Unknown	39	9	39	13	9	5
S11	Female	70	Congenital hearing loss	21	12	93	14	9	6
S12	Female	42	Congenital hearing loss	27	13	79	14	9	4
Average		56		41	14	65			

Speech perception scores are given as percentage phonemes correct (Ph%) in phonetically balanced monosyllabic (CVC) words.

CVC, consonant-vowel-consonant

Assessment of Electrode Position

The position of the electrode array, and thereby the individual electrode contacts, was determined from a postoperative CT scan, which is part of the clinical CI program. To measure the exact position of the electrodes, a multiplanar reconstruction (MPR) was generated from the CT scan (Verbist et al. 2005). A system of coordinates was placed in the postoperative MPR, using a custom Matlab computer program (MathWorks, Natick, MA). This method has been previously described elsewhere (Snel-Bongers et al. 2011). The angular positions of the electrode contacts used in this study were measured from the round window (Verbist et al. 2010a; Verbist et al. 2010b). Three cochlear locations, basal, middle and apical, were selected for this study at 120 degrees (electrode contact 13-14), 240 degrees (electrode contact 6-10) and 360 degrees (electrode contact 2-6) respectively, (Table 1). Corresponding contacts were determined for all patients.

The influence of the surgeon on the electrode array position in the cochlea was limited, as we concluded from the small range of the selected basal electrode contacts (13 -14). The differences are largely determined by the anatomy of the cochlea, which resulted in apical electrode contacts 2-6 being closest to the 360-degrees position.

The CT-scan was further used to determine the distance from the electrode contacts to the medial wall of the cochlea. After locating the electrode contacts individually, a line was generated from each contact to the centre of the modiolus. The distance to the medial wall was calculated along this line, after identifying the location of the medial wall.

Psychophysical experiments

Two psychophysical experiments were performed: pitch discrimination and measurement of the interaction index (as described in the following sections). These experiments were performed using the research tools BEDCS (Bionic Ear Data Collection System, Advanced Bionics, Sylmar, CA) for the electrical stimulus configuration and PsychoACoustic Test Suite (Advanced Bionics, Niel, Belgium) for the psychophysical tests. Stimuli were bursts of biphasic pulses with phase duration of 32 µs and a rate of 1400 pulses per second. The total burst duration varied among the experiments. Between each burst was a pause of 500 msec.. Dual-electrode stimuli were always delivered simultaneously. The proportion of the total current directed to the more basal electrode contact of the dual-electrode pair is denoted as α. The current steering coefficient varies from $\alpha = 0$, where all current is directed to the apical electrode contact and $\alpha = 1$, where all current is directed to the basal electrode contact. A staircase procedure was used for both experiments. The procedure was that they stopped after 10 reversals (i.e. changes in the direction of the signal level), where the test outcome was calculated over the last six reversals. However, in cases where a downward or upward trend was detected on the last six reversal points by the program (PsychoACoustic Test Suite), the test was extended assuming that either the adaptive procedure had not yet converged to the subject's discrimination limit or in the latter case lost it again because of, for example, a loss of attention (Reference note 3).

Pitch discrimination

Before starting, most comfortable loudness levels (MCLs) were first determined for each of the six preselected electrode contacts individually. The subject was asked to indicate when the signal sounded most comfortably loud (MCL). All levels were carefully loudness balanced within and across electrode pairs, as in normal clinical practice.

To determine the “just noticeable difference” (JND) of α, a three-alternative forced choice, 1-up/2-down staircase procedure was used. The reference stimulus had a value $\alpha = 0$ (all current to apical electrode contact) and the probe stimulus a value of $\alpha>0$. Both stimuli had a total duration of 300 msec and were presented on MCL. The reference stimulus was presented twice and the probe stimulus once. In each trial, the presentation order of the three stimuli was randomized. The subject was asked to select which stimulus was different in pitch. A loudness roving of 10% (considered to be moderate) was applied to the current levels to avoid any potential bias from loudness cues (Vanpoucke, Reference note 4). The experiment started with probe α of 0.9. Over the 10 reversals, α was altered in steps of 0.1 for the first two, in steps of 0.05 for the second two, and in steps of 0.025 for the remaining six. When a subject was not able to discriminate the probe from the reference (α approaching 1), the test automatically terminated after five attempts.

Channel interaction

The interaction index (*S*) (Boex et al. 2003) can be used as a measure of channel interaction. It compares the detection threshold on a certain channel in the presence of another channel, which is in the present study 2 dB lower than threshold level (TL). In the absence of channel interactions and channel masking, the interaction index is zero.

The formula is as follows:

$$S = (T_p - T_{p+m}) / 2\,(T_m - \mu) \qquad \text{Eq. 1}$$

Where T_p is the TL of the probe alone, T_m is the TL of the masker alone, T_{p+m} is the TL of the masker and probe together, and μ is the amount (the equivalent of 2 dB, in µA) that the masker level is lower than the probe level (see later). Moreover, all other values in Eq. 1 are expressed in µA. When *S* reaches zero, there is almost no interaction, and when *S* reaches 1 or -1, there is a high interaction. A negative value of *S* means that when the probe and masker are stimulated together, more current is needed than when the probe is stimulated alone. A positive value designates the opposite.

For the sequential interaction index, thresholds were determined for the probe, masker and probe + masker condition using a three-alternative forced choice, 1-up/2-down staircase procedure. Two experiments were conducted. In the first experiment, the interaction index of two consecutive single-electrode stimuli was measured. The probe covered electrode contact "e" and the masker electrode contact "e+1" (Figure 1A). The second experiment is a variation in which the interaction index of two current steered channels was conducted. Here, the probe and masker were both a dual-electrode stimulus with α = 0.5. The probe covered

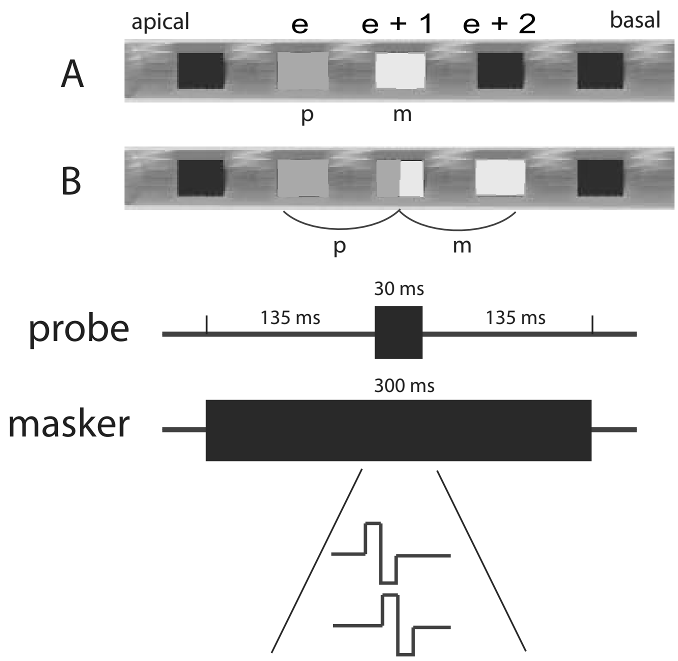

Figure 1. *Electrode contact pairs used in channel interaction experiment for single-electrode stimulation (SES) (A) and dual-electrode stimulation (DES) (B). The most apical electrode contact of a pair is denoted as e and either 120 degrees, 240 degrees or 360 degrees from the round window as selected on the basis of a computed tomography scan. The probe (p), a stimulus of 30 msec, is either e or DES of e and e+1 and the masker (m), a stimulus of 300 msec, is either e+1 or DES of e+1 and e+2. The probe starts 135 msec later than the masker. Probe and masker are presented sequentially, which is shown in the last line, where the probe is the first pulse and the masker the second.*

electrode pair "e" and "e+1" and the masker covered pair "e+1"and "e+2" (Figure 1B).

For both experiments, three thresholds needed to be determined. All the stimuli were presented randomly per part. In the first part, the threshold of the probe alone (T_P) was determined. The probe (the apical electrode contact of the pair) had burst duration of 30 msec (Figure 1) and was presented once in the three alternatives. In the second part, the threshold of the masker alone (T_M) was determined. The masker (the basal electrode contact of the pair) had burst duration of 300 msec (Figure 1) and was also presented once in the three alternatives. In the third part, the threshold of the probe in the presence of the masker (T_{P+M}) was determined. The probe and masker were presented sequentially (in phase) in the test signal, where the probe started 135 ms later than the masker (Figure 1). All trials started with the probe set to most comfortable level (MCL). The masker was presented 2 dB below T_M during the test. The reference stimulus consisted of the masker signal alone (2 dB below T_M) and was presented twice. Following each three-burst sequence, the subject was asked in which interval the signal was heard. The amplitude of the test signal was altered in the first 4 of the 10 steps with 15% and in the remaining 6 steps with 7%.

Objective measures

Electrical field imaging (EFI)

The intracochlear electrical fields exhibit considerable patient variability, depending on factors such as the state of cochlear tissues and the electrode placement and insertion angle. In a patent scala tympani, a wide spread of the current will be observed, whereas in an ossified region, the electrical spread curves are much steeper (Vanpoucke et al. 2004). To identify which intracochlear potential fields were combined with the DES stimuli, we recorded the intracochlear fields with the EFIM (Electrical Field Imaging Measurement) research tool (Advanced Bionics, Niel, Belgium). Each contact along the electrode array is stimulated in monopolar mode, and the EFIM tool then makes an accurate recording of the intracochlear potential induced on each contact along the electrode array. The stimulus used was a 3 kHz sinusoid of 1 msec duration. The spread of the electrical current in the cochlea can be derived from this measurement. To characterize the decay of the intracochlear potential by a single metric, i.e. the width, an exponential line was fitted through the data points separately for the apical and basal side of the expected peak position. The width of the graph was measured at 75% of the peak amplitude and expressed in number of electrode spacings.

Spread of excitation

A forward-masking method was used to obtain the eCAP with Neural Response Imagining via Research Studies Platform for Objective Measures (Advanced Bionics, Niel, Belgium). For determining the location of the neurons responding to a stimulus, SOE method with fixed probe and variable masker (Cohen et al. 2001) was measured in awake subjects, both for SES and DES. The masker preceded the probe with an interpulse interval of 398.7 µs, i.e. well below the refractory period, such that fibers recruited by the masker can no longer respond to the probe stimulus. The SOE function was measured using the eCAP method as psychophysical measurements were judged too time consuming. The test started with determining the most comfortable loudness level (MCL) of the probe electrode contact(s), because the test took place at MCL. In the first experiment, the probe was set to a fixed single electrode contact. In the second experiment, the probe was expected to be shifted towards the base by approximately half an electrode contact with DES pitch ($\alpha = 0.5$). The recording electrode contact was located two electrode contacts apical to the probe electrode contact. The masker, stimulated at MCL determined for the probe, was roved along all electrode contacts apart from the recording electrode contact and was a mono electrode stimulus in both experiments.

The subtraction method (Abbas et al. 2004; Brown et al. 1998) was used to separate the neural activations from the electrical artefacts. The stimulus (probe and masker) consisted of a biphasic pulse with phase duration of 32.3 µs. The gain at the recording contact was set to 300 X and the sampling rate of the stimuli to 56 kHz. The ECAP response was computed by averaging each recorded response 32 times.

To quantify the selectivity or side of stimulation (X) of the probe electrode in a single-width metric, an exponential line was fitted separately for the apical and basal side of the peak position over the graph depicting the response magnitude as a function of masker position (Cohen et al. 2003). The peak was based on the data points of the graph and is not necessarily at the same position as the probe. Selectivity was determined as the graph width at 75% of the peak amplitude expressed as number of electrode contacts (Hughes and Abbas 2006a). The X was determined in two different ways; (i) the position of the peak of the graph (X_p) and (ii) the center point along the 75% line (X_c), both expressed as position along the electrode array.

Statistical Analysis

For the comparisons between SES and DES for SOE and the interaction index, a Student t-test was used. In the other comparisons, there were multiple data points per patient. Therefore, a linear mixed model was used as this method can take several parameters into account in the same analysis. With this method, direct correlation will give a result for the group but not for the individual patient. It is even possible that the overall result can give a positive correlation, whereas all individual patients have a negative correlation of their own data points(Fitzmaurice et al. 2004). The difference between the two methods will be illustrated by additionally using a Pearson's correlation for all the comparisons.

As speech perception cannot be measured on three different locations along the array, the comparison between speech perception and the other parameters was performed using a Pearson's correlation. Differences were considered significant at the 0.05 level. All data were analyzed using the SPSS 16 (Statistical Package for the Social Sciences, SPSS inc. Headquarters, Chicago, IL).

Table 2. *Statistical outcomes of the linear mixed model (LMM) and Pearson correlation for all the measured parameters for the influence of the electrode contact location in the cochlea (180 degrees vs. 360 degrees measured from the round window) and in comparison with alpha.*

	Statistical test		Alpha	Sequential interaction index (SES)	Sequential interaction index (DES)	Selectivity SES (elec.)	Selectivity DES (elec.)	EFI	Distance medial wall (mm)
Influence of place	LMM	*p*	0.462	0.869	0.982	0.014 *	0.049 *	0.001 *	0.143
Alpha vs.	Pearson correlation	R^2	-	-0.119	-0.234	0.125	0.080	0.077	0.370
		p	-	0.488	0.197	0.481	0.653	0.657	0.026 *
	LMM	*p*	-	0.026 *	0.375	0.913	0.233	0.859	0.806

For both tests, the p value and the Pearson correlation R^2 are given.

* Differences were considered significant at the 0.05 level.
SES, single-electrode stimulation; DES, dual-electrode stimulation; EFI, electrical field imaging

Results

Electrode position

The LMM can take several indicators into account, of which the electrode location in the cochlea is one. For all the parameters, it was investigated whether the electrode position was of influence on the outcome, of which the *p* values are shown in Table 2 in the first row. Both SOE and EFI show a significant difference for the three locations ($p < 0.05$). This only indicated that there is a difference between the three locations but not which ones differ from each other.

The differences between the three locations were further analyzed with a standard (two-sided) Student *t*-test, the results of which are shown in table 3. The basal region gives a significantly smaller 75% width of the graph than apical, indicating better selectivity in this region. There was no significant difference between apical and middle and between middle and basal sites. There was, however, a significant difference between apical and basal sites. For EFI, the LMM also showed an influence of the position of the electrode in the cochlea (Table 2). The Student *t*-test (Table 3) calculated a significant difference in width between middle and basal and between apical and basal locations. There was, nevertheless, no difference between the width at apical and middle locations. This indicated more current spread in the apical and middle regions than in the basal region. The other parameters were not different for the three locations (Table 2).

Comparison between SES and DES

The comparison between SES and DES for SOE and sequential interaction index is shown in Figure 2. No difference ($p = 0.708$) was found between SES (4.32 +/- 2.43) and DES (4.45 +/- 2.36) for the width at 75% of the SOE graph (Figure 2A). Figure 3 shows the results from a typical subject (S3), where the width for SES appears similar to DES, which also demonstrates the similarity between SES and DES. This figure also demonstrates that the exponentials nicely fitted the data points (R^2 between 0.90 and 0.98), which is the case in all subjects (the average R^2 is 0.89 +/- 0.09). The sequential interaction index also showed no difference ($p = 0.9$) between SES (-0.24 +/- 0.12) and DES (-0.23 +/- 0.14), which is illustrated in Figure 2B.

Table 3. *Statistical outcomes of the standard (two-sided) Student's t-test for selectivity SES and DES and EFI.*

	Selectivity SES	Selectivity DES	EFI
120 degrees vs. 240 degrees	0.161	0.218	0.005 *
120 degrees vs. 360 degrees	0.004 *	0.015 *	< 0.001 *
240 degrees vs. 360 degrees	0.077	0.168	0.233

The three different locations are compared with each other, because of the significant influence found with the linear mixed model (see table 2 first row). The p-values are shown.
** Differences were considered significant at the 0.05 level.*
SES, single-electrode stimulation; DES, dual-electrode stimulation; EFI, electrode field imaging.

The last comparison between SES and DES was for the X (the site of stimulation). The peak of the SOE graph (X_p), determined using the intercept of the fitted lines, and the center of the excitation area (X_c, half way along the 75% line) are used as measures of X; both X_p and X_c are expressed in electrode contact number. The dashed line in Figure 3 indicates X_p and the arrow in Figure 3B indicates X_c., which are both hypothesized to be identical to the number of the probe contact. With DES, this can be a fractional number, e.g. 6.5 when DES on contacts 6 and 7 with α = 0.5 is used for the probe. Figure 4 shows X_p (A) and X_c (B) between SES and DES for the three locations separately (triangle (120^0), square (240^0) and dot (360^0)). The expected place of X_p and X_c for DES is indicated by a dashed gray line (at 0.5). Note that the SES on the apical contact of the pair was used as a reference stimulus and is indicated by the horizontal solid line at zero. The bars represent the average

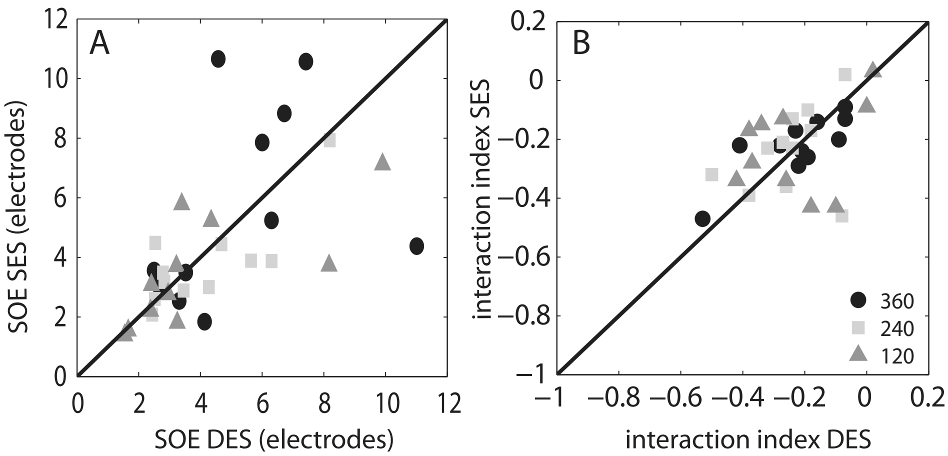

Figure 2. *The comparison between single-electrode stimulation (SES) on the y axis and dual-electrode stimulation (DES) on the x axis for spread of excitation (SOE) (A) and channel interaction (B). The dot represent the data derived from apical (360 degrees), the square the data from middle (240 degrees) and the triangle the data from basal (120 degrees).*

shift per electrode location. Despite the wide spread of the individual data points, the averages of X_p along the array are not significantly different from the electrode contact number of SES (p = 0.99) or the predicted location of DES (p = 0.744). In comparison with SES on the apical contact of the DES pair, an average shift of 0.54

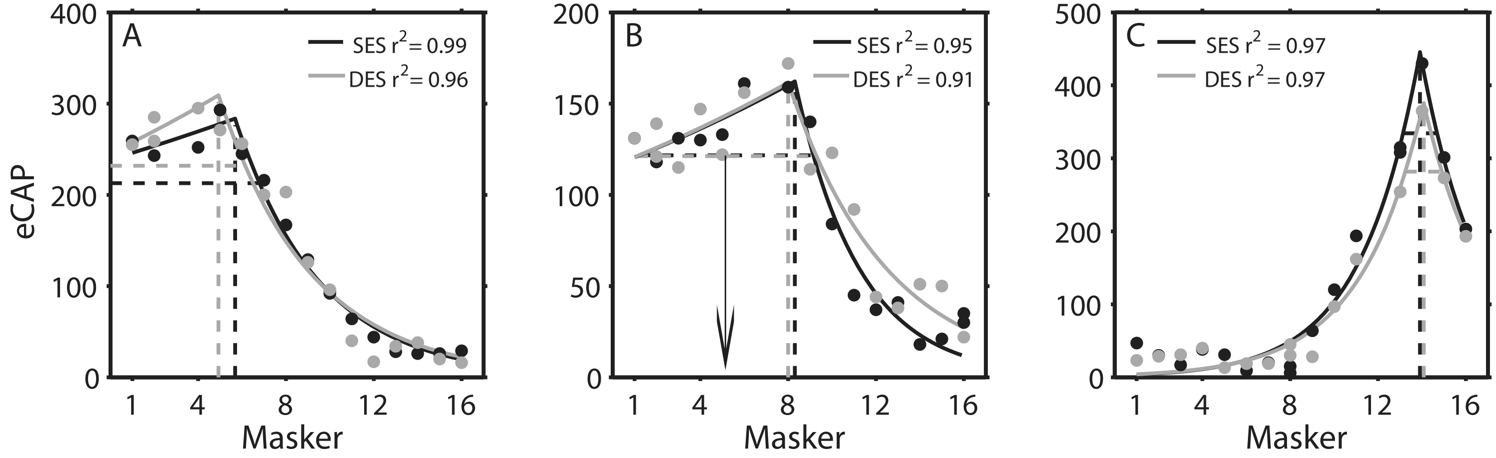

Figure 3. *The spread of excitation curves from S3 for the three locations in the cochlea, 360 degrees (A), 240 degrees (B) or 120 (C). The black dots and line represent the data from single-electrode stimulation (SES) and the grey dots and line represents the data from dual-electrode stimulation (DES) on adjacent electrode contacts. The vertical dashed line denotes X_p of the graph on the electrode array, and the horizontal dashed line denotes the width of the graph at 75% of the peak amplitude. The arrow in (B) denotes X_c.*

(+/- 0.77) electrode contacts to basal was shown for DES (with α=0.5), which is highly significant (p = 0.0002) and completely in line with expectations. This shift is also illustrated in Figure 3 for subject S3. In contrast, the averages of X_c are significantly different from the electrode number of SES (p = 0.003) or the predicted location of DES ($p < 0.001$). The location along the array for SES is 0.69 (+/- 1.3) electrode contacts more apical to the electrode number of the probe, which is demonstrated in figure 3B. The average difference of X_c between SES and DES (with α=0.5) is 0.57 (+/- 1.2) electrode contacts (X_c for DES being more basal), which is a significant one (p = 0.007) of the expected size and direction (Figure 4B).

Predictors of pitch discrimination and speech recognition

To be able to predict JND α from the other measures, at least one parameter must correlate significantly with it. As shown in Figure 5 A-D and listed in Table 2 in the second row, only the electrode contact distance to the medial wall showed a significant, but rather weak (R^2 = 0.370, p = 0.026) correlation with JND α. None of the other measured parameters (interaction index, selectivity and EFI) seemed to correlate with JND α. However, as argued before, a Pearson's correlation is not the correct way to address this issue, and a LMM is more appropriate here. First, the relationship between the different cochlear locations and the measured parameters was determined. As described above and listed in Table 2 in the first row, only SOE an EFI differed for the three locations.

The LMM was applied on JND α with all the other parameters (Interaction index, SOE, EFI and distance to the medial wall). For SOE and EFI, the electrode contact location was embedded in the test. Unlike the Pearson's correlation, a significant relationship between JND α and the sequential interaction index was found (p = 0.032). There was no significant correlation for the electrode distance to the medial wall (p = 0.806). The former result implies that lower channel interaction typically occurs with a lower JND α. The difference between the correlation and the LMM for channel interactions can be explained with the individual results shown in Figure 5F. Five of the 12 subjects (S1, S3, S4, S5 and S10) showed a decrease in JND α together with less interaction. The other parameters were too diverse and showed no relation with JND α (table 2).

For the comparison with speech perception scores, the average of the three values from the different locations for all parameters for each subject was used. Only one apparent relationship was observed (Figure 5E): JND α showed a significant correlation with the speech perception score (R = -0.6, p = 0.038).

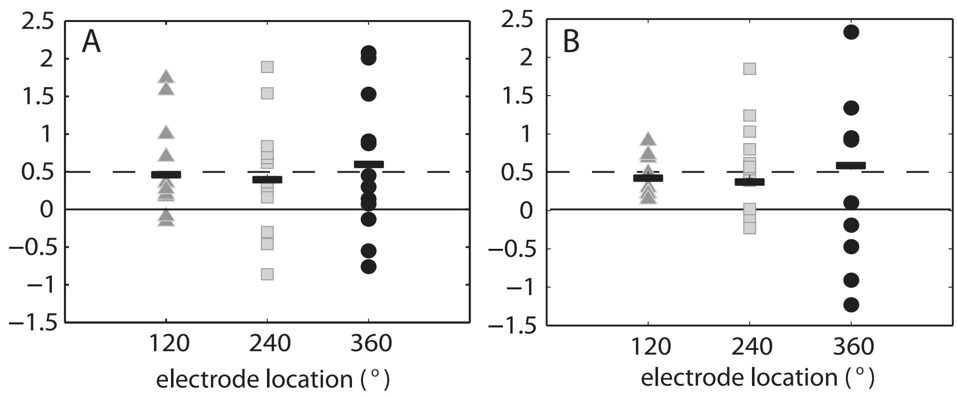

Figure 4. *The difference X between single-electrode stimulation (SES) and dual-electrode stimulation (DES) for X_p (a) and for X_c (b), where SES is made equal to zero. The y axis represents the place on the electrode array expressed in electrode number. The horizontal dashed line represents the expected shift of 0.5 for α = 0.5. The solid black bars are the average of all the data points for that location. The symbols demonstrate the individual data.*

Discussion

The main goal of this study was to examine whether DES exhibits the same characteristics as SES for SOE, sequential interaction and the site of stimulation (X). The former two parameters were indistinguishable for SES and DES, which implies that a "software electrode" behaves similarly to a real physical electrode contact. This implies that DES can be used in a strategy similar to continuous interleaved sampling (CIS) (Wilson et al. 1991) and if this is true it is likely that DES produce similar speech recognition scores to SES. Moreover, these results are consistent with previous studies (Busby et al. 2008; Saoji et al. 2009).

If DES can be used to improve tonotopical resolution, this could result in improved speech perception in general and possibly also in improved speech perception in noise and better music perception. Indeed, some studies have indicated that an increased number of electrode contacts is beneficial to speech in noise (Nie et al. 2006). Firszt et al. (2009) compared HiRes (SES) with HiRes120 (a DES implementation, theoretically delivering 120 channels) in CII and 90K cochlear implant users. They found a significant improvement in speech recognition with HiRes 120 compared with HiRes for words in quiet and sentences in noise as well as

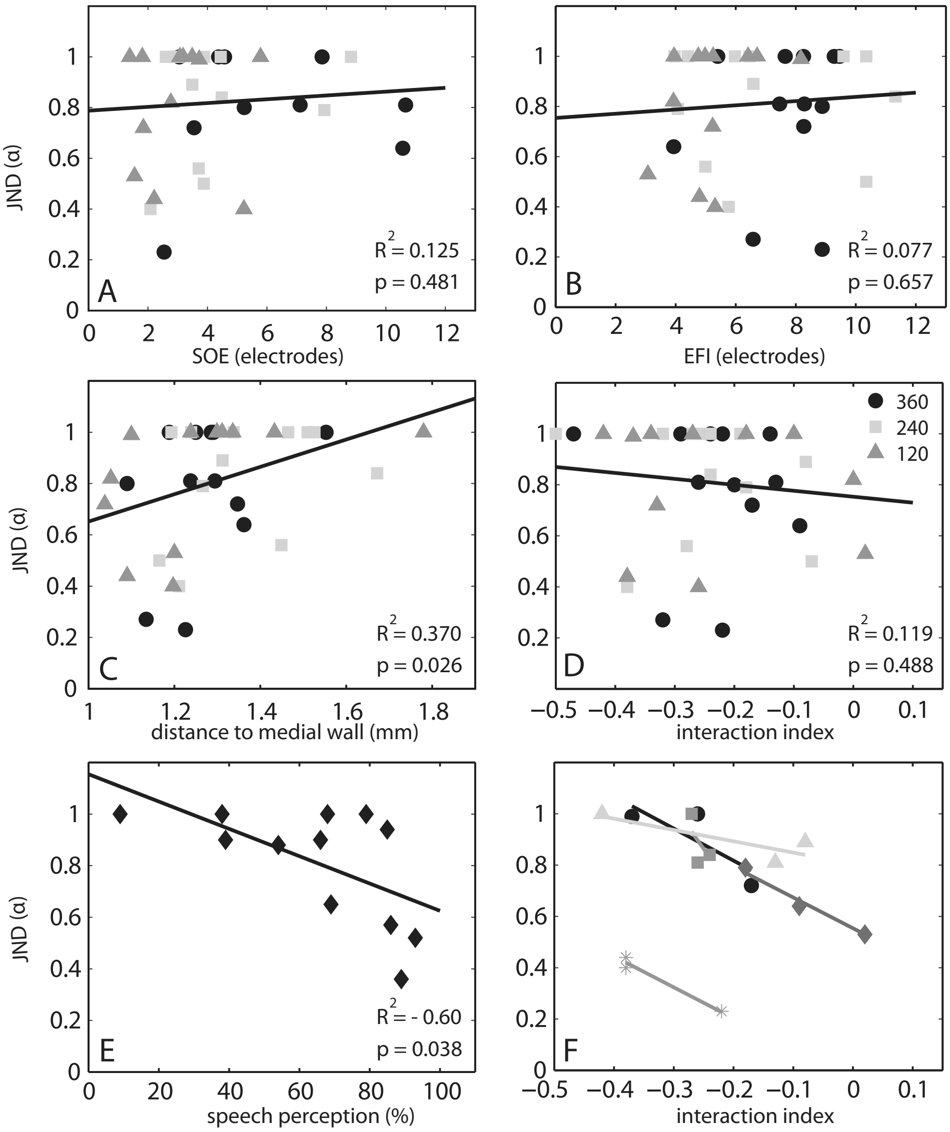

Figure 5. *The first four graphs show the correlation between just noticeable difference (JND) α and spread of excitation (A), electrical field imaging (EFI) (B), electrode distance to the medial wall (C) and channel interaction (D). The dot represent the data derived from apical (360 degrees), the square the data from middle (240 degrees) and the triangle the data from basal (120 degrees). The correlation between JND α and speech perception (E) and the individual results or the channel interaction experiment for 5 of the 12 subjects (F) are also shown.*

music ratings of pleasantness and instrument distinctness. This suggests that use of DES results in significant improvement of performance, although this improvement may be modest. On the contrary in a recent study, Donaldson et al. (2011) found no difference between the two strategies, HiRes or HiRes 120, for speech perception with or without background noise. Some subjects had better speech perception with HiRes 120, but there were also subjects who exhibited initial decrements. The subjects who participated in the present study did not use HiRes 120, and so a direct comparison between the studies is not possible, but the subjects who participated in this study had a relatively high JND α compared with subjects in other published studies (Donaldson et al. 2005; Firszt et al. 2007; Koch et al. 2007; Townshend et al. 1987). When using the formula used in former studies (Firszt et al. 2007; Koch et al. 2007) to calculate the number of spectral channels per electrode array, an average of 20 spectral channels for the whole array applies to our subject group with a range from 8 till 46. It is therefore not clear whether the subjects in the present study would benefit from HiRes 120. It may be that individual allocation of the number of spectral channels implemented using DES, based on the JND α determined for a couple of electrode contact pairs, could optimize the speech coding strategy for individual users.

The SOE produced by current steering has been investigated previously. Saoji et al. (2009) compared the SOE of a simultaneously spanned signal with that produced by an intermediate physical electrode contact in Advanced Bionics CI users (e.g., comparing the SOE produced by electrode contacts 3 and 5 stimulated simultaneously with that produced by electrode contact 4 alone). In line with the findings at the present study, they found that both configurations produced comparable areas of excitation. Busby et al. (2008) determined whether there were any consistent differences between the electrophysiological SOE functions produced by simultaneous DES and SES for subjects with the Nucleus Freedom cochlear implant. They also found that dual-electrode SOEs were similar to those for single electrodes with respect to SOE width. The latter outcomes could, however, have been influenced by impedance differences between the two contacts, as electrode coupling was used to divide the current over the contacts. Hughes and Goulson (2011) used subjects with either an advanced bionics CI or a nucleus Freedom CI and compared physical contact with virtual channels for three different ECAP responses, threshold and slope of the input/output function, measure of refractory recovery and relative location of SOE. They found no difference between a physical contact (SES) and a virtual channel (DES) for all their measures and the location of the SOE from a virtual channel was situated between the two flanking physical electrode contacts.

Classically, uncontrolled channel interaction has been identified as a phenomenon that easily degrades speech perception with CI. Speech perception outcomes generally improved after the introduction of sequential stimulation, such as was first used by the CIS strategy (Wilson et al. 1991), which results in less channel interaction. Boëx et al. (2003a) measured the interaction produced by sequential and simultaneous stimulation and confirmed that sequential biphasic stimuli on different contacts produce lower interactions than simultaneous stimuli. With DES, controlled channel interaction is exploited in a favorable way to produced additional pitch percepts. In line with this, the present study could not demonstrate any difference in terms of sequential electrical interaction or width of SOE between SES and DES. This means that DES channels in many respects behave like physical contacts and could be implemented as such in the CIS strategy, without negative effects due to channel interaction.

This study demonstrates that eCAP forward-masking curves, which are mostly used to determine the SOE of a single-electrode contact, are an appropriate method for distinguishing the stimulation site for DES and SES. In line with our findings, Saoji et al. (2009) concluded that the “center of gravity” was comparable for DES and SES. Of course, one would also expect that there are differences between DES and SES at the edges of the region of excitation, but we are not aware of any evidence in the literature in this respect. Snel-Bongers et al. (2011) used a pitch matching experiment that used spanned electrode contacts to find the actual X produced by DES. Again, in that study, a current steered signal was compared with an intermediate physical electrode contact. They found that equal current distribution (α = 0.5) corresponded with a physical electrode contact exactly in between the driven contacts. In the present study, the excitation area was determined by using eCAP-based SOE curves. For the site of the neural excitation zone, a difference of 0.5 electrode contacts between SES and DES was predicted. A significant shift in X_p of 0.54 electrode contacts towards the base relative to the X_p of the probe with SES was observed, which was not significantly different from the expected value of 0.5. So, the maximal X for α = 0.5 is situated half way between the two driven electrodes contacts, just as predicted and in line with the study of Snel-Bongers et al. (2011). However, this was not the case when the centre of gravity was used as a measure of excitation site, i.e., the middle of the 75% width line. Here, the shift differed significantly from the expected shift of 0.5. In line with this, for SES also, the centre of gravity of the 75% SOE width was shifted apical relative to the stimulating contacts. It is not equivocally clear which of the two methods is the most appropriate. A theoretical advantage of the first method (X_p) is that it does not require or assume symmetry, whereas the second method does. Among others, Briaire et al. (2000) showed that there is no symmetry in the current pathways in the cochlea. The current distribution to basal is larger than to the apical region, which results in an asymmetry in the SOE curves (van de Beek, reference note 5). A limitation of the first method is that it depends on the fit of an exponential curve to the data points, which is not per se correct. However, the correlation coefficient of the fitted line is high in all cases tested here.

Two studies already mentioned above (Saoji et al. 2009; Snel-Bongers et al. 2011) have tried to identify X of DES by making use of spanning, i.e. current steering between nonadjacent electrode contacts. The question arises whether eCAP forward-masking curves give the same results for spanning as was found in the present study with neighbouring contacts. This will be subject of future investigation. The initial outcomes suggest that the findings can be extended to spanned electrode pairs.

The location of the electrode array is influenced by the surgical insertion and by the anatomy of the cochlea. As shown in Table 1, the electrode contact closest to 120 degrees from the round window was quite constant in our subjects, ranging from 13 to 14. This means that in this population, the insertion position of the electrode contact was constant. Nevertheless, there was a wide range in contact number for the electrode contact used at the apical (360 degrees) position (which is between contacts 2 and 6), demonstrating that the insertion angle varies considerably among individuals for outer wall electrodes like the HiFocus J. This is most likely a result of the variable anatomy (especially size) of the cochlea, which means that the actual location of any particular electrode contact may vary widely among subjects when it is defined by electrode contact number as is done in many studies. In the present study, however, all measured parameters were correlated with the electrode contact location rather than number: EFI and SOE however, showed significant differences between the three locations in the cochlea. The EFI recordings showed more current spread in the apical region and, accordingly, the eCAP SOE measures yielded broader spatial selectivity curves in the apex. This was previously predicted by Briaire and Frijns (2006) in a computer model of the cochlea but has, to our knowledge, not yet been demonstrated in patients. Previous studies investigating the influence of the location on SOE (Hughes and Abbas 2006a; van Weert et al. 2005) found no difference between apical, middle or basal electrode contacts. However, their selection of electrode contacts was based on contact number instead of more precise electrode location.

One of the principal aims of this study was to find a parameter that predicts the ability of a subject to discriminate intermediate pitches. Using a Pearson's correlation, only the electrode distance to the medial wall showed a significant correlation with JND α. However, a Pearson's correlation is not the optimal method when a subject has more than one data point with the same experiment because, in this situation, an individual might show a significant correlation, while the group does not. With a LMM, the individual and other different parameters can be taken into account. Using this approach, only the sequential interactions index showed a significant correlation with JND α but only on a per-patient basis. Therefore, the sequential interaction index in itself is not a useful predictor for JND α.

As mentioned earlier, four subjects reach floor performance, i.e. they have a JND α = 1. Three of these four subjects (S6, S8 and S9) also participated in the study of Snel-Bongers et al. (2011), where spanning offered the possibility to measure JND α above 1. If their smallest JND α from that study (2.85, 1.94 and 1.76, respectively) is included in the statistics of the present paper a significant correlation with the distance to the medial wall is found (R^2 = 0.649, p = 0.043). This means that a lateral placement of the electrode array would lead to a higher JND α, which is in contrast with our initial hypothesis. Further studies in larger patient groups have to elucidate this.

As an addition, all the parameters from the present study were compared with the speech perception of the subjects measured at 6 months after implantation. JND α showed a significant correlation with speech perception. Subjects who are good at discriminating intermediate pitches tend to have high scores in speech understanding, which is in contrast with the findings from Firszt et al. (2007). The other parameters of the present study showed no correlation with speech perception, which is in line with previous studies (Cohen et al. 2006; Hughes and Abbas 2006b; Hughes and Stille 2008).

An explanation for finding better pitch discrimination with higher speech perception scores could be that these subjects have better or more evenly distributed neural survival (Briaire and Frijns 2006). If some neurons are missing in a crucial cochlear location for a given pitch, it is logical that a subject will not be able to discriminate between two signals which stimulate that area. This would suggest that current steering is only beneficial for subjects who have optimal conditions for speech perception from the outset. Contrary to this hypothesis, Firszt et al. (2009) report that they could not predict the benefit from current steering on the basis of performance with HiRes, Donaldson et al. (2011) do not analyze this explicitly, but from the data they present, it is not evident that better performance with HiRes would predict more benefit from HiRes120.

In summary, the results of the present study showed that SES and DES are equal with regard to SOE and channel interaction, which indicate that DES channels could be used in a CIS strategy. The excitation site of DES has the predicted displacement compared with the excitation region induced by SES measured with SOE. Furthermore, the variation in number of intermediate pitches created with DES along the array is correlated with channel interaction.

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Chapter 3

The use of partial bipolar stimulation in cochlear implants to create spectral channels apical to the stimulated electrode pair

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Ear and Hearing, submitted

Abstract

Objectives: Cochlear implant electrode arrays have a more shallow insertion depth than the physiological place-to-frequency distribution, as a deep insertion could lead to intra-cochlear trauma. An alternative for a deeper insertion can be the so-called phantom channel, which is partial bipolar stimulation, with non-equal amplitudes on the two stimulating contacts. Through the use of psychophysical experiments and computational modeling this study investigates the neural excitation, place of stimulation and the perceived loudness of a phantom channel.

Design: Ten postlingually adult deafened users of the HiRes90K cochlear implant with a HiFocus1J electrode array were selected to participate in this study. The stimulation level required to maintain equal loudness with monopolar stimulation was determined with a psychophysical loudness balancing experiment. The largest achievable pitch shift by varying the bipolar coefficient was determined in two steps, using a pitch-ranking procedure followed by a pitch matching experiment. Through use of a computational model of the cochlea, the mechanism underlying phantom stimulation was studied, predictions concerning the current correction required to reach similar excitation widths and the largest pitch shift for three different cochlear morphologies with the electrode array in both medial and lateral position.

Results: (1) More current is needed on the primary electrode when increasing the current on the compensating electrode to maintain equal loudness. (2) All subjects exhibited an apical pitch shift with an average of 1 electrode contact. (3) The psychophysical results are in line with the predictions of the computational model. (4) The computational model predicts that the electrode array in lateral position exhibits a larger pitch shift to apical than the medial position.

Conclusion: Both the computational model of the cochlea and the psychophysical data show that it is possible to stimulate in a more apical region with phantom stimulation and that more current is needed to maintain equal loudness. The model predicts, however, that stimulating at lower levels decreases the pitch shift and the electrode array in a lateral position would generate a larger pitch shift than in medial position.

Introduction

Cochlear implants (CIs) are widely used as a treatment for profoundly hearing impaired children and adults. There is some evidence that speech recognition by implant users is improved when the acoustic input frequency is matched to the cochlear location that normally processes that frequency range (Baskent and Shannon 2004). However, if an electrode array does not span the desired frequency range, which is the case in the CI types of Advanced Bionics and Cochlear (typical length of standard electrode arrays 18-24 mm, extending up to maximal 1 ½ turns of the cochlea), a matched map would result in the loss of low frequency information (Carlyon et al. 2010). One way to resolve this issue is a deeper insertion into the cochlea. The electrode arrays used in Med-EL devices can be considerably longer than the arrays from other manufacturers, following the concept of full cochlear coverage. Their standard arrays are 28 to 31 mm long, which is almost the complete length of the basilar membrane. Recent studies have shown the transmission of very low frequency information, either electrically or acoustically, can improve speech perception scores from implant users in general (Dorman et al. 2005; Gantz and Turner 2004; Gantz et al. 2004; Riss et al. 2011; Turner et al. 2008; von Ilberg et al. 2011; von et al. 1999). However, when most currently available electrode arrays are inserted very deeply into the cochlea they tend to produce more intra-cochlear trauma, with placement of the electrode array in the scala vestibuli instead of the scala tympani, loss of residual hearing and reduction of the neural substrate (Boyd 2011). Skinner et al. (2007) and Finley et al. (2008) showed that misplacement in the scala vestibuli or deep insertion have a negative influence on speech perception, leading to the use of shorter arrays to reduce possible trauma. Another way to reach the apical region is by stimulating electrically beyond the position of the physical electrode array. Phantom electrodes (Saoji and Litvak 2010) or pseudo-monophasic pulses (Macherey et al. 2011) are examples of such stimulation in the more apical region and probably can both be an alternative to a deeper electrode array insertion. Similarly, it is also possible to stimulate in the more basal direction, when an electrode array is over inserted.

A phantom channel is a form of partial bipolar stimulation, with non-equal amplitudes on the two stimulating contacts (Saoji and Litvak (2010)). A biphasic pulse (cathodic – anodic) is presented on the apical electrode contact, also called “primary” electrode. An out-of-phase biphasic pulse (anodic – cathodic) with lower amplitude is presented on the adjacent basal electrode contact, also called “compensating” electrode. The ratio between amplitudes of the compensating electrode and the primary electrode is termed σ. This means that when σ = 0, only the primary electrode is stimulated (as in a monopolar configuration), and when σ = 1, stimulus levels of the primary and compensating electrodes are equal, as in bipolar stimulation.

Because the currents to the neighboring contacts are applied out of phase, the intracochlear electrical field is pushed away from the compensating electrode, to the other side of the primary electrode (Saoji and Litvak 2010). This makes it possible to create spectral channels beyond the electrode array. Saoji and Litvak (2010) showed that it is possible to shift the percept from 0.5 to 2 contact spacings beyond the primary electrode.

Another way to stimulate beyond the electrode array is with pseudo-monophasic pulses (Macherey et al. 2011). Here two electrodes were stimulated in a bipolar fashion with an initial short, high-amplitude anodic phase (relative to the most apical electrode) followed by a long, low-amplitude phase of opposite polarity. This resulted in a place pitch shift between 0.55 and 1.1 mm (0.5 to 1 electrode contacts) in an apical direction.

To supplement clinical data, simulations of phantom electrode excitation were performed using a computational model of the implanted human cochlea. The model (Briaire and Frijns 2000; Briaire and Frijns 2005; Briaire and Frijns 2006; Frijns et al. 2001; Frijns et al. 2009a; Frijns et al. 2009b) provides insight into CI-induced electrical potential distributions and their resulting neural excitation patterns in a three-dimensional human cochlear geometry. By simulating the psychophysical experiments and objective measures of CI recipients, an electro-anatomical model can therefore shed light on the internal workings of new excitation strategies such as phantom electrode stimulation.

Most studies are currently performed at most comfortable loudness (MCL) level, as in the study by Saoji and Litvak (2010). A recent study from Snel-Bongers et al. (2013) showed that when current steering is performed near threshold level (TL), the current compensation needed to maintain equal loudness is different than at MCL level. Using computational modelling, Frijns et al. (2009b) showed differences in excitation profiles between current steering at MCL and at TL. This study will investigate the effect of lower stimulation levels on a phantom electrode using computational modeling.

To summarize, in this study the phantom stimulation technique has been investigated. The following issues are addressed: 1) the stimulation level to maintain equal loudness; 2)the σ with the largest pitch shift in apical direction and the size of this shift; 3) the consistency between psychophysical data and computational modeling; 4) the influence of the position of the electrode array; 5) the effect of lower stimulation level on the size of the shift.

Method

Subjects

A group of 10 postlingually deafened adults was recruited. All were unilaterally implanted at the LUMC in the period between 2002 and 2007 and received a HiRes90k implant with a HiFocus-1j electrode array (Advanced Bionics, Valencia, CA). No problems were reported during surgery or the subsequent rehabilitation program. Subject information is provided in Table 1. All subjects achieved a phoneme recognition score above 50%, obtained with the standard Dutch speech test from the Dutch Society of Audiology (Bosman and Smoorenburg 1995). Written informed consent was obtained before any study procedures were conducted. This study was approved by the Medical Ethical Committee of the LUMC under number P02.106.M.

Table 1. *Subject demographics.*

	Gender	**Age (years)**	**Aetiology**	**Duration of deafness (years)**	**CI side**	**CI usage (months)**	**CVC Ph%**	**Electrodes tested**	
								180°	**360°**
S1	Female	59	Familiar progressive	29	left	54	87	10	3
S2	Male	58	Unknown	3	right	48	86	12	5
S3	Male	56	Loudness	4	right	73	84	13	6
S4	Female	70	Familiar progressive	10	right	30	91	10	4
S5	Male	46	Familiar progressive	16	right	60	95	11	4
S6	Female	48	Familiar progressive	30	right	38	65	10	4
S7	Female	44	Congenital	36	right	37	86	11	5
S8	Female	58	Congenital	10	right	38	77	9	2
S9	Female	56	Rubella intra uterine	50	right	40	66	11	5
S10	Female	59	Unknown	50	left	45	54	11	4
Average		55		23		46			

Speech perception scores are given as percentage phonemes correct (Ph%) in phonetically balanced monosyllabic (CVC) words.

Assessment of Electrode location

The intracochlear position of the all electrode contacts was determined from a postoperative CT-scan which is administered as part of the clinical CI program. To measure the exact position of the electrode contacts, a Multiplanar reconstruction (MPR) was made from the CT-scan (Verbist et al. 2005). A system of coordinates, described in previous papers (Snel-Bongers et al. 2011; Snel-Bongers et al. 2012), was applied to the postoperative MPR using a custom Matlab application (MathWorks, Natick, MA). All electrode contacts were marked by an experienced physician. In accordance with the consensus on cochlear coordinates, the angles used in this study were calculated with the round window as the 0° reference (Verbist et al. 2010a; Verbist et al. 2010b). To control for variation in insertion depth and in cochlear dimensions, electrode contacts at the same rotational angle were selected for test. For each subject the electrode contact closest to 360° (apical site, AS) and the one closest to 180° (basal site, BS) were selected from the electrode array (Table1) and used in the following experiments. Although the infra apical stimulation is of interest, the experiments were performed on electrodes in the middle of the electrode array. This made it possible to perform the experiments at the same location for each subject and to compare the pitch produced by phantom with that produced by current steering.

Psychophysical experiments

The psychophysical experiments were performed with PACTS (PsychoACoustic Test Suite, Advanced Bionics Europe, Niel, Belgium) and the BEDCS (Bionic Ear Data Collection System, Advanced Bionics, Valencia, CA) research tool for the electrical stimulus configuration. Stimuli were bursts of biphasic pulses with phase duration of 32.32 µs, pulse rate of 1,400 pulses per second and total burst duration of 300 msec. A pause of 300 msec was inserted between stimulus bursts.

With Current Steering (CS), stimuli were simultaneous and in-phase, applied on adjacent electrode contacts. The proportion of the total current directed to the more basal contact of the stimulated pair is denoted as α. This coefficient varies from $\alpha = 0$, where all current is directed to the apical electrode (AS or BS) to $\alpha = 1$, where all current is directed to the basal electrode (Donaldson et al. 2005). For phantom stimulation, stimuli were also simultaneous, but out of phase, also applied on two adjacent electrode contacts. The apical electrode was used as the primary electrode, or the stimulating electrode, while a basal electrode was used as the compensating electrode. The ratio of the current magnitude applied to the compensation electrode divided by that applied to the primary electrode is denoted by compensation coefficient σ (Saoji and Litvak 2010).

The output current of the implant device is limited by the voltage compliance limit of the internal electronics. To characterize the actual stimulation in the patients at levels above compliance the current sources of the HiRes90K implant were scrutinized by recording the output voltage of a clinical implant with a microprobe at the electrode contact. The current sources demonstrated a linear behavior right up to the saturation level (7.13 V with a load of 5kOhm). Specifying higher output levels does not change the actual output, it stays at this saturation level. It also turned out that the amplitude of the first half of the pulse phase is up to 2.6% higher than that of the second half. This phenomenon, occurs however, also with pulses below saturation level (1.2% on average, without a clear trend with respect to stimulation level). This relative stable pulse shape and the fixed output charge makes it a valid approach to use the saturation current as output level for current levels above the saturation point.

Before starting with the experiments, the electrode contact impedances were measured for all sixteen contacts using a pulse width of 32.32 µs/phase and amplitude of 40 µA. The values were used to calculate the saturation current (µA) assuming a maximum voltage of 7.0 V. If the saturation level was exceeded, the effective stimulating current was equal to the maximum current output level for this electrode. This maximum current was used to calculate the actual σ value presented to the patient (see Table 2). To make sure there is no pollution of the results, the entire analysis in this paper was limited to data points obtained below saturation level.

Stimulation level adjustment

The Most Comfortable Loudness levels (MCLs) were determined for the primary electrode (σ = 0) and for six phantom electrode compensations (σ = 0.38, 0.5, 0.63, 0.75, 0.88, 1) at both the AS and BS locations. The subject was asked to indicate when the signal sounded most comfortably loud (MCL). Next, equal loudness contours (EqL) were obtained by balancing the loudness of a phantom electrode to a comfortably loud stimulus produced by the primary electrode alone. Two ascending and two descending tracks were used for balancing. The final result was the average of the 4 levels. The subjects listened in alternation to the stimulus from the primary electrode alone and the stimulus from the phantom electrode while they adjusted the current level of the phantom electrode stimulus in steps of 1 µA using an unmarked turning knob (Saoji and Litvak 2010). When the current level of the primary electrode got above saturation level and therefore remained constant, the increasing levels of the compensating contacts was responsible for further loudness growth, allowing the subjects to finish the task without problems. The EqLs were used in the next experiments (pitch ranking, pitch matching).

Place pitch phantom electrode

The pitch shift was determined in two steps. First, the σ that induced the presumable lowest pitch was determined using a pitch-ranking procedure. The subject heard two sounds and was instructed to indicate the sound that was lower in pitch. The stimuli were presented at equally loud levels, using the levels determined in the EqL experiments described above. No feedback was given. The pairs consisted of two different σ's, where a σ was compared with the neighboring higher σ and the next one in line. For example, $\sigma = 0$ was compared with $\sigma = 0.38$ and $\sigma = 0.5$ and $\sigma = 0.75$ was compared with $\sigma = 0.88$ and $\sigma = 1.00$. This resulted in eleven different comparison pairs . In the pitch ranking task, each stimulus pair was presented on eight randomized trials and subject' responses were recorded. When the stimulus with the higher σ was chosen, the answer was scored as correct. The outcome could vary between 0% and 100%. A pitch ranking score of 100% was awarded when the subject consistently identified, for example, $\sigma = 0.38$ as lower than $\sigma = 0$. A pitch ranking score of 50% was interpreted as the subject not being able to differentiate between the pair of stimuli. If the score was lower than 50% the result was interpreted as the subject perceiving the second σ as having a higher pitch, in other words a pitch reversal having taken place. The σ delivering the lowest pitch sensation was defined as the lowest value of σ from the set [0,0.38,0.5,0.63,0.75,0.88,1], which is found to sound lower in pitch than both its adjacent values. This definition will always identify a σ that is below the first reversal threshold, even if the pitch is not monotonically rising for higher values of σ.

In the second step the resulting pitch shift was estimated with a pitch matching experiment. To compensate for potential errors in the first step not only the σ at first pitch reversal but also the two neighboring values were tested. For this experiment a non-marked turning knob was programmed to change the pitch of the matching stimulus. The matching stimulus could shift along the whole array using current steering with a step size of $\alpha = 0.05$. If applicable, the contacts involved in the pair would shift to the neighboring pair to allow for a continuum along the array. The MCL level for the current steering pairs was based on the monopolar MCL level of the individual contacts. Several studies validated that no current correction is needed to maintain equal loudness for the different α's between neighbouring contacts (Donaldson et al. 2005; Snel-Bongers et al. 2011) A loudness roving of +/-10% (in linear units, considered to be moderate) was applied to the stimulation current of the current steered stimulus in order to avoid any potential bias from a loudness cue. This current steered stimulus was generated between two adjacent electrode contacts for all the possible contact pairs, thereby making use of the earlier finding that the pitch for current steering varies monotonically with α (Snel-Bongers et al. 2011). Four tracks were performed. For the odd numbered tracks, trial 1 and 3, the pitch matching started on the contacts of the phantom pair (with current steering coefficients α=0.4 and 0.6 respectively), while the adjacent apical electrode pair was used for the even numbered trials (with a of α=0.6 and 0.4 respectively). The subject heard the matching stimulus and the phantom stimulus in alternation and was asked to adjust the matching stimulus to the phantom stimulus by using the unmarked turning knob.

Cochlear computer model

Model simulations of phantom electrode stimulation were performed using a computational model of the implanted human cochlea, which has been developed over the years at the Leiden University Medical Center and used to analyse stimulation paradigms such as current steering and phased array (Briaire and Frijns 2000; Briaire and Frijns 2005; Briaire and Frijns 2006; Frijns et al. 2001; Frijns et al. 2009a; Frijns et al. 2009b). The first part of the model is a volume conduction section, which employs a realistic three-dimensional representation of an implanted cochlea in order to calculate electrical potentials induced by electrical stimulation. Secondly, an active nerve fiber model simulates neural responses of 320 modelled nerve fibers to electrical stimuli. Figure 1 shows the three cochlear geometries used for this study. CM1 (Cochlear Model) and CM2 (Figures 1A and B) were based on two different histological slices of a human cochlea obtained by F. Linthicum (House Ear Institute), while CM3 (Figures 1C) was based on reconstructions from micro-CT data of a human cochlea provided by Advanced Bionics and the University of Antwerp. Generally speaking the three geometries have mostly subtle differences in the shapes of their internal structures; however there is some variability in the length of the basilar membrane, which is 35.7 mm for CM1, 32.5 mm for CM2 and 32.7 for CM3. Since CM1 and CM2 were both based on one histological slice each, the trajectories of their cochlear ducts and internal structures had to be mathematically interpolated, unlike the more accurate CM3. Apart from the size the three cochlea models differ in geometry, especially in the distance of the basal turn from the apical turns (smallest in CM2 and largest in

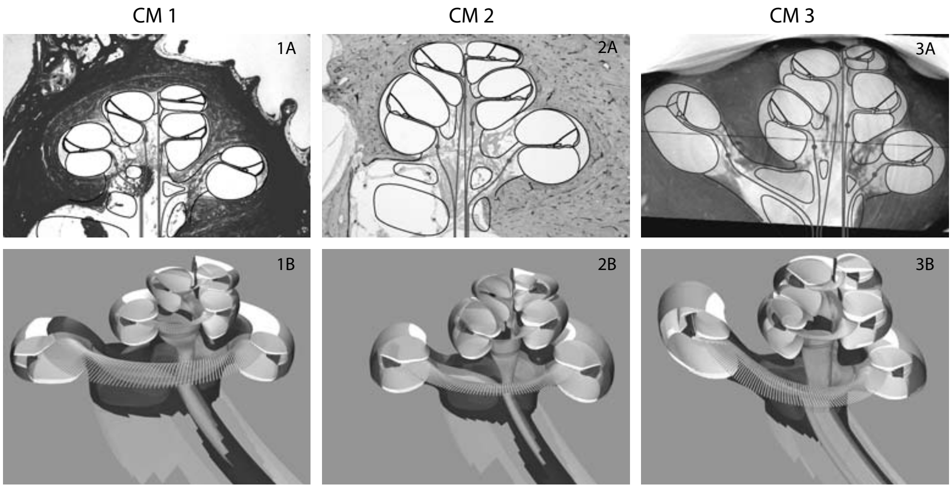


Figure 1. *Illustrations of the cochlear geometries: (A) CM1, (B) CM2 and (C) CM3. The above pictures show the histological mid-modiolar cross-sections (A&B) and micro-CT reconstruction (C) used to define the geometries, along with the mesh boundaries and nerve fibres in that plane. The pictures below are ray traced images of the full 3D models. Histological slices for CM1 and CM2 were provided by F. Linthicum of the House Ear Institute, the micro-CT data for CM3 was provided by Advanced Bionics and the University of Antwerp.*

CM3). Moreover, the turns are more or less stacked on top of each other in CM2, while the apical ones are more embedded in the basal turn in CM1 and CM3. Such variations are in line with the histological findings of Erixon et al. (2009), who described large variations in spiral length and also stated that each cochlea has its own 'fingerprint', an individual design with variable proportions. From previous modeling work (Frijns et al. 2001) it is expected that such anatomical differences have an impact on the outcome of cochlear implantation.

The anatomical models were implanted with realistic representations of the HiFocus-1j electrode array (Advanced Bionics, Sylmar, CA, USA) in the scala tympani. To study the effect of the distance of the electrode to the neural elements, simulations were included for electrodes in medial and lateral positions. Phantom electrode simulations were made for contacts at BS and AS, with σ-values ranging from 0 (monopolar stimulation) to 1 (bipolar stimulation) in increments of 0.1. Stimulation was applied for every value of σ, for each electrode pair. Results of the model simulations were plotted as excitation profiles: the grey shade coded maps show as a function of stimulus current which model nerve fibers were excited and which part of the fiber was responsible for spike initiation. Every nerve fiber in the cochlear model was assigned a characteristic pitch determined by the Greenwood frequency at the location of its peripheral tip along the basilar membrane (Greenwood 1990). These values were used as the y-axis when plotting excitation profiles. The theoretically perceived pitch of a region of excited fibers was determined by its center of excitation along the basilar membrane. This was determined by calculating the center of gravity of the excited neurons (at their tips below the organ of Corti), which was in turn converted to an equivalent pitch using the Greenwood map. In this manner, excited pitch was calculated for the dynamic range of all electrode configurations. The dynamic range of a contact pair was taken to be the current range over which the stimulated nerve fibers occupied between 1 and 4 mm of the basilar membrane. For the modelling data, the current level which results in 1 mm of the basilar membrane being excited is simply referred to as threshold (Snel-Bongers et al. 2013). The current level needed to produce 4 mm of basilar membrane excitation is called I_{4mm} (Briaire and Frijns 2000). To facilitate comparison between stimulus modalities, stimulus levels in the model are presented relative to the threshold for each situation. Where applicable, absolute current levels will be mentioned.

For comparison with the clinical data, a loudness correction experiment and maximal pitch shift experiment were simulated in the computational model. Additionally, the effect of current on the pitch shift was determined in the model for the σ with the largest shift.

Statistics

All statistical analysis was performed with the SPSS 16 (Statistical Package for the Social Sciences, SPSS inc., Chicago, IL) statistic software package. For the psychophysical experiments a linear mixed model (Fitzmaurice et al. 2004) and a paired sample Student's T-test were used. Differences were considered significant at the 0.05 level.

Results

Voltage compliance

The high impedance for both locations in subject S2 and S3 prevented to reach MCL level for most of the values of σ used. Therefore, these subjects were left out the analysis of all experiments (Table 2). Subjects S1, S4, S5 and S7 ran into voltage compliance limits before first pitch reversal, as shown in Table 2. These data points (mostly for apical electrode contacts) were therefore omitted from the analysis of the pitch ranking and pitch matching experiments.

***Table 2. σ** after recalculation with the maximum current.*

	AS						BS					
σ	**0.38**	**0.50**	**0.63**	**0.75**	**0.88**	**1**	**0.38**	**0.50**	**0.63**	**0.75**	**0.88**	**1**
S1	0.38	0.50	0.63	0.75	*0.94*	0.94	0.38	*0.50*	0.63	0.75	1.06	0.85
S2	0.42	0.68	0.97	0.98	0.98	0.98	0.45	0.77	0.93	0.93	0.93	0.93
S3	0.38	0.50	0.69	1.02	1.09	1.09	0.38	0.50	0.85	0.98	0.98	0.98
S4	0.38	0.50	0.63	*0.56*	0.53	0.53	0.38	0.50	*0.63*	0.75	1.01	1.00
S5	0.38	0.50	0.63	0.79	*1.42*	1.51	0.38	0.50	*0.63*	0.75	0.09	1.02
S6	0.38	*0.50*	0.63	0.75	1.00	1.00	0.38	*0.50*	0.63	0.75	0.94	1.02
S7	0.38	0.50	*0.69*	0.85	0.99	1.11	0.38	0.50	0.63	*0.75*	0.88	1.00
S8	0.38	0.50	0.63	*0.75*	1.19	1.45	*0.38*	0.50	0.63	0.84	1.05	1.17
S9	0.38	0.50	*0.63*	0.75	0.94	1.00	0.38	0.50	0.63	*0.75*	0.93	1.93
S10	0.38	0.50	0.63	0.75	*0.88*	1.01	0.38	0.50	0.63	0.75	0.85	0.85

Gray square: different σ from original
underlined: σ at first pitch reversal from pitch ranking experiment.

EQL

Psychophysical experiments

The EqL results for the different values of σ normalized to the monopolar configuration of the primary electrode, are shown in Figure 2 for BS (A) and AS (B) on MCL. The individual data are plotted with a different symbol for each subject.

Several data are missing for σ 0.88 and σ 1. Because of the high impedance, it was not possible to reach MCL for these σ's for several subjects. None of the subjects for AS were able to reach MCL level for all the σ's and for BS 2 subjects were able to reach MCL level for all the σ's. When using a linear mixed model, no significant difference (p = 0.308) was found between the two locations in the cochlea. EqL increases as the σ value increases, as shown for all the situations in Figure 2. Figure 2A includes one subject (S7), were the current first increases until σ = 0.75 and then rapidly decreases.

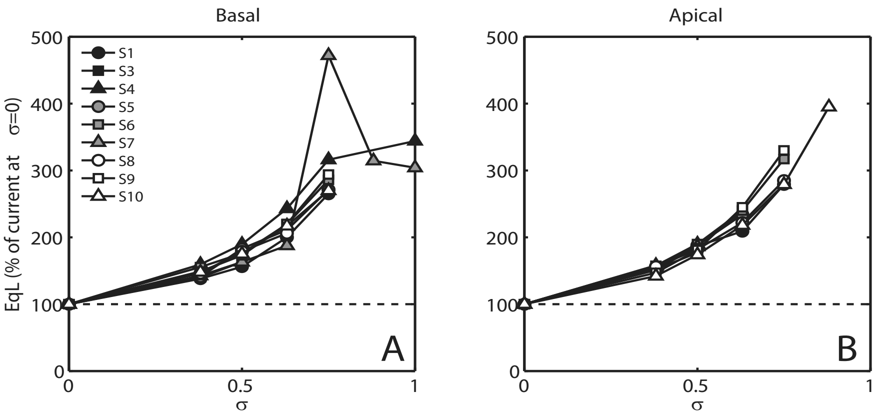


Figure 2. *Individual data of the loudness correction experiment, the loudness balanced EqL (A,B) for basal (A) and apical (B) sites. The individual data are represented for each subjects with a different symbol. The different σ values are denoted on the x axis and the EqL (MCL σ / MCL σ=0) expressed in percentage, normalized on the 'primary' electrode (σ=0), on the y axis.*

Computational model

I_{4mm} as a function of σ is shown in Figure 3 for three cochlear models (CM1, CM2, and CM3), of lateral (A, B and C) and medial (D, E and F) contacts at BS and AS. Since I_{4mm} is considered equivalent to MCL in the model, these plots can be directly compared to the EqL curves in Figure 2. In Figure 3A, B and C all curves show an increase in I_{4mm} when σ is increased starting from σ=0, which is comparable with the individual graphs from figure 2. Two curves reach a maximum at some value of σ, after which the current needed to reach 4 mm of BM excitation starts to decrease again (BS, figure 3A,C). In comparison with the clinical data, the subject

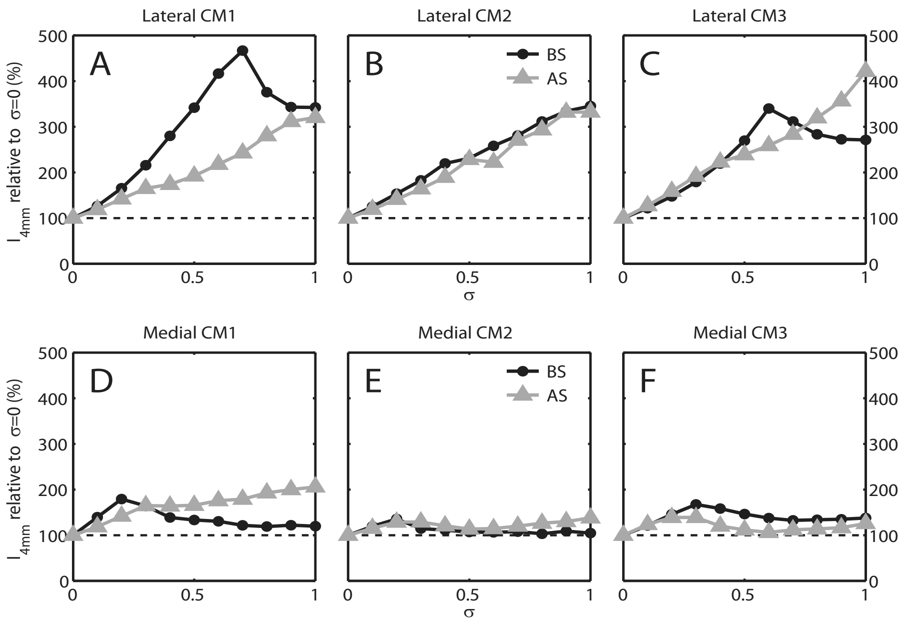


Figure 3. *Curves showing the amount of current needed for phantom stimulation in order to achieve 4 mm excitation of the basilar membrane in the model. Horizontal axes indicate the value of σ, vertical axes indicate the current delivered on the main contact of the phantom electrode pair, in percentage relative to monopolar stimulation (σ=0). Black dots are for contacts at BS, grey triangles are values at AS. The left (A,D), middle (B,E) and right (C,F) graph correspond to cochlear models 1, 2 and 3 respectively. The graphs on the first line represent the data for the lateral position (A, B and C) and on the second line for the medial position (D, E and F).*

(S4) illustrated with the squares (Figure 2A), also shows a small decrease, but then from σ=0.88. Subject S7 decreases from σ=0.75 for BS (Figure 2A), which almost equals CM 1 in lateral position (Figure 3A). In this model the contacts in the apical region (AS) show no decrease in I_{4mm} between σ=0 and σ=1, but flatten towards σ=1, which is also seen in the clinical data. The difference between the three models can be explained by the difference in geometry. The influence of the position of the electrode array is shown in Figure 3D, E and F, where an almost flat line for the three cochlear models is demonstrated, where BS in CM1 (Figure 3D) shows an increase at first and decreases after σ=0.3, which is also shown in CM3 for both AS and BS (Figure 3F). None of them are comparable with the clinical data.

Largest pitch shift

Psychophysical experiments

Figure 4A shows the results from one subject (S7) for stimulation site AS in a bar graph for the pitch ranking experiment. With increasing σ, a change in perception is shown. At first the larger σ of the pair (for example σ= 0.5 in pair (0.38 ; 0,50)) was judged to be lower in pitch, up until σ = 0.63. For larger values of σ the smallest σ of the pair was considered lower in pitch, indicating a pitch reversal. Therefore it can be inferred that σ = 0.63 yielded the (first) lowest pitch sensation for this phantom

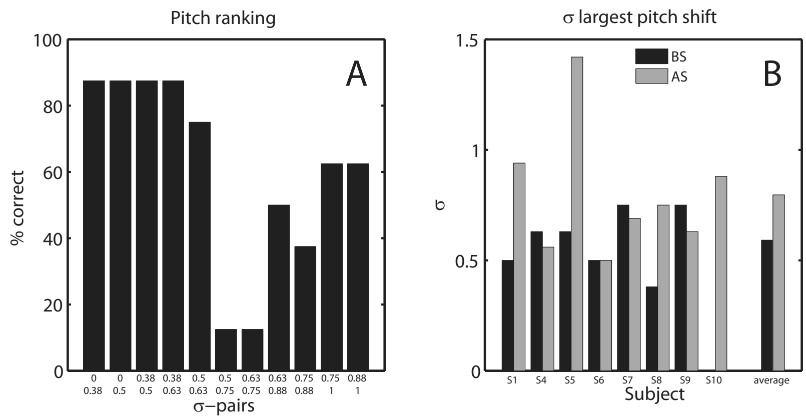


Figure 4. *Data of one subjects (S7) for stimulation site AS of the pitch ranking experiment (A), with the pairs denoted on the x axis and the percentage where the lowest pitch was correctly chosen on the y axis. The individual and average data of the pitch ranking experiment (B), with the subjects denoted on the x axis and the σ at first pitch reversal on the y axis shown with the bars. The light gray bar represents the apical position and the black bar the basal position.*

pair. As can be seen in Figure 4B, the σ at first pitch reversal differs between subjects. The data of S10 are missing for the basal position because the subject got tired during testing and was unable to complete the test session. In table 2 isshown that some of these σ's at first pitch reversal (underlined) are a recalculated σ (for AS S1, S4, S5). These subjects were left out the further analysis of the pitch ranking and pitch matching experiment. In two data points subject S8 AS and S9 BS) the flanking σ is a recalculated σ. These σ are in both cases higher than the σ at first

pitch reversal. These data points can therefore be used in the pitch matching experiment.
The σ at first pitch reversal that induced a pitch shift to apical was first determined using pitch ranking measures per subject per electrode position. Results from BS were not significantly different from those obtained at AS ($p = 0.298$). First pitch reversal was obtained for a σ of 0.60 on average, which is closest to σ 0.63, with σ = 0.38 as a minimum and σ = 0.75 as a maximum.

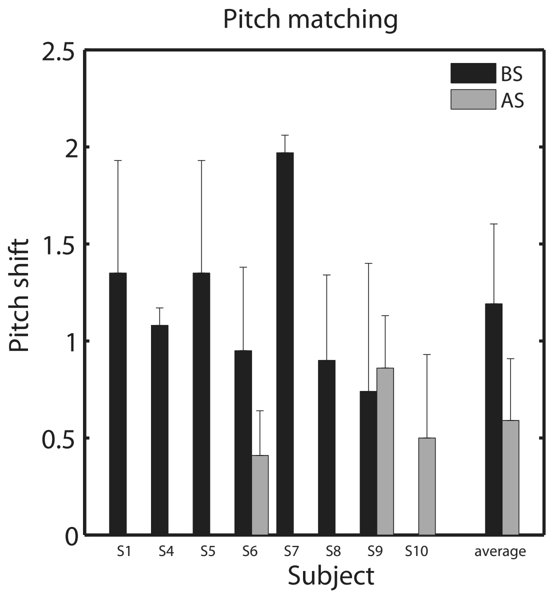


Figure 5. *The individual and average data of the pitch shift at first pitch reversal experiment at MCL, with the subjects denoted on the x axis and the pitch shift expressed in electrode contact spacing on the y axis. The light gray bar represents the apical position and the black bar the basal position.*

Pitch found at the σ at first pitch reversal measured with the pitch matching experiment is demonstrated in Figure 5 expressed in electrodes along the array for both AS and BS at MCL. As indicated in the material and methods, the two σ's adjacent to the σ's at first pitch reversal shown in Figure 4, were also tested. The figure shows the data for the σ with the pitch shift as determined by pitch matching only. This did not occur at the same σ as found in the pitch ranking experiment for all subjects. The mean shift for the σ found with the pitch ranking experiment was

0.75 electrode contacts and for the flanking σ's respectively 0.63 and 0.52 electrode contacts. Six of the ten σ's found with the pitch ranking experiment, had with the pitch matching experiment the largest pitch shift. In the other four cases, one of the flanking σ's had a larger shift. All subjects showed a pitch shift in the apical direction from the apical electrode of the pair. For both locations, 2 data sets (S8 apical and S10 basal) were not collected because of subject fatigue during testing. The smallest shift was 0.41 electrode contacts and the largest shift was 1.97 electrode contacts, with a highly significant average shift of 1.07 electrode contacts ($p < 0.001$). Also the shifts per location were highly significant ($p<0.001$): BS had an average shift of 1.19 electrode contact and AS an average shift of 0.59 electrode contact. Interestingly, also the difference between the shifts of the two locations was a highly significant ($p<0.001$).

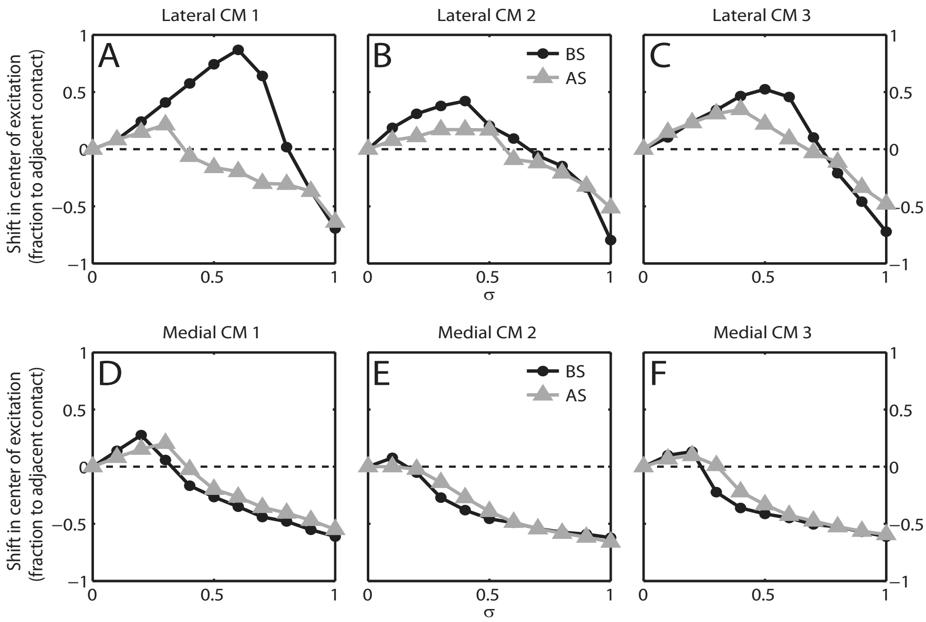


Figure 6. *Pitch excited in the model with phantom stimulation as a function of σ (x axis), at* I_{4mm}. *On the y axis the shift of the center of excitation is shown expressed in fraction to the adjacent electrode. The largest pitch shift for the lateral (A, B and C) and medial position (D, E, and F) are shown. Black dots are for contacts at BS, grey triangles are values at AS. The left (A,D), middle (B,E) and right (C,F) graph correspond to cochlear models 1, 2 and 3 respectively.*

Computational model

The simulated pitch shift (y-axis) excited at I_{4mm} is shown in Figure 6 for contacts at BS and AS in the three cochlear models for lateral and medial located electrode contacts, for varying values of σ (x-axis). The shift of the center of excitation expressed in electrode distance compared to monopolar stimulation (the horizontal dashed line) is shown on the y-axis. In all contacts there is an initial range of σ where the pitch excited by the contact decreases for increasing σ, due to the region of excitation moving in the apical direction. The largest pitch shift, approximately 1 electrode contact, is seen in figure 6A for the basal electrode contact at lateral position. The other simulations show a shift smaller than half a

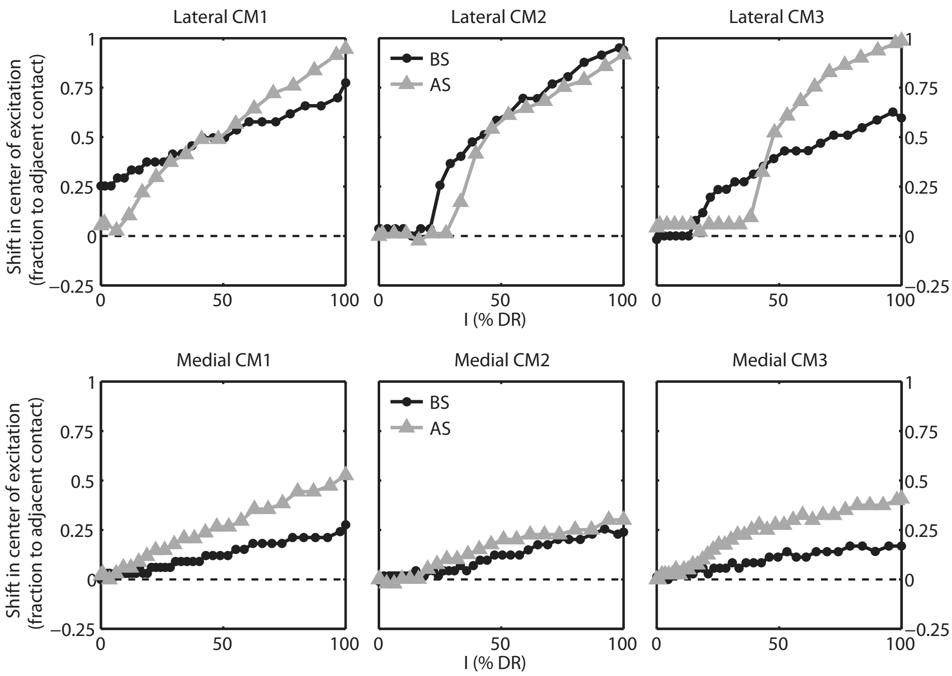


Figure 7. *Model pitch excited by phantom stimulation as a function of stimulus intensity. Horizontal axes indicates the dynamic range from threshold to I_{4mm}, expressed in a percentage (0% corresponds to threshold and 100% corresponds to I_{4mm}). Vertical axis indicates the shift in center of excitation expresses in fraction to adjacent contact. Black dots are for contacts at BS, grey triangles are values at AS. The left (A), middle (B) and right (C) graph correspond to cochlear models 1, 2 and 3 respectively. The graphs on the first line represent the data for the lateral position (A, B and C) and on the second line for the medial position (D, E and F).*

contact spacing. The largest pitch shift found in the psychophysical experiments was overall larger than the shift predicted by the model, although the average is comparable to cochlear model 1 in BS (Figure 6A). The apical shift is larger at BS than at AS, which was also shown in the psychophysical pitch matching data. At higher values of σ however, the center of excitation shifts more in the basal direction. The medial curves show a small shift in the apical direction with a maximum of 0.3 electrode contacts in Figure 6D for BS. Beyond σ=0.2 there is no apical shift.

In Figure 7 the pitch shift of phantom electrode stimulation in the model is plotted against stimulus level (given as percentage of the Dynamic Range (DR)), for a single value of σ with the largest pitch shift (shown in figure 6). With shift in center of excitation expressed as a fraction of the adjacent contact spacing on the y-axis, the apical and basal data can be plotted in the same graph and the difference in pitch shift becomes more easily comparable. It is immediately apparent that the shift in pitch caused by phantom electrode stimulation is dependent on stimulation level for all three cochlear models for both the lateral and medial position of the electrode contacts. Here again the shift in apical direction is larger for the lateral position than for the medial position. Also, the change in current has more influence on the shift in apical direction of the lateral position.

Excitation profiles

The computer model was used to study the relative width of the region of excitation for the various stimulus modalities and values of σ in phantom electrode stimulation. As data from the various cochlear models were not essentially different, only the data from cochlear model 1 are presented here. It also turned out that the excitation profiles for apical and basal sites were not essentially different, apart from the fact that at AS more fibers are excited in their peripheral process. Figure 8 compares monopolar stimulation on the apical contact of the pair (A), current steering for α=0.5 (B) and phantom electrode stimulation for σ=0.6 (C)

for a lateral contact. To simplify comparison, the outline of the excitation profile in A is plotted as a grey dashed line in B and C. The center of excitation (indicated with a triangle on the vertical dashed line) for CS shifts in basal direction (B) and for phantom stimulation in apical direction (C) in comparison with monopolar stimulation. The threshold level, by definition zero dB in the graph, is higher for partial bipolar stimulation (0.66 mA) than for the monopole and CS (0.37 mA and 0.41 mA, respectively). The width of the excitation pattern of phantom stimulation is thinner than with current steering. As a result, I_{4mm} , as indicated by a vertical black dashed line in Figure 8, is much higher for phantom stimulation than for the other two conditions, predicting a higher stimulus level needed to reach MCL with phantom stimulation. Although it seems from Figure 8 A and B that CS has a lower electrical dynamic range than monopolar stimulation, this varies largely between cochlear models and BS and AS. This is mainly determined by threshold variations, as the absolute value of I_{4mm} is equal within 10% for both stimulus configurations in all three cochlear models, both for AS and BS.

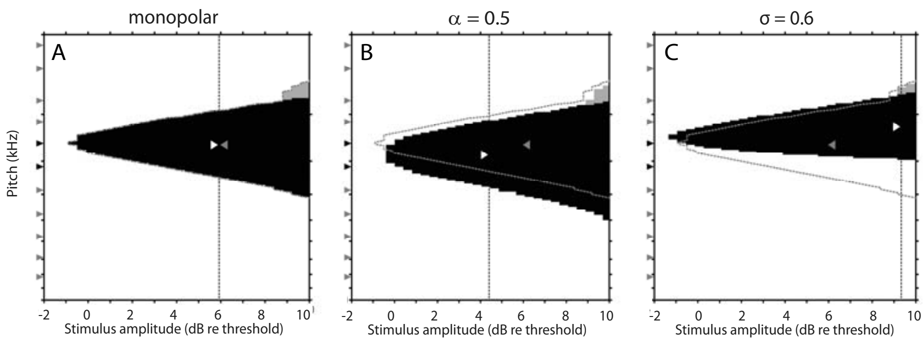


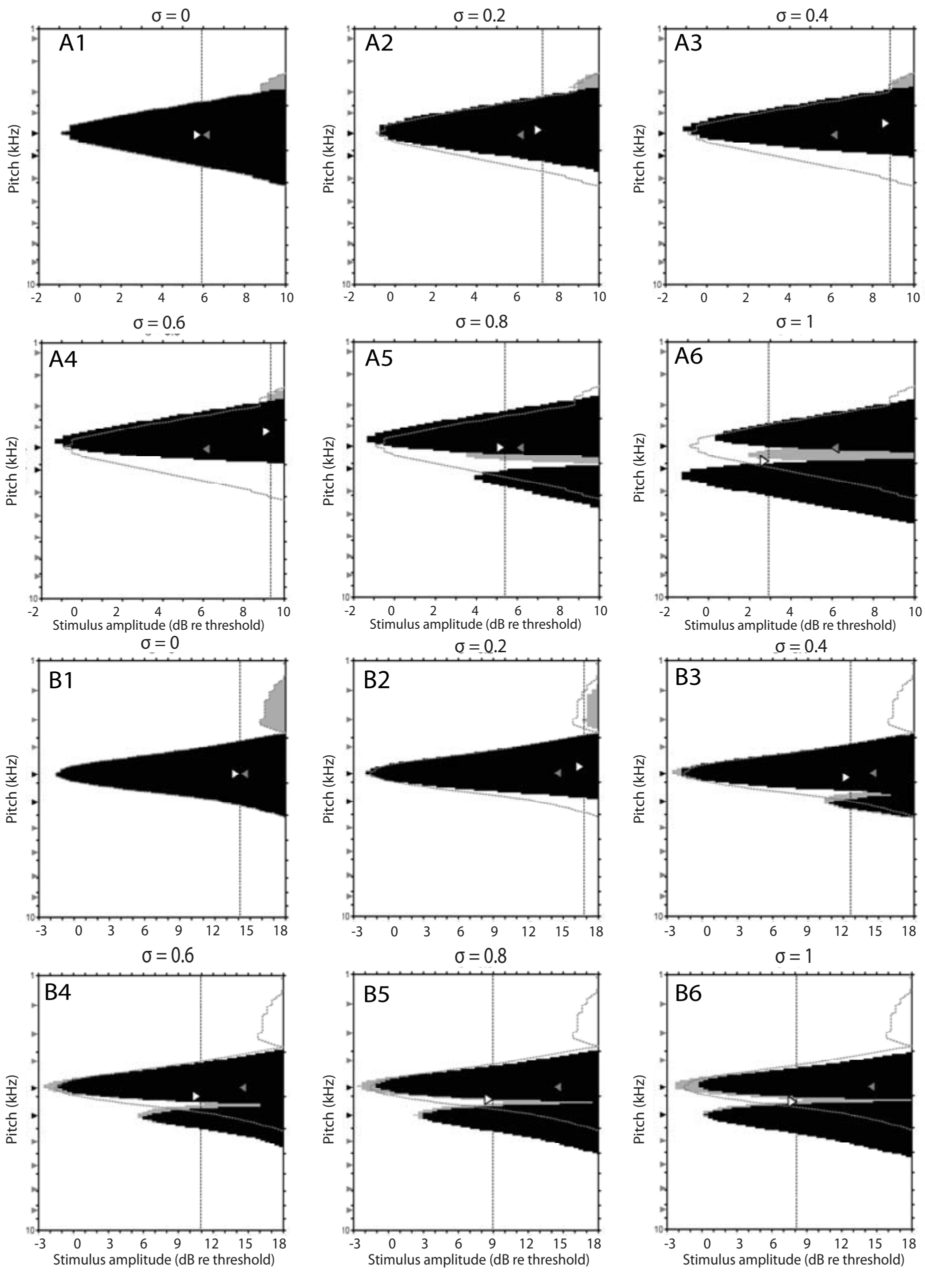
Figure 8. *Excitation profiles of monopolar stimulation (A), current steering with α=0.5 (B) and phantom stimulation with σ=0.6 (C) on a lateral contact at BS in cochlea model 1. The excitation profiles show neural stimulation patterns in a section of the cochlea for a range of stimulus levels. Horizontal axes indicate stimulation level in dB relative to* threshold of the applied stimulus configuration (due to loudness differences the absolute currents varies between the graphs)*, the vertical axes denote the tonotopic frequencies of model fibers as determined by the Greenwood map. The triangles on the y axis denote the position of the electrode contacts. Black coloured areas indicate stimulation in the axons, grey coloured areas correspond to stimulation at the peripheral process and white areas indicate no stimulation. The vertical black dashed line in each panel marks the current level where the excited fibers occupy a total of 4 mm along the basilar membrane. The white triangle on this line indicates the center of excitation at 4 mm. The grey dashed line in each panel marks the contour of the excitation pattern and the grey triangle marks the center of excitation at 4mm of the monopolar situation.*

Excitation profiles of Phantom Electrode stimulation on a lateral contact at BS are shown in Figure 9A, with different values of σ in each panel. I_{4mm}, again indicated by a vertical black dashed line in each panel, increases up until σ=0.6, after which it decreases, as has already been shown in Figure 3 (A and C). The grey dashed curve in each panel marks the contour of the excitation pattern of the monopolar situation seen in Figure 9A (σ=0). With increasing σ, the basal flank of the black area decreases. As a consequence the center of the excitation profile shifts in an apical direction, which is also indicated here with a triangle on the vertical dashed line. From σ = 0.8 onwards the excitation area of the compensating electrode appears, and the total area is broader than the excitation area of the monopolar stimulation (σ=0). At this point the center shifts back again in the basal direction and at σ = 1.0 a bipolar stimulation pattern is visible. The excitation profiles of Phantom Electrode stimulation on a medial contact at BS are shown in Figure 9B (cochlear model 1). The excitation area is smaller for σ=0 in comparison with lateral position. Further, the excitation area of the compensating electrode appears with σ=0.4, which results in a smaller to almost no shift in apical direction (Figure 6 D – F).

Discussion

This study showed that with a partial bipolar configuration, where pulses are delivered simultaneously to electrode contacts but with opposite polarity, the pitch percept is pushed away from the primary electrode contact in the contralateral direction from the compensating electrode contact. Therefore it may be possible in the future to stimulate beyond the electrode array in the apical region of the cochlea, which is in line with previous research (Saoji and Litvak 2010). The ratio σ (of current on the compensating contact to that on the primary one), which generated the pitch shift at first reversal and the place of stimulation of the phantom electrode turned out to be different across subjects. However, seven out of nine subjects were able (at a significance level of 0.05) to perceive a pitch more apical than the most apical stimulating physical contact, with a minimum shift of 0.41 electrode contacts. However, to create a phantom electrode more current correction is required to maintain equal loudness between monopolar stimulation and phantom stimulation than with current steering (Figures 2 and 3; (Frijns et al. 2009b; Snel-Bongers et al. 2011)) .

Figure 9. *Excitation profiles of phantom stimulation on a lateral(A) and medial (B) contact at BS in cochlea model 1, for different values of σ in each panel. The excitation profiles show neural stimulation patterns in a section of the cochlea for a range of stimulus levels. Horizontal axes indicate stimulation level in dB relative to* threshold of the applied stimulus configuration (due to loudness differences the absolute currents varies between the graphs)*, the vertical axes denote the tonotopic frequencies of model fibers as determined by the Greenwood map. Black coloured areas indicate stimulation in the axons, grey coloured areas correspond to stimulation at the peripheral process and white areas indicate no stimulation. The vertical black dashed line in each panel marks the current level where the excited fibers occupy a total of 4 mm along the basilar membrane. The white triangle on this line indicates the center of excitation at 4 mm. The grey dashed line in each panel marks the contour of the excitation pattern and the grey triangle marks the center of excitation at 4mm of the monopolar situation seen in the upper left panel (σ=0).*


σ = 0
σ = 0.2
σ = 0.4
σ = 0.6
σ = 0.8
σ = 1
A1
A2
A3
A4
A5
A6
B1
B2
B3
B4
B5
B6
Pitch (kHz)
Stimulus amplitude (dB re threshold)

EQL

The initial increase (and sometimes decrease) in current found in the psychophysical experiment determining EqL contours (Figure 2) was comparable to the results from the computational model of the cochlea for the lateral position. However, several subjects exceeded voltage compliance for the higher σ's (σ = 0.88 and σ = 1) with our standard phase duration of 32.32 µs. When phantom will be used in clinical practice a broader pulse is necessary for several subject to prohibit exceeding voltage compliance.

Saoji and Litvak (2010) also described an initial increase in current with σ but from σ = 0.75 a flattening of the curve. The model shows that the initial increase in current needed to achieve 4mm excitation (equal to MCL) is caused by the negative stimulus on the compensating contact (Figure 10). The negative stimulus is counteracting some of the current spread of the primary contact. This makes it more difficult for the electrical current to reach the neurons. At sufficiently high values of σ however, the amplitude of the negative stimulus becomes high enough to start exciting neurons in its own right and creates an extra area of excitation near the compensating contact (Figure 9 A5). This is essentially bipolar stimulation, and the additionally excited fibers subsequently make it easier to reach 4mm excitation. This stimulation potentially leads to a down wards slope in the EqL-curves. It appears that it highly depends on the amount of channel interaction whether this down wards slope occurs, and at which point it starts.

From both Saoji and Litvak (2010) and the present study it is clear that creating a phantom electrode at MCL is possible. The model provides insight at the point, where the apical shift became smaller with decreasing stimulus level (Figure 7) and, at the lowest levels, no shift occurred at all. From the excitation profiles in Figure 10 it is clear that for excitation around threshold level, the excitation place remains at the contact position (denoted with triangles on the y axis). The model indicates that the steering of the center of excitation is caused by a suppression of the excitation on the basal side, while the fibers at the main contact are still excited. This is achieved at the price of higher current levels needed to produce the same loudness. At low levels the number of fibers that can be suppressed on one side is smaller and thus the phantom effect is diminished.

Pitch shift at first pitch reversal

Each subject showed a pitch shift in the apical direction with increasing σ, where the extent of the shift differed from 0.41 to 1.97 times a contact spacing. Also the σ at first pitch reversal differed between subjects. The used psychophysical method to determine the largest the pitch shift is unable to detect a theoretically possible second pitch reversal with an even larger pitch shift. Only the σ at first pitch reversal and the flanking σ's were used in the pitch matching experiment. And an possible higher pitch shift could have been be missed in the current setup. The computer model, however, showed only one pitch reversal. The presented data therefore, are expected to be representative of the real pitch shift.

The computer model of the cochlea gives an explanation for this underlying mechanisms of the pitch shift. For all contacts there is an initial range of σ where the pitch excited by the contact decreases for increasing σ. The region of excitation will move in the apical direction as a result of increasing channel interaction. At higher values of σ however, the excitation pattern takes the same form as that produced by bipolar stimulation (Figure 9 A5). The additional region of excitation caused by the compensating contact shifts the center of excitation in the basal direction, increasing the excited pitch. The point at which the excitation pattern becomes bimodal is heavily dependent on the amount of channel interaction.

The pitch of phantom electrode configurations was examined in 10 subjects by Saoji and Litvak (2010). They used several pitch ranking tests to evaluate the largest pitch shift and found a shift of between 0.5 and 1.2 electrode contacts with a pitch matching experiment using monopolar stimuli on physical contacts in between a partial bipolar pair spanning several contacts. To further substantiate this outcome, the current study used, in addition to the pitch ranking test, current steering in a pitch matching procedure to determine the size of pitch shift at first pitch reversal for partial bipolar stimulation on adjacent electrodes. Moreover, the pitch matching experiment confirmed the pitch ranking data on the value of σ associated with the first pitch reversal. However, the group of subjects was small. Therefore cannot be concluded which of the two methods is most accurate.

Current steering

CS and phantom stimulation differ fundamentally from each other. Firstly in polarity of the pulses, but also in excitation profiles as shown in Figure 8. The width of the excitation profile for phantom stimulation as predicted by the model is much thinner than the profile of CS, thus providing potentially with better spatial resolution. As expected the current level to reach I_{4mm} is higher for phantom stimulation than for the other to stimulation types. The almost equal current for monopolar stimulation and current steering is comparable with previous studies (Frijns et al. 2009b; Snel-Bongers et al. 2011; Donaldson et al. 2005).

The influence of contact position

The intended position of the HiFocus-1J electrode array is near the lateral wall of the cochlea. The psychophysical results are therefore best comparable with the computational model results of the lateral position. According to the model, however, a medial position will lead to different results, as in medial contacts, the amount of interaction between channels is less than in outer wall contacts. This is due to the closer proximity to the neurons and leads to less 'fanning out' of the electrical current before it reaches its target. In channels with low interaction, the compensating stimulus can excite a second region of neurons relatively independently from the primary stimulus. This is well illustrated by comparing Figures 9 A and B, where it is clear that for a peri-modiolar electrode a second lobe (basal to the main one) is elicited by the compensating current for lower values of σ than for the electrode in an outer wall position. This explains the lower values of the pitch shift in apical direction for the medial position in comparison with lateral position (Figure 6), as well as the fact that the pitch is more dependent on stimulus level for lateral positions than for medial ones (Figure 7).

Future perspectives

The phantom electrode technique works. However, more current is required to maintain equal loudness and the pitch shift at first pitch reversal differs by subject. The increase in current will lead to higher battery consumption, which can be inconvenient for CI users. Whether CI users will benefit from phantom stimulation and whether it is possible to use the phantom electrode in a speech coding strategy should be tested in a chronic clinical trial. Here speech perception scores from a normal clinical setting should be compared with speech perception scores obtained with a speech coding strategy employing phantom stimulation. In this trial it is also of importance to test whether subjects with a shallow insertion benefit from more apical stimulation. Previous studies (Hamzavi and Arnoldner 2006; Hochmair et al. 2003; Qi et al. 2011) indicated that stimulating in more apical regions enhances speech perception. They all switched off the 4 most apical electrodes in a Med-EL cochlear implant and found that the speech perception was significantly lower in this situation, than when these electrode contacts were switched on. Contrary to this finding, Gani et al. (2007) found that some patients benefit from switching off the most apical electrode contacts in a Med-EL device. Probably this is explained by high channel interaction, which can lead to pitch confusion in the apex (Boyd 2011).

Conclusion

Based on the psychophysical data and the predictions of the computational modeling it can be concluded that phantom stimulation on an electrode array in lateral position makes it possible to stimulate more apically by about 1 electrode contact distance (1.1 mm). However, more current is required to maintain equal loudness and the model predicts that stimulating at lower current levels will probably result in a smaller pitch shift.

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Chapter 4

Influence of widening electrode separation on current steering performance

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Abstract

Objectives: Current steering between adjacent electrodes makes it possible to create more spectral channels than the number of electrodes in an electrode array. With current steering on non-adjacent electrodes, here called “spanning”, it could be possible to bridge a defective electrode contact or potentially reduce the number of electrode contacts for the same level of access to the auditory nerve. This study investigates the effectiveness of spanning in terms of the number of intermediate pitches, loudness effects, and linearity of the current weighting coefficient (α) with respect to the perceived pitch.

Design: Twelve post-lingually deafened users of the HiRes90K cochlear implant with HiFocus1J electrode were randomly selected to participate in this study. Electrode contacts were selected at two locations in the cochlea, as determined on multi slice CT (MSCT): 180º (basal) and 360º (apical) from the round window. For both cochlear locations three psychophysical experiments were performed using simultaneous stimulation of electrode contacts. An adaptive staircase based procedure was used. The number of intermediate pitches was assessed with a 3AFC pitch discrimination task, and the extent of current adjustment required when varying the current weighting coefficient (α) was determined with loudness balancing (2AFC). Finally, the pitch of a spanned channel was matched with the pitch of an intermediate physical electrode in a 2AFC procedure to assess the place of the spanned channel on the electrode array.

Results: Spanning required significantly more current compensation to maintain equal loudness than current steering between adjacent electrode contacts. A significant decrease of discriminable intermediate pitches occurred with spanning in comparison with current steering between adjacent electrode contacts. No significant difference was found between the pitch matched current steering coefficient and the theoretical coefficient corresponding a priori with the intermediate physical electrode. No significant difference was found between the data from the apical and the basal sections of the electrode array.

Conclusions: Spanning over wider electrode distance is feasible. With increasing electrode spanning distance, more current compensation is needed to maintain equal loudness and a gradual deterioration in the just noticeable difference for pitch is observed. However, the pitch progression is linear. For a spanned signal with equal proportions of current delivered to both electrodes, pitch is equivalent to that produced by an intermediate physical electrode.

Introduction

Contemporary cochlear implants (CI) contain 12 to 22 intra-cochlear electrode contacts, implying a highly quantized spatial access to the auditory nerve when using standard CI sound processing algorithms. For CI recipients this coarse electrical tonotopy may result in significant difficulties with speech understanding in background noise and appreciating music (Frijns et al. 2003; Shannon et al. 2004). A logical remedy is to increase the resolution of spatial access to the auditory nerve, and thereby hopefully increase the number of distinct pitches a subject can discriminate. Townshend *et al.* (1987) and McDermott and McKay (1994) showed that the perception of pitch can be varied between two adjacent electrodes by delivering the current either simultaneously (Townshend et al. 1987) or non-simultaneously (McDermott and McKay 1994) to both contacts. Recipients systematically reported a single-sound percept with a pitch that was between the base pitches of the individually stimulated contacts. Donaldson *et al.* (2005) were the first to investigate the number of discriminable pitches generated between two adjacent contacts with simultaneous dual-electrode stimulation, also called current steering. Their study concluded that a two- to nine-fold increase in the number of pitches was possible. This was later also found for non-simultaneous stimulation (Kwon and van den Honert 2006). Firszt *et al.* (2007) and Koch *et al.* (2007) extended the study of Donaldson *et al.* (2005) by estimating the number of discriminable pitches (also called spectral channels) that could be generated using current steering. For the whole electrode array, this ranged from 8 to 451 with an average across subjects of 63 spectral channels (Firszt et al. 2007).

A sound processing strategy, called HiRes 120, based on current steering was implemented by Advanced Bionics (Brendel et al. 2008). Several studies (Buechner et al. 2008; Firszt et al. 2009) evaluated this sound processing strategy and found significantly better speech perception for HiRes 120 compared to HiRes. This strategy was also evaluated in a European multi centre HiRes 120 study (Eklöf, reference note 1). Some subjects from the study group at the Leiden University Medical Centre (LUMC) had a non-active electrode (a gap) in their programs. In contrast to the subjects without an electrode gap, this group had poorer speech perception outcomes for the HiRes 120 program than for the HiRes program (Boermans, reference note 2). This led us to consider the possibility that current steering could be used to replace the missing electrodes. Previous research has shown that it is possible to create an intermediate pitch for electrode separation up to and including 4 mm for simultaneous (Saoji, reference note 3) and non-simultaneous (McDermott and McKay 1994) dual-electrode stimulation. We will refer to current steering on non-adjacent electrodes as spanning. If spanning is as effective as current steering on adjacent electrodes, it can be used to bridge, defective contacts. Eventually it could lead to a new electrode design with the same sound perception quality, but with a lower number of physical electrode contacts on an array.

With current steering on adjacent contacts, due to electric field summation, no or very little adjustment of the current is needed to maintain equal loudness (Donaldson et al. 2005; Frijns et al. 2008; Frijns et al. 2009). However, it is not known what happens with current adjustment when increasing the spanning distance. With spanning, there is presumably less overlap between the regions of neural excitation produced by the two electrode contacts, which is comparable with sequential stimulation. With computational modelling has been shown that sequential stimulation needs current adjustment (Frijns et al. 2009). Given the potential importance of spanning in future sound processing strategies, we endeavored to study the amount of current compensation needed to maintain equal loudness with spanning in our subject group.

As a new research element, we intended to study the pitches evoked by spanning in comparison to current steering on adjacent electrode contacts. We focused particularly on the number of intermediate pitches i.e., the possibility of creating the same number of intermediate pitches with spanning as with current steering on adjacent contacts and on the progression of the pitch percept. The number of intermediate pitches can be calculated with a formula, where the just noticeable difference (JND) is used (Firszt et al. 2007; Koch et al. 2007). The latter tests the assumption that, when the current is equally distributed to both electrode contacts and the neural survival is equally distributed, the generated percept is centered exactly between the physical contacts. The question arises whether there is a linear correlation between pitch and the proportion of current going to each of the spanned electrode contacts. One way to look into this issue is to determine the proportion of current that matches the pitch of an intermediate physical contact (linearity of the mapping). This way defective electrodes can be replaced while maintaining exactly the same pitch percept.

In terms of electrode location several studies have shown that, with current steering, more intermediate pitches can be discriminated in the apical region than in the basal region (Firszt et al. 2007; Koch et al. 2007; Kwon and van den Honert 2006). These studies selected test electrodes based on their rank number on the electrode array. However there are important differences between subjects regarding insertion angle, size of the cochlea and electrode position, which will most probably influence the outcome (Kos et al. 2005; Skinner et al. 2007). Consequently, for standardized comparison, data from electrode contacts at the same position in the cochlea are preferred. We therefore, selected the electrodes based on their location in the cochlea, using a CT-scan to determine the exact electrode position (Lane et al. 2007; Skinner et al. 1994; Verbist et al. 2005).

To summarize, this study investigates whether spanning - up to four electrodes - is as effective as current steering on adjacent electrodes. The following issues are addressed: 1) the extent of current adjustment required to maintain equal loudness due to spanning; 2) the change in number of intermediate pitches with spanning; 3) the linearity of the pitch percept with respect to place; 4) The importance of cochlear location on the psychoacoustic outcomes.

Methods

Subjects

A group of 12 postlingually deafened adults was unilaterally implanted at the LUMC in 2007. Each received a HiRes90K implant with a HiFocus-1j electrode array (Advanced Bionics, Sylmar, CA). No problems were reported during surgery or the subsequent rehabilitation program. Subject information is provided in Table 1. All subjects participated in the first two experiments. Only six of the twelve subjects (S2, S3, S4, S10, S11 and S12) were willing to participate in the third experiment. The average phoneme recognition score of 75 % (range 38-96%), obtained with the standard Dutch speech test of the Dutch Society of Audiology (Bosman and Smoorenburg 1995), is representative for that of the total cochlear implant population at LUMC. Written consent was obtained. This study was approved by the Medical Ethical Committee of the LUMC under number P02.106.J.

Electrode locations

As part of the clinical CI program every CI candidate undergoes a preoperative and a postoperative CT-scan. The latter was used to locate the position of the electrode array. Multiplanar reconstructions (MPR) were made through the cochlea parallel to the basal turn and perpendicular to the modiolus (cochlear view), i.e., in the plane of the electrode array (Vitrea 2 software, Vital Images, Minnetonka, MN).

This procedure was completed using a dedicated Multi slice CT scan data acquisition protocol developed in our center (Verbist et al. 2005).

Table 1. *Subject demographics.*

	Gender	Age (years)	Aetiology	Duration of deafness (years)	CI side	CI usage (months)	CVC Ph%	Electrodes tested 180°	360°
S1	Female	42	Congenital hearing loss	36	right	13	86	11	5
S2	Female	54	Rubella intra uterine	50	right	16	66	11	5
S3	Male	60	Congenital hearing loss	55	right	13	54	9	2
S4	Male	61	Meningitis	57	right	18	38	10	4
S5	Female	47	Progressive hearing loss	15	left	10	80	8	1
S6	Male	74	M. Meniére	24	right	8	74	9	2
S7	Female	54	Congenital hearing loss	46	right	11	85	12	6
S8	Female	69	Congenital hearing loss	21	right	10	93	11	6
S9	Male	48	Meningitis	42	right	8	68	11	4
S10	Female	43	Unknown	39	left	6	39	11	5
S11	Male	63	Otosclerosis	23	right	17	89	11	5
S12	Female	43	Congenital hearing loss	5	right	9	96	10	4
Average		55		34		12	75		

Speech perception scores are given as percentage phonemes correct (Ph%) in phonetically balanced monosyllabic (CVC) words.

To measure the exact position of the electrodes, a system of coordinates was placed in the postoperative MPR, with a custom Matlab computer program (MathWorks, Natick, MA). In this program, the z-axis was placed through the modiolus and the 0^{o} reference angle was placed through the most lateral point of the lateral semicircular canal. All electrode contacts were marked by an experienced physician. Correction of the angular system to angles measured from the round window was done using the angular position of the round window, as recorded from the preoperative scan of the individual subject. The angles measured from the round window were used in this study, thereby conforming to an international consensus (Verbist et al. 2010). The electrode contact numbering is ascending from apex to base in line with the manufacture's convention. For each subject the electrode contact closest to 360 degrees (apical site, AS) and the one closest to 180 degrees (basal site, BS) were selected (Table1). The average location of these sites was respectively at 354 degrees (+/- 9 degrees) and 181 degrees (+/- 7 degrees). Current steering was conducted between the apical contact (at 360^o or 180^o) and the next four more basal electrode contacts. Throughout this paper a pair, consisting of electrode contacts e and e+i, will be referenced to as 'pair e+i' (with i ranging from 1 to 4).There was no overlap of the two contact groups. The first two experiments took place on both locations, the third experiment was conducted only for the apical site.

Experiments

Experiments were performed with the research tool BEDCS (Bionic Ear Data Collection System, Advanced Bionics, Sylmar, CA) for the electrical stimulus configuration and PACTS (PsychoACoustic Test Suite, Advanced Bionics Europe, Niel, Belgium) for the psychophysical tests. Stimuli were bursts of symmetric biphasic pulses with phase duration of 32 µs, pulse rate of 1400 pulses per second and total burst duration of 300 ms. Between the stimuli was a pause of 500 ms. Dual-electrode stimuli were always simultaneous (i.e., current steering was employed). The proportion of the total current directed to the more basal contact of the dual-electrode contact pair is denoted as α. This coefficient varies from α = 0, where all current is directed to the apical electrode to α = 1, where all current is directed to the basal electrode. The individual loudness growth of each electrode contact was taken into account with linear correction between the two electrode contacts in a pair. Before testing, electrical threshold levels (TL) and most comfortable levels (MCL) were determined for all electrode contacts.

This study consisted of three different experiments; loudness balancing, pitch discrimination and pitch matching. The loudness balancing was conducted first, to determine whether spanning requires current adjustment to maintain constant loudness. These data were used in the other two experiments to equalize loudness between presentations. After each experiment the subject was asked to describe the percepts which they had received. In all experiments a staircase procedure was used (Levitt 1971). The specific type varied between experiments. The procedure required ten reversals (i.e. changes in the direction of the signal level), where the test outcome was calculated over the last six reversals. If the variance (standard deviation) on the last six reversal points was considered too large by the program

(PACTS), determined using an algebraic algorithm (Reference note 4), the test was extended to determine a few (1-12) more reversal points.

Loudness balancing

TLs and MCLs were determined for each of the ten preselected electrode contacts. The subject was asked to indicate when the signal on the physical contacts was just heard (TL) and also when the signal sounded most comfortably loud (MCL). All levels were carefully loudness balanced within and across electrode pairs, as in normal clinical follow-up. Linear correction then took place between the electrode contacts. Because of the correction for possible differences in MCL, the influence of loudness difference on the outcome of this experiment is reduced to a minimum. Using a two-alternative-forced-choice (2AFC) 1-up/1-down staircase procedure, equal loudness was determined for the intermediate percepts compared to the apical electrode contact of the stimulated pair. Stimulus A, with $\alpha = 0$, was presented at MCL. Stimulus B, with $\alpha = 0.5$, started at 120 percent of MCL. In each trial, the order of presentation of stimulus A and B was randomized. The subject

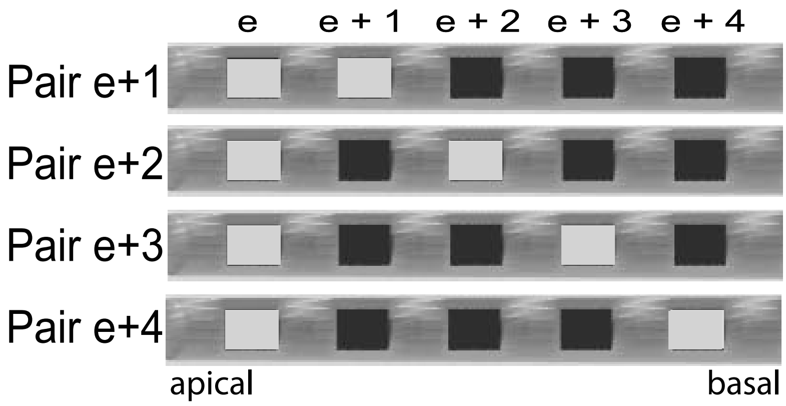

Figure 1. *Electrode pairs used in loudness balancing and pitch discrimination experiments. The most apical electrode of a pair is denoted as e and is either AS (360^o from round window) or BS (180^o from round window) as selected on the basis of a CT-scan. The light gray squares are the stimulated electrode contacts with dual-electrode stimulation in the experiments. A pair consist of e, the apical electrode and 'e+i', the basal electrode, where 'i' varies between 1 and 4.*

was asked which stimulus was louder. Through 10 reversals, the current for stimulus B decreased or increased in 15 percent increments for the first four reversals and in 7 percent increments for the last six reversals. For both cochlear locations (AS and BS), four different electrode pairs with increasing spanning distance (figure 1) were evaluated. The experiment always started with the AS pair e+1, followed by AS pair e+2 and so on.

Pitch discrimination
The just noticeable difference (JND) in current weighting coefficient α was determined with a 3 AFC, 1-up/2-down staircase procedure for the four different spanning pairs at each cochlear location: AS and BS. The reference stimulus had a value α = 0 (apical electrode) and the probe stimulus a non-zero α between 0 and 1. The reference stimulus was played twice and the probe stimulus once. In each trial, the presentation order of the three stimuli was randomized. The subject was asked which stimulus was different in pitch. A loudness roving of 10% (considered to be moderate) was applied to the stimulation current in order to avoid any potential bias from a loudness cue (Vanpoucke, reference note 5). The experiment started with α = 0.9. Of the ten reversals, the first two were altered in steps of 0.1, the second two in steps of 0.05, and the last six in steps of 0.025 of α. When a subject was not able to discriminate the physical electrode in the pair (α evolving to 1), the test automatically stopped after five attempts.

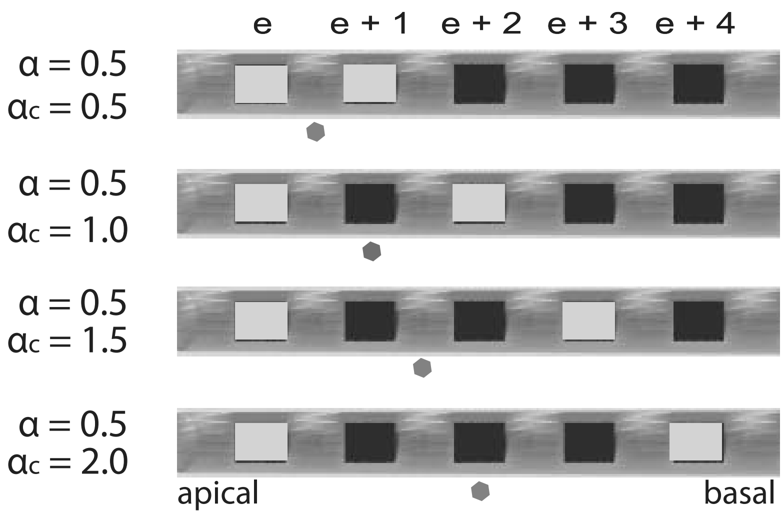

Figure 2. *Explanation of the corrected α (α_c), as defined by Equation 1. The light gray squares are the electrode contacts stimulated with current steering in the pitch discrimination experiment. The dots indicate the location associated with α = 0.5, the actual fractions of the current going to the basal contact of the spanned pair. α_c is after computing with Equation 1, expressed in electrode spacing.*

The variable α has a different basis for each spanning distance. To be able to compare the outcome of this experiment between the different spanned electrode pairs, a common scale must be used for the position between the contacts. Using electrode spacing provides this common reference. The position of $\alpha = 0.5$ for adjacent contacts will correspond to a 0.5 electrode spacing measured from the apical electrode of the pair. For $\alpha = 0.5$ with two bridged contacts, pair e+3 will correspond to a 1.5 electrode spacing. Therefore, in the data analysis, normalization was applied expressing all JNDs in terms of the so-called corrected α, α_c, defined as follows (see figure 2). :

$$\text{JND } \alpha_c = \text{JND } \alpha \times (EL_{basal}-EL_{apical}) \qquad \text{(Eq. 1)}$$

With JND α = JND for that specific electrode pair expressed in electrode spacing measured from the apical electrode of the pair, EL_{basal} = basal electrode of the current steered pair and EL_{apical} = apical electrode of the current steered pair.

Pitch matching

This pitch matching experiment was conducted to compare the pitch of a monopolar physical electrode contact with the pitch of a spanned stimulus. As described above, it is presumed that $\alpha = 0.5$ with three bridged contacts (pair e+4), will correspond to 2 electrode spacing, which is equal to the position of physical electrode e+2. Similarly, $\alpha = 0.33$ with two bridged electrode contacts (pair e+3) will correspond to 1 electrode spacing and is equal to physical electrode contact e+1. With a 2 AFC, 1-up/1-down staircase procedure, α was determined for a dual-electrode contact pair for six different pair combinations (shown in figure 3) at the AS cochlear location only. Similar loudness roving (10%) as for 'pitch discrimination' was used. The reference stimulus A was given through a monopolar physical electrode contact lying between the electrodes contacts comprising the spanning pair. The test stimulus B was a spanned signal using one of the spanning pair. In each trial, stimuli A and B were presented in random order. The subject had to determine which of the two stimuli sounded higher in pitch. The staircase procedure converged on the value of α that best matched the pitch of the reference stimulus. For the ten reversals, α was altered in steps of 0.1 during the first two, in steps of 0.05 during the second two, and in steps of 0.025 during the remaining six. The experiment started alternating with $\alpha = 0.1$ and $\alpha = 0.9$, both tested twice for all six electrode pairs presented randomly. The averaged was calculated of these four outcomes per pair.

Statistical Analysis

All data were analyzed with the SPSS 16 (Statistical Package for the Social Sciences, SPSS inc., Chicago, IL) statistic software package. For loudness balancing and pitch discrimination experiments a linear mixed model (Fitzmaurice et al. 2004b) was used. In the pitch matching experiments, the Student's t-test was used to compare the mean α with the expected α, corresponding to the intermediate physical electrode. Differences were considered significant at the 0.05 level.

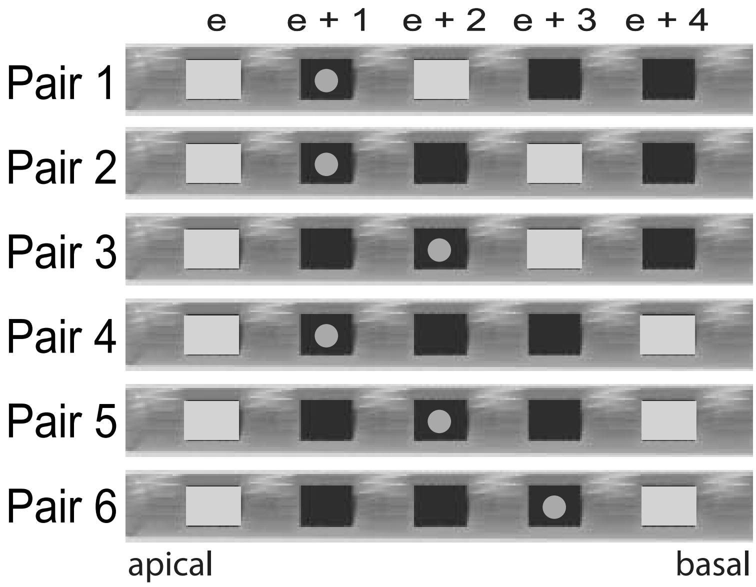

Figure 3. *Electrode pairs used in pitch matching experiments. The light grey squares are the stimulated electrodes with dual-electrode stimulation. The dots correspond to the intermediate electrode contact i.e., the physical reference contact.*

Results

Loudness balancing

The group results are shown in figure 4. Stimulation currents ($I_{MCL}(\alpha)$) are normalized such that the current needed for MCL as measured for α = 0, was set at 100%. The results are shown for both cochlear locations, AS and BS (dot and triangle resp.). There was no significant difference between apical and basal locations ($p = 0.7$). The results of the individual subjects differed substantially, which is illustrated by the large standard deviations. In general, current adjustment needed to create the same loudness for different electrode pairs, increased significantly ($p = 1.0 \times 10^{-6}$) with increasing spanning distance. The current compensation ranged from 103% (0.2 dB)

the other pairs. However, using a statistic spline model (Fitzmaurice et al. 2004a), significance could not be confirmed ($p = 0.06$) at this point. Looking at the individual results (Figure 5) several differences among the subjects are shown. First, across subjects there is an alternation between AS and BS for which required the largest amount of current adjustment. Second, a decrease in current on e+1 is

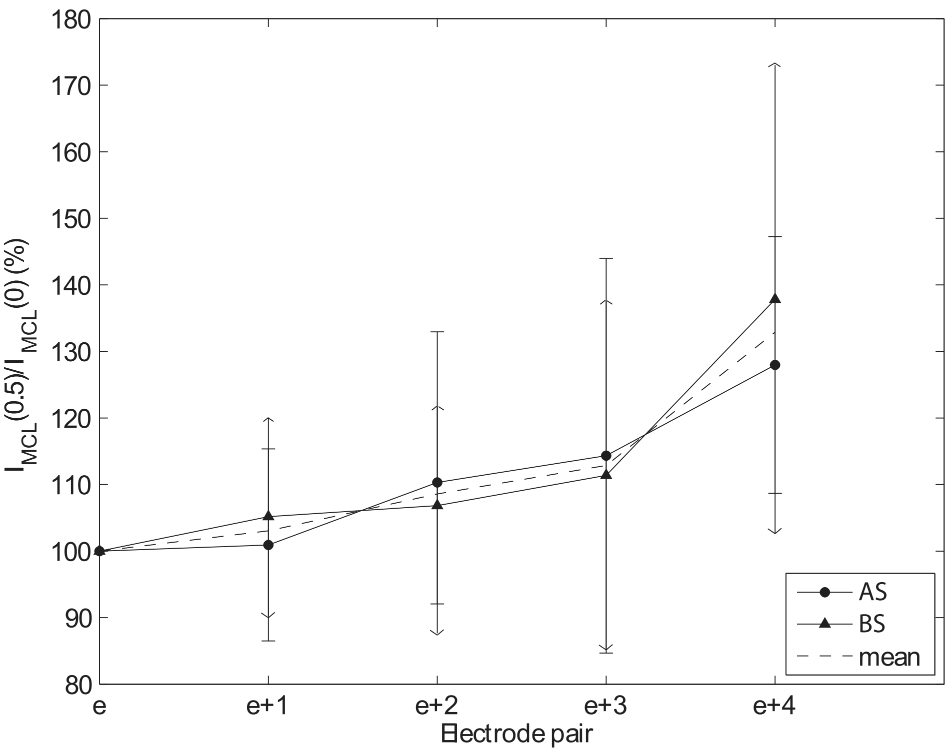

Figure 4. *Average data of the loudness balancing experiment, for AS (dot), BS (triangle) and the mean (dashed line). The current at most comfortable level (MCL) measured on e (I_{MCL} (0)) was set at 100%, the other currents (I_{MCL} (0.5)) are expressed in percentages of this value. The electrode pairs are denoted on the horizontal axis.*

shown in subjects S1-BS, S2-AS, S3-AS, S4-BS and S11-both. Some subjects (S7-BS, S10-BS and S12-AS) demonstrate an increase on e+1 and then a decrease on e+2.

Subject S5-AS, S7-AS, S8-BS and S9-BS needed less current at pair e+3. The remaining subjects illustrate a gradual increase in current over all the pairs, which is consistent with the mean shown in figure 4. An exception was subject S6, whose data deviated for both locations. No correct current could be measured for electrode pair e+4 on the BS while the AS showed a large decrease of current for pair e+4. This subject's data were excluded from further analysis, because this subject perceived two separate pitches (for pair e+2, e+3 and e+4) instead of one and was therefore, not able to complete the experiment.

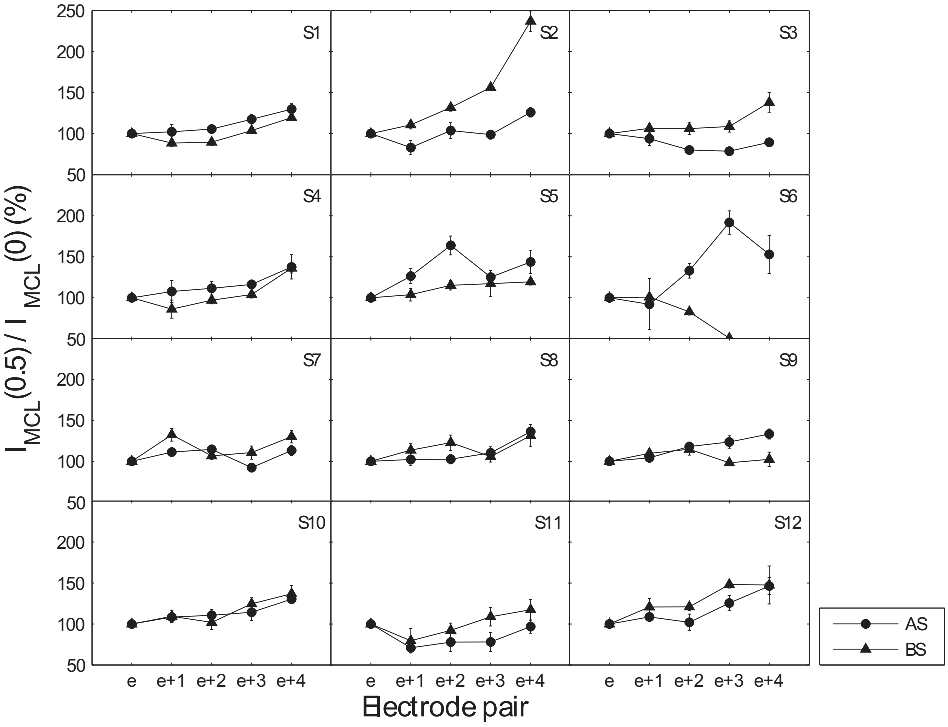

Figure 5. *Individual results for the twelve subjects (S1-12) of the loudness balancing experiments, presented in the same way as the group results in Figure 4. The dots represent the data of the AS of the array and the triangles the BS of the array.*

Pitch Discrimination

The JND for pitch, expressed in α_c, averaged over all subjects is plotted in figure 6 as a function of spanning distance. No significant difference was found between the two cochlear locations ($p = 0.6$). The average α_c for e+1 was 0.83 and for e+4 it was 1.75. This is approximately a doubling, which represents in a significant loss of intermediate pitches ($p = 3.6 \times 10^{-7}$). JND α_c increased approximately by 0.3 per contact distance (1.1 mm) spanned. Using the formula by Firszt et al (2007), $N_{channels} = 2 + (1/JND-1)$, the number of spectral channels (intermediate pitches plus the 2 electrodes) can be calculated. This results in $N_{channels} = 2.2$ for e+1, which is much lower than the results of Firszt et al. (2007) and Koch et al. (2007) (7.1 and 5.0 resp.)

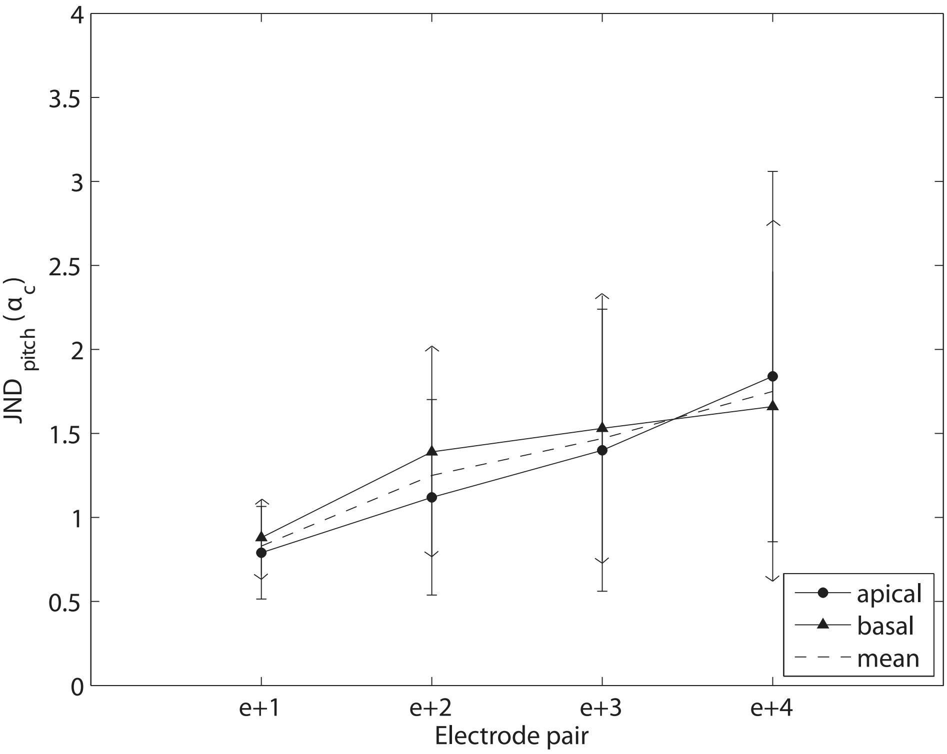

Figure 6. *Average data of the pitch discrimination experiment, for AS (dot), BS (triangle) and the mean (dashed line). The vertical axis denotes the JND of the α_c (JND_{pitch} (α_c), calculated on the basis of Equation 1, while the electrode pairs are denoted on the horizontal axis.*

Four of the twelve subjects (S4, S7, S9 and S12) were not able to distinguish between two adjacent electrode contacts (pair e+1). In that situation the test aborted at α = 1.0. The JND α expressed in electrode spacing could therefore, be higher, which might influence statistics and could lead to a decrease in intermediate pitches. However, when leaving pair e+1 out the linear mixed model, the loss of intermediate pitches is still significant ($p = 0.002$).

The individual pitch discrimination data are shown in figure 7, demonstrating large inter-individual variability. For a number of subjects, the just noticeable pitch difference could be maintained with increasing spanning distance (e.g. S1-BS, S3-AS, S5-BS, S10-AS, S11- and S12-AS), for others (S1-AS, S2, S3-BS, S4, S5-AS, S6, S7, S8 and S9) the JND increases significantly with increasing spanning distance.

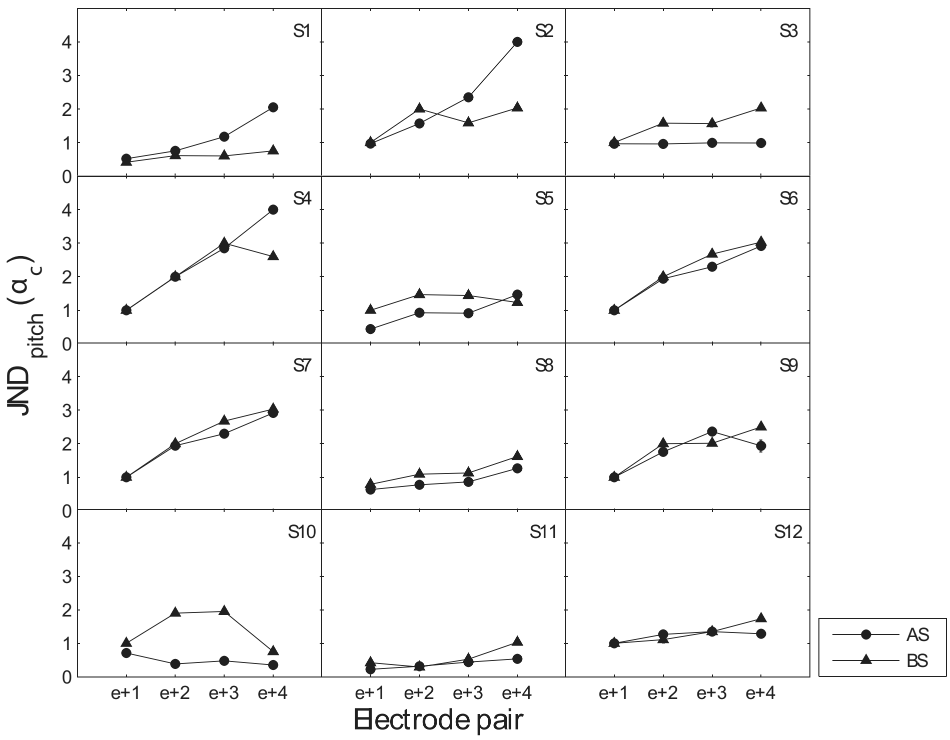

Figure 7. *Individual results for the twelve subjects (S1-12) of the pith discrimination experiments, for AS (dot) and BS (triangle), presented in the same way as Figure 6.*

Pitch matching

In figure 8 the average α per electrode pair (the triangle) is shown. The horizontal solid bars represent the physical contacts used in the spanning pair and the arrow is pointing to a filled square at the place of the theoretically expected value of α. The individual data are presented with light gray dots. These dots represent the average of the four measurements per subject, two times started at 0.1 and two times at 0.9. The standard deviation for these data points varied, with an average of 11.7. There was a significant difference between the data obtained with starting point α = 0.1 or α = 0.9 (p = 0.005). The data from α = 0.1 was mostly indicated

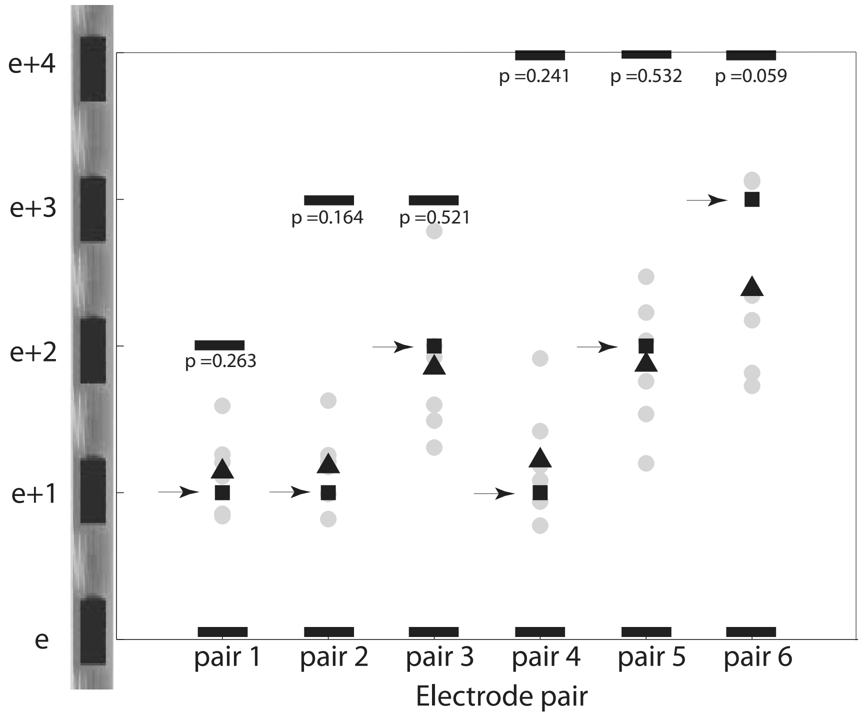

Figure 8. *Average and individual data of pitch matching at AS for six different electrode pairs (horizontal axis). On the vertical axis the position along the electrode array is plotted. The thick horizontal bars represent the places of the spanned electrode pair on the electrode array. The squares marked by an arrow represent the physical reference contacts, the triangles represent the average αs. The light gray dots represent the individual data. The p-values (Student's t-test with null-hypothesis that the triangles and the squares have the same position on the graph) are shown under the horizontal bars for each electrode pair.*

lower than expected and the data from α = 0.9 higher than expected (Carlyon, reference note 6). The average per electrode pair shows no significant difference between the place of the spanned signal and the physical electrode both expressed in electrode spacing, although pair 6 seems lower.

Discussion

Loudness balancing

Our results show a consistent pattern. At larger spanning distances simultaneous dual electrode stimulation is still possible, but precision in addressing the auditory nerve is reduced. For example, for the reference situation of current steering on adjacent electrodes our finding that no current compensation was needed to maintain equal loudness is consistent with the literature (Donaldson et al. 2005; Frijns et al. 2008; Frijns et al. 2009).Gradually, with increasing distance, an approximately linear current adjustment (0.52 dB/mm) is required to maintain loudness.

In a recent study Frijns *et al.* (2009) demonstrated that sequential dual electrode stimulation requires current correction to maintain constant loudness with varying α on adjacent electrodes. On the basis of computational modelling they inferred, that in sequential dual electrode stimulation, current compensation serves to fuse two separate excitation areas to a single one. They also concluded that simultaneous current steering between adjacent contacts provides a single area of excitation. The fact that current compensation is also needed with simultaneous spanning is an indication that with increasing electrode separations the electrical field summation reduces and that two separate excitation areas exist around each electrode contact of the pair.

To illustrate this reasoning further, figure 9 shows intra cochlear potentials for a subject (not from this study) in our centre, measured with the EFIM (Electrical Field Imaging Method) research tool (Advanced Bionics, Niel, Belgium). These electrical potentials are measured along the electrode array, and therefore are only an approximation of the electrical potentials at the location of the auditory nerve. However, this approximation is good enough to illustrate the effect of increasing spanning distance. The thin grey lines denote the potentials applied by the individual electrode contacts. The dotted horizontal line denotes the hypothetical threshold of neural excitation. Nerve fibres in the zone with a potential above this threshold are assumed to react to electrical stimulation, while those below this

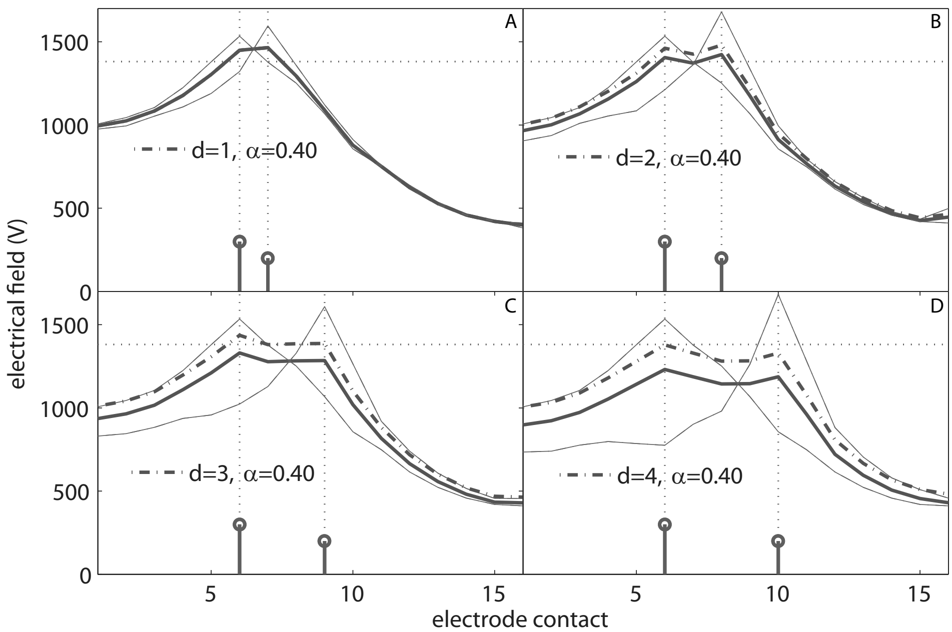

Figure 9. *Intracochlear potentials with a spanned field for a coefficient α = 0.4 and four inter-electrode distances (1.1 (A) – 4.4 mm (D)). The thin grey lines denote the potentials generated by the individual electrode contacts, as measured with Electrical Field Imaging in a patient for a HiRes90K implant with HiFocus1j electrode array. The dotted horizontal lines denote a hypothetical threshold of neural excitation. The thick line denotes the situation when no current compensation is applied. The dash-dot line denotes the situation with the addition of 4% extra current per additional contact distance spanned.*

threshold would not respond. When dual electrode stimulation is applied without current compensation, the summed field (in bold) is created. The figure shows the spanned field for a coefficient α = 0.4 and four inter-electrode separations (1.1 (A) – 4.4 mm (D)). The graphs differ in height and width; these differences are the consequence of the conductance change of the surrounding tissue as can be clinically found in patients. For increasing spanning distance essentially two phenomena are observed: (1) the peak of the spanned field decreases leading to perceivable loudness effects (cf. Figure 4) – the stimulation level potentially becoming sub-threshold (panels C and D) and (2) the width of the electrical field broadens. The dash-dot line denotes the situation with 4% additional current per additional (1.1 mm) electrode distance. This compensation current, intended to ensure constant loudness of the percept, elevates the potential over a broader region and thus adds fibres to the zone with assumed electrical stimulation, thereby fusing the regions of excitation around each electrode contact.

Pitch discrimination

In the present study the number of intermediate pitches observed for spanning is reduced by approximately 0.3 per electrode contact distance (1.1 mm) spanned. The widening of the spanned electrical field is assumed to be the root cause for this gradual loss of pitch discrimination observed with increasing spanning distance. Nevertheless, in the present paper current steering on adjacent electrodes also had a low number of intermediate pitches in comparison with previous research (2.2 vs. 7.1 and 5.0) (Firszt et al. 2007; Koch et al. 2007). Although the experimental setup was comparable with these earlier two studies, some minor differences can be listed, which are not likely the cause of the differences in outcome. First, the difference in electrode selection (same position in the cochlea vs. same contact number) might influence the number of spectral channels. Secondly, our definition of α is different. In the above- mentioned studies, $\alpha = 0$ accounts for all current on the basal electrode, where $\alpha = 0$ in this study indicates the apical contact (in line with the definition used by Donaldson et al. (2005)). Thirdly, the experimental set-up differed i.e., a 3AFC 1up/2down procedure in this study, versus a 2AFC 1up/3down in the previous ones. Fourthly, our experiment included loudness roving, while previous experiments did not. Considering these four items, the last item seems the most plausible cause of the difference between the studies. In the present study a considerable variation in performance existed among the subjects. Other studies in our clinic with good performers showed similar results to Firszt et al (2007) and Koch et al (2007). In line with this observation, also the good performers in the present study also tended to have a smaller JND α than the

poorer ones. The subjects (S1, S5, S7, S8, S11 and S12) with a speech perception score > 75%, had a significantly ($p = 0.017$) lower JND α (0.70) than the subjects with a speech perception score < 75% (0.97).

Furthermore, not every subject was able to discriminate between the pitches of two adjacent physical electrode contacts, which is consistent with previous research (Donaldson et al. 2005; Firszt et al. 2007; Koch et al. 2007). Some subjects in our study were not even able to discriminate between contacts several millimetres apart. In theory, this leads to fewer spectral channels than physical electrode contacts. Consequently, the number of spectral channels as described in the studies of Firszt *et al.* (2007) and Koch *et al.* (2007) may be overestimated for subjects, who were not able to discriminate between two adjacent electrode contacts.

The pitch discrimination performance measured for adjacent contact current steering and spanning varies widely among subjects. Some of the inter subject variability is likely due to differences in the intra cochlear electrical fields electrode placement and neural survival. Therefore, it would be interesting to investigate whether these or other parameters are able to predict the JND of α.

Pitch matching

In the present study we used pitch matching between a spanned pair and intermediate physical electrode contact to assess the relationship between the pitch and α. We expected, e.g., that the pitch of monopolar coupled electrode contact e+2 would be the same as that for α=0.5 in pair 5 (spanned pair e+4). This expectation was confirmed. None of the electrode contact pairs showed a significant difference between the place pitch of the physical electrode and the pitch of the corresponding spanned stimulus. Based on this result, spanning is believed suitable for replacing a defective electrode contact with a comparable signal. Saoji et al. (2009) also compared a spanned signal with an intermediate physical electrode, but used spread of excitation instead of a psychophysical experiment. Their outcome was not expressed in electrode place on the electrode array. They also concluded that the centre of gravity was comparable for a spanned signal and the signal of a physical electrode contact.

Although the average data were not significantly different, the individual data were not close to the expected value for every subject (figure 8). The exact stimulation site between the two electrode contacts could be influenced by the asymmetry of the electrical fields due to the tapering of the cochlea. Also, the shape of the cochlea, the arrangement of the nerve fibers (Sridhar et al. 2006), or the survival of the nerve fibers could influence outcome (Briaire and Frijns 2006), since they can differ between subjects. Which of these factors is of greatest influence on the variance between the subjects is not clear? This will be examined in the near future in our computer model of the cochlea (cf. Frijns et al. 2009). If it turns out that the shape of the cochlea has any systematic influence, it must also be taken into account in the clinical setting, when determining the number of intermediate pitches to be incorporated in future current steering based speech processing strategies. In our opinion, such an approach is likely to be an improvement over the method that is currently used in the HiRes 120 strategy.

Electrode location

All experiments were performed at two different locations on the electrode array viz., a basal- and an apical site (at 180° and 360° from the round window, respectively). In contrast with previous research (Firszt et al. 2007; Koch et al. 2007), for current steering between adjacent electrode contacts we found no significant difference in the number of intermediate pitches between basal and apical sites. An explanation for this dissimilarity could be the difference in the way electrodes were selected (same position in the cochlea vs. same contact number). In the present study, the number of the reference apical contact (e) varied between 1 and 6. Similarly, a range of between 8 and 12 was used for the basal contact (Table 1). These selections were required to compensate for anatomical and surgical variability. Electrode selection based upon location in the cochlea, on the basis of a CT-scan, is a reliable and standardized method. We prefer this approach since it allows comparison of comparable parts of cochleae across subjects.

General conclusion

Our results indicate that with current steering spanning is possible at larger electrode contact separations. With increasing electrode spanning distance, more current compensation is needed to maintain equal loudness. Moreover, a gradual deterioration in the JND for α_c is observed, which implies that the total number of intermediate pitches decreases when increasing the spanning distance. Nevertheless, spanning provides a potential opportunity to fill in gaps in the tonotopic map for subjects with defective electrode contacts. This is likely a better solution than skipping regions of the cochlea. In that respect, the spanning results are promising and therefore, spanning should be implemented in future speech coding strategies.

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Chapter 5

Threshold levels of dual electrode stimulation in cochlear implants

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Abstract

Simultaneous stimulation on two contacts (current steering) creates intermediate pitches between the physical contacts in cochlear implants. All recent studies on current steering have focused on Most Comfortable Loudness levels and not at low stimulation levels. This study investigates the efficacy of dual electrode stimulation at lower levels, thereby focusing on the requirements to correct for threshold variations.

With a current steered signal, Threshold Levels were determined on 4 different electrode pairs for 7 different current steering coefficients (α). This was done psychophysically in twelve postlingually deafened cochlear implant (HiRes90K, HiFocus1J) users and, in a computer model, which made use of three different neural morphologies.

The analysis on the psychophysical data taking all subjects into account showed that in all conditions there was no significant difference between the Threshold Level of the physical contacts and the intermediate created percepts, eliminating the need for current corrections at these very low levels. The model data showed unexpected drops in threshold in the middle of the two physical contacts (both contacts equal current). Results consistent with this prediction were obtained for a subset of 5 subjects for the apical pair with wider spacing (2.2 mm). Further analysis showed that this decrease was only observed in subjects with a long duration of deafness.

For current steering on adjacent contacts the results from the psychophysical experiments were in line with the results from computational modelling. However, the dip in the threshold profile could only be replicated in the computational model with surviving peripheral processes without an unmyelinated terminal. On the basis of this result, we put forward that the majority of the surviving spiral ganglion cells in the cochlea in humans with a long duration of deafness still retain peripheral processes, but have lost their unmyelinated terminals.

Introduction

Cochlear implants (CIs) are widely used as treatment for profoundly hearing impaired children and adults. The main goal of a CI is to recover a perception of sound and, in particular, speech information. However, implanted adults and children are still experiencing problems in challenging listening situations, such as background noise or listening to music. One reason for this might be reduced spectral resolution caused by the limited number of physical electrodes in the array (Brendel et al. 2009; Hughes and Goulson 2011). Dual electrode stimulation (DES), either simultaneous (Donaldson et al. 2005; Townshend et al. 1987) or sequential (Kwon and van den Honert 2006; McDermott and McKay 1994), has been proposed as a method to increase the number of perceivable pitches with CIs. In simultaneous DES (also called current steering), the summation of two electrical fields produces excitation of nerve fibers intermediate to the stimulated contacts. Therefore it can lead to generation of additional pitch percepts beyond those generated by stimulation of a single contact. The percept is controlled by a current steering coefficient α. This coefficient is defined as the fraction of the total current delivered through the more basal contact of the pair. Therefore, α = 0 denotes stimulation of the apical contact only and α = 1 pure stimulation of the basal one. The number of intermediate percepts thus created along the whole array varies among CII/HiRes 90K implant users (ranging from 8 – 466 percepts) and between studies (the average ranging from 20-93 percepts) (Firszt et al. 2007; Koch et al. 2007; Snel-Bongers et al. 2012).

The perceived pitch depends on the neural excitation pattern induced by the DES. Frijns et al. (2009b) examined the neural excitation pattern for both simultaneous and sequential DES, both psychophysically and using computational modeling. For current levels close to Most Comfortable Loudness level (MCL), they found that the excitation area moves smoothly between the contacts as a function of α producing an almost constant loudness (Figure 1C and D). However, the computational model also showed that, in some situations, there was discontinuous stimulation for the different α-values, especially at the lowest stimulation levels (Figure 1A and B). Similar effects were found while evaluating DES in animals using neural recordings (Bonham and Litvak 2008). Consequently, the centre of excitation jumped from one electrode contact region to the other. Both our model and the physiological studies suggest that at a constant stimulation level the number of activated neurons changes for different α-values. To stimulate at Threshold Level (TL) for various α-values then requires a current level correction during DES.

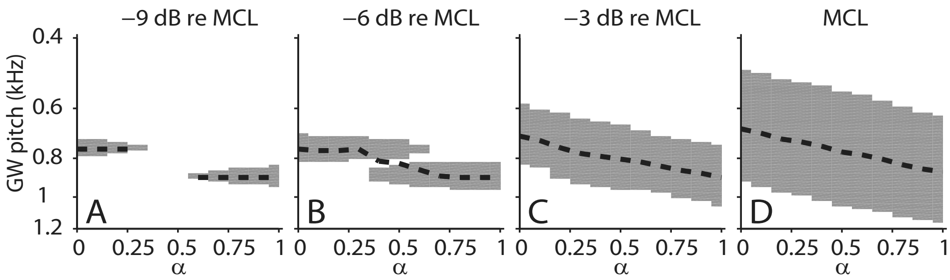

Figure 1. *Current steering plots for AS contacts in a HiFocus 1 electrode (outer wall position) calculated by Frijns et al. (2009b). The nerve fibers exhibit a peripheral process without an unmyelinated terminal (UT). The ordinate axis denotes the associated place pitch of the fibers according to the Greenwood (GW) map. The excitation area is shaded grey and its center is indicated by a dashed line. Panes from left to right show results for stimulation levels from near threshold (-9 dB re MCL) to MCL.*

The human cochlea model developed at Leiden University Medical Center has been used to evaluate effects of intra-cochlear position (Frijns et al. 2001), neural degeneration (Briaire and Frijns 2006) and effects of multipolar stimulation (Frijns et al. 2011) on thresholds and spread of excitation. The realistic tapering structure of the cochlear model allows for the evaluation of excitation differences between the base and the apex of the cochlea. In the model, TL has been shown to depend on variables such as the position of the electrode contacts in the scala tympani (i.e. lateral or peri-modiolar positions) and the presence or degeneration of the peripheral axonal processes. The model consists of two parts, a volume conduction part simulating the current flow through an implanted cochlea and a neural part simulating the response of the nerve fibers (Briaire and Frijns 2000; Briaire and Frijns 2005; Briaire and Frijns 2006; Frijns et al. 2001; Frijns et al. 2009a; Frijns et al. 2009b). In the present study this model will be used to evaluate the behavior of the threshold under different current steering conditions.

All recent studies on current steering have focused on MCL level and not on TL. When current steering is used in speech coding strategies, it is of interest to know what happens at TL. Firstly, because sounds are presented at levels ranging from threshold to MCL level and not only at MCL level. If large corrections were needed then if, for example, one bit of the frequency spectrum were dominated by a component whose frequency caused it to be sent entirely to one electrode, and another region had a frequency content that led to current sharing, this could distort the representation of the frequency spectrum. In addition, TL is part of the clinical fitting procedure. At MCL, a current correction is needed to maintain constant loudness for non-simultaneous DES on adjacent electrodes, while it is not for most simultaneous DES (Donaldson et al. 2005; Frijns et al. 2009b; Snel-Bongers et al. 2011; Snel-Bongers et al. 2012). Based on the findings with our computational model described above (Figure 1A, 1B), it was hypothesized that such a current correction is also needed when current steering is employed close to TL. This was evaluated in the present study by computational modeling and with a psychophysical experiment. Experiments were conducted at two locations along the cochlea (apical and basal), for two adjacent contacts and for two non-adjacent contacts with one electrode in between (Snel-Bongers et al. 2011).

Method

Subjects

12 postlingually deafened adults implanted at LUMC in 2007 with a HiRes 90K HiFocus-1J^{TM} cochlear implant (Advanced Bionics, Sylmar, CA) took part. All subjects had at least one year experience with their implant and a phoneme score of at least 70%, measured at 65 dB SPL with the standard Dutch monosyllabic word speech test (Bosman and Smoorenburg 1995). Specific subject information is provided in Table 1. The study was approved by the Leiden University Medical Center Ethics Committee under number P02.106.L. Written informed consent was obtained from the participants.

Assessment of electrode position

The position of the electrode array and, thereby, the electrode contacts, was determined from post-operative CT-scans which are a routine part of the clinical CI program. To measure the exact position of the electrode contacts, a multiplanar reconstruction (MPR) was made (Verbist et al. 2005). A system of coordinates, according to an international consensus (Verbist et al. 2010), was entered in the postoperative MPR, using a custom Matlab application (MathWorks, Natick, MA) as described in a previous paper (Snel-Bongers et al. 2011). All electrode contacts were marked by an experienced physician. In line with the consensus, the angles used in this study were calculated with the round window as the 0º reference.

Table 1. *Subject demographics.*

	Gender	Age (years)	Aetiology	Duration of deafness (years)	CI side	CI usage (months)	CVC Ph%	Electrodes tested	
								180^o	360^o
S1	Male	64	Otosclerosis	23	right	23	89	11	4
S2	Female	69	Meningitis	36	right	52	81	11	5
S3	Male	60	Medication	4	left	52	92	13	6
S4	Female	57	Unknown	27	right	44	83	11	3
S5	Female	58	Unknown	42	right	33	87	9	2
S6	Female	77	M. Meniére	12	right	52	72	11	5
S7	Male	55	loudness	4	right	61	84	13	6
S8	Female	44	Unknown	36	right	20	92	11	5
S9	Male	71	Familiar progressive	26	left	29	84	11	4
S10	Male	50	Otosclerosis	6	left	38	96	12	4
S11	Female	72	Familiar progressive	30	right	37	86	11	4
S12	Male	53	Unknown	43	left	32	89	9	2
Average		61		24		39	86		

Speech perception scores are given as percentage phonemes correct (Ph%) in phonetically balanced monosyllabic (CVC) words.

For each subject the electrode contact closest to 360º (apical site, AS) and the one closest to 180º (basal site, BS) were selected on the electrode array (Table 1). Current steering was applied between the contact at the reference angles e (360º and 180º), and the two contacts in the basal direction (e+1 and e+2), creating two pairs with a spacing of one and two contacts (1.1 mm and 2.2 mm) respectively. Throughout this paper the pairs consisting of electrode contacts (e and e+1) and (e and e+2), will be referred to as 'pair e+1' and 'pair e+2' respectively.

The CT-scan was further used to determine the distance from the electrode contacts to the medial wall of the cochlea. After locating each electrode contact individually, a line was generated from the contact to the center of the modiolus. After identifying the location of the medial wall, the distance was calculated along this line (Snel-Bongers et al. 2012).

Computer model

For the modeling part of this study, a computational model of the implanted human cochlea, which has been developed over the years at Leiden University Medical Center, was used (Briaire and Frijns 2005; Frijns et al. 2001; Frijns et al. 2011; Frijns et al. 2009a). The first part of the model consists of a volume-conduction model that calculates electrical potentials at the auditory nerve fibers located in a realistic three-dimensional representation of a human cochlea implanted with a geometrically accurate representation of the HiFocus electrode array (Advanced Bionics, Sylmar, CA, USA). Secondly, an active nerve fiber model simulates neural responses to specific stimulation patterns produced by the cochlear implant, using the calculated potentials at the location of the nodes of Ranvier of the primary auditory nerve fibers. Neural excitation profiles were generated at the same electrode locations and with the same stimulus configurations as investigated in the subject group, except that the current steering parameter (α) ranged from 0 to 1 in increments of 0.1. Three sets of 320 nerve fibers with different stages of degeneration were created, based on the morphology with an unmyelinated cell body as described in Briaire and Frijns (2005). The first set contained intact neurons with an unmyelinated terminal (UT) added at the tip of the peripheral process (Figure 2). Based on earlier research the length of this UT was set to 10 μm (Liberman and Oliver 1984; Parkins and Colombo 1987). Previous research (Kujawa and Liberman 2009; Lin et al. 2011) demonstrated that the UT is the first part that degenerates after acoustic overexposure with moderate hearing loss as a consequence. The second set therefore, simulates an initial stage of degeneration with peripheral processes, but now without an UT, replacing it by a 1 μm node. The third set consisted of neurons in a further stage of degeneration, without peripheral processes but with their cell bodies and central axons still intact (Briaire and Frijns 2006). The undegenerated peripheral processes followed non-radial trajectories based on data from Stakhovskaya et al. (2007) as described in Frijns et al. (2009b).

From the excitation profiles it was possible to determine how the width of the excitation area depends on the stimulus level. This excitation width is expressed as the length spanned by the tips of the peripheral processes, in other words, the equivalent length along the basilar membrane that corresponds to the neural activation. Based on this loudness definition equivalent loudness was considered to be the equivalent width of excitation in mm along the basilar membrane. Current levels were determined for total basilar membrane excitation lengths ranging from 0 mm (i.e. absolute threshold) to 4 mm. The value of 4 mm excitation was

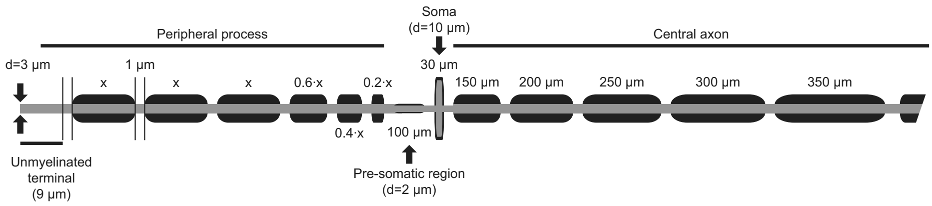

Figure 2. *Representation of the nerve fiber morphology. The peripheral process consists of six scalable segments to adjust for the variable length from the organ of Corti to the cell body, with the unmyelinated terminal (UT) at the end.*

considered to correspond to maximum comfortable loudness (Briaire and Frijns 2006). Throughout the manuscript two definitions for TL were defined: the minimum amount of current needed to excite at least one fiber ("0 mm width") (Briaire and Frijns 2006) called 1st fiber threshold (TL_{0mm}) and a model equivalent of the perceptual threshold (TL_{1mm}) where 1 mm of the length along the basilar membrane is excited.

Psychophysical experiment

The main outcome for this experiment was the TL_{Φ}, when the signal was just heard, at various values of the current steering coefficient α. The experiment was performed using the Bionic Ear Data Collection System (BEDCS, Advanced Bionics, USA) for the stimulation configuration and using the PsychoACoustic Test Suite (PACTS, Advanced Bionics, Belgium) for the psychoacoustic tests. Stimuli were 300 ms bursts of symmetric biphasic pulses with phase duration of 32 µs and 1400 pulses per second. The inter-stimulus interval was 500 msec. Dual electrode stimuli were always simultaneous.

Rough TLs and most comfortable loudness levels were first determined for each of the six pre-selected electrode contacts individually. The subject was asked to indicate when the signal was just heard (rough TL) and also when the signal sounded most comfortably loud (MCL).

A single run of a 2-Alternative-Forced-Choice, 1-up/2-down adaptive procedure was used to determine TL_{Φ} (Levitt 1971) for each α = 0, 0.17, 0.33, 0.50, 0.67, 0.83, or 1 for all four electrode pairs. The target stimulus consisted of a dual-electrode stimulus at a current level between MCL and TL. The reference stimulus was 0 mA. Within each trial, the two stimuli were presented in a random order. The subject was required to select the stimulus that generated a sound percept. A response was considered to be correct when the subject chose the target stimulus. The current level of the target stimulus was decreased until the subject chose the wrong interval because no sound was heard for either stimulus. The procedure covered ten reversals (i.e. changes in the direction of the signal level), where the test outcome was calculated over the last six reversals. The current level was altered in steps of 15% increments or decrements for the first four reversals and in steps of 7% for the remaining six. If a downward or upward trend was detected over the last six reversal points by the program (PACTS), determined using an algebraic algorithm (website, 2009), then the test was extended, assuming that either the adaptive procedure had not yet converged to the subject’s discrimination limit or that the measurement was unreliable due to the behavioral status of the subject, for example loss of attention (Snel-Bongers et al. 2011).

To correct for the variation in the absolute thresholds between all subjects and the four stimulated positions, the data were normalized. TL for each α was normalized on both ends ($\alpha = 0$ (TL_0) and $\alpha = 1$ (TL_1)) with linear interpolation in between, using the following formula:

$$TL_{normalized} = TL_{\alpha} / (TL_0 + \alpha\,(TL_1 - TL_0)) \qquad \text{(Eq.1)},$$

where TL_{α} is the TL for that specific α ($0 \leq \alpha \leq 1$).

As a consequence, all threshold corrections are calculated relative to $TL_{normalized}$, and do not reflect the absolute current level.

Statistical analysis

For the threshold detection experiments a linear mixed model analysis (Fitzmaurice et al. 2004) was performed on the normalized data. A linear mixed model can take several data points from one subject into account, and gives an overview of the interaction of all these data with the main values, the comparison of all data with one data point and corrects for the individual subject (Snel-Bongers et al. 2012). Further, the linear mixed model corrects for missing data. A Bonferroni correction was applied to all statistical tests, to correct for the fact that (up to five) different tests were performed on the same data, resulting in a significance criterion of $p<0.01$.

All data were analyzed using the SPSS 17 (Statistical Package for the Social Sciences, SPSS inc., Chicago, IL) statistics software package.

Results

Electrode position

The mean location of the apical and basal electrode sites, measured from the round window, was at 364° (±11°) and 180° (±7°) respectively. The apical electrode contacts were significantly closer ($p = 0.026$) to the medial wall (1.19 mm +/- 0.11) than the basal contacts (1.33 mm +/- 0.12).

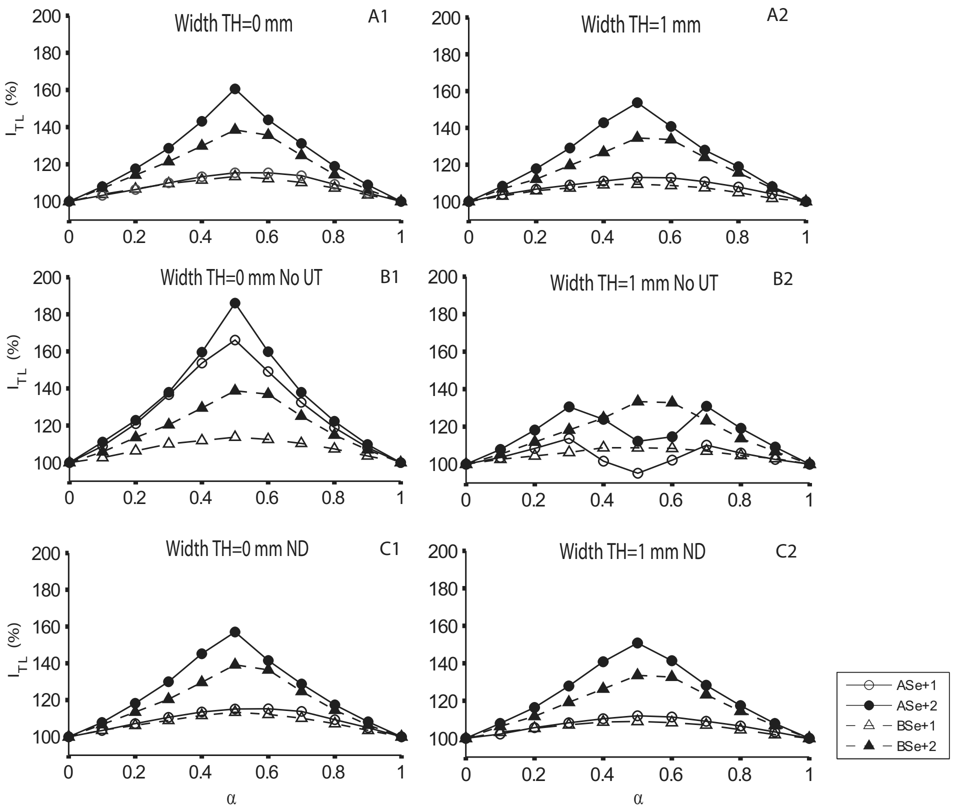

Figure 3. *Computational modeling results of the loudness balancing experiment for the model with a peripheral process with an UT (A), a peripheral process without UT (B) and without peripheral processes (C). The circles represent the data at the AS of the array and the triangles data at the BS of the array, where the open symbols are pair e+1 and the filled symbols pair e+2. The data was normalized on both ends ($\alpha = 0$ and $\alpha = 1$) (eq. 1) and the other currents (I_{TL}) are expressed in percentages of this values. Panes on the left show results for excitation lengths of 0 mm and of 1 mm on the right.*

Computer model

Figure 3 shows normalized current levels needed to achieve 0 mm (TL_{0mm}), and 1 mm (TL_{1mm}) excitation along the basilar membrane in a cochlear model with either intact neurons (SG cells with a peripheral process) with an UT (3A), without an UT (3B, No UT) and a degenerated peripheral process (3C, DPP), for current steered and spanning pairs (e+1: open vs. e+2: filled symbols) at AS and BS (AS: triangles vs. BS: circles). Generally speaking, the e+1 pair needs less current correction than the e+2 pair and the apical pair needs more current correction than the basal pair, regardless of the threshold criterion. Further, more current correction is needed in the fiber model without UT in comparison with the other two fiber degeneration states.

In Figure 3B1, it is visible that apically more current correction is needed to reach TL_{0mm} than basally. The curve for e+1 at BS is almost flat, while the others peak more or less around α = 0.5. The basal electrodes have the same pattern for the TL_{1mm} condition (Figure 3B2). However, for the apical sites current levels for 1.0 mm show a clear dip of 60% relative to the TL_{0mm} condition. Interestingly, in the case of the dip, the calculated excitation profiles showed that initial excitation takes place at the peripheral processes, while it occurs in the central axons in most other cases.

This reduced TL around α = 0.5 can also be seen in Figure 1, which was generated with nerve fibers with peripheral processes, but without an UT. From Figure 1A (for stimuli 9 dB below MCL) it is clear there is a dependence of the number of excited fibers on α, even resulting in an absence of excited fibers at the center (α= 0.5). This indicates that the current level needs to be varied (increased) as a function of α if a constant number of excited fibers has to be maintained regardless of α. In figure 1B the situation for a 3 dB higher current level is shown. The center of the excitation now consists of two regions (one around each individual contact). For α = 0.5, both regions co-exist and lead to a higher number of excited nerve fibers (i.e., increased loudness with the same amount of current). As a result, the current to maintain constant loudness over the whole range of α from 0 to 1 shows a minimum at α=0.5.

Figure 3A and 3C show the plots for the other two neural conditions (with UT and without peripheral process, respectively). These plots are not essentially different for the basal pairs. For the apical pairs however for TL_{0mm}, particularly pair e+1, less current correction is needed to reach TL (Figure 3A1 and 3C1) in comparison with the graphs in Figure 3B1. Contrary to Figure 3B2, Figure 3A2 and Figure 3C2 do not show a dip for apical electrode pairs.

For both cases (Figure 3A and 3C), the excitation region will be a single area that shifts gradually between e and e+x. However, the excited region does decrease in size as α approaches 0.5 for low current levels. In line with this, the required stimulus levels are elevated for pair e+1by approximate 10% around α = 0.5 for both TL criteria (first fiber, or on the basis of a distinct width of the excited region). With elevation up to 65%, this effect is larger for pair e+2 than for adjacent electrode contacts.

Psychophysical results

In Figure 4, the individual psychophysical results, normalized on both the apical and basal electrode of the pair (Eq.1), are shown for the two different positions in the cochlea (AS: circles vs. BS: triangles) and both measured electrode pairs (e+1: open vs. e+2: filled symbols). The average results are shown in Figure 5. Linear mixed modeling performed on the data excluding α = 0.0 and α = 1.0 showed that there is no difference between the curves for the four electrode pairs ($F_{(221)}$= 1.822, P = 0.145). The average curves suggest (figure 5) that the pairs e+2 need on average more current,correction like in the computer model (figure 3), but the e+1 (101.29%) and e+2 (104.26%) pairs were not significantly different ($F_{(223)}$= 1.969, P = 0.144) from each other. Also the position in the cochlea had no significant ($F_{(223)}$= 1.969, P = 0.162) effect on TLs (AS: 101.35% and BS: 104.20%), which is in line with the model predictions, which use 1 mm excitation as threshold criterion. No relation was found between TL_{Φ} and the distance to the medial wall ($r^2_{(24)}$ = -0.072, P = 0.737).

Contrary to some of the model predictions, the TL_{Φ} for intermediate values of α are not significantly different ($F_{(265)}$= 0.774, P = 0.569) from the flanking electrodes (α = 0 and α = 1), as demonstrated with the linear mixed model run on all data together. In line with this result, TL_{Φ} found with α = 0.5 on both adjacent (pair e+1) (103.55% on average) and nonadjacent electrode (pair e+2) (100.88% on average) pairs were not significantly different from those of the apical contact ($t_{(22)}$= -1.380, P = 0.182 and ($t_{(23)}$= -1.132, P = 0.269, respectively).

The model outcomes, shown in Figure 3B2, exhibit a dip for α = 0.5 in TL_{1mm} at AS, which is also visible in the psychophysical results for pair e+2 at 360° (Figure 5). A standard Student's T-test showed a decrease of the TL_{Φ} of α = 0.5 (94.33 %) compared with α = 0.33 (104.03 %), but no difference with α = 0.67 (102.87 %) ($F_{(66)}$ = 1.505, P = 0.042, and 0.072 respectively). After application of the Bonferroni correction, these differences did not meet the significance criterion.

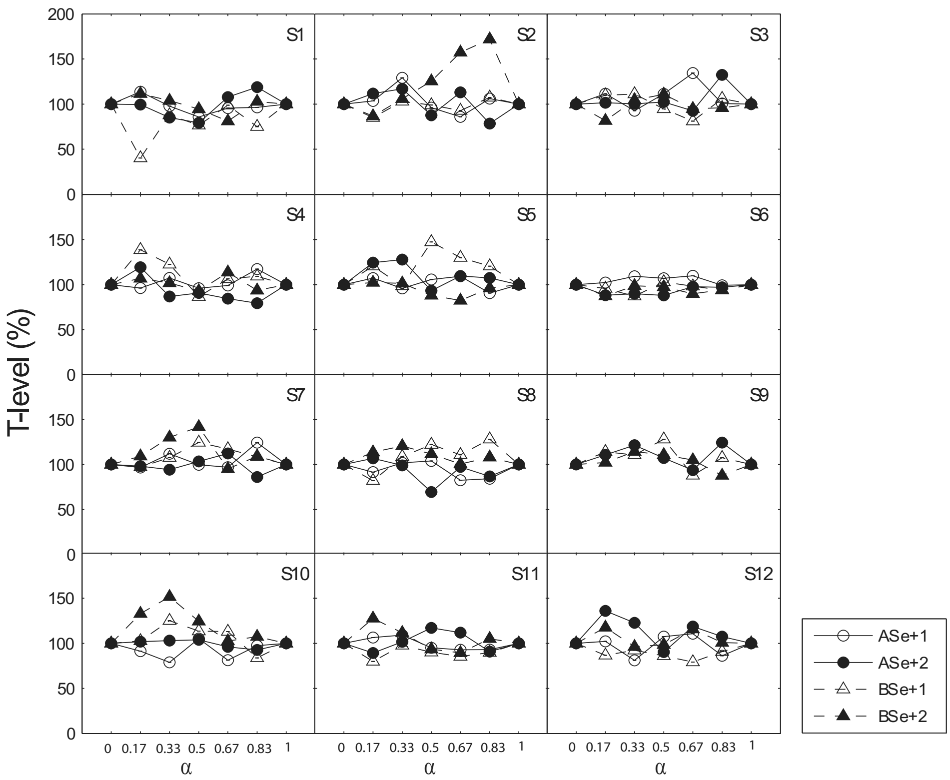

Figure 4. *Individual results for the twelve subjects (S1-12) on the loudness balancing experiment. The circles represent the data of the AS pairs and the triangles the BS pairs, where open symbols are for pair e+1 and filled symbols are for pair e+2. The data were normalized and are expressed in percentages. The different values of α are denoted on the horizontal axis.*

From Figure 4, it is clear that such a dip in AS pair e+2 (at least 10 % lower threshold values at $\alpha = 0.5$ compared to $\alpha = 0.33$ and $\alpha = 0.67$) is visible in the individual results of subjects S1, S2, S5, S8 and S12. To find out, whether these subjects share a common factor, the subjects were divided into two groups, one group with the dip (5 subjects) and a group lacking it (7 subjects). A post-hoc analysis with a standard Student's T-test was performed, using p = 0.01 as the level of significance after correcting according to Bonferroni. The average duration of deafness for the group without a dip (15.5 years) was significantly lower ($t_{(10)}$= 3.599, P = 0.005) than that for the group with a dip (36.0 years), while the parameters age at implantation, electrode distance to the medial wall and the absolute value of TL_{Φ} showed no significant difference between these groups ($t_{(10)}$= -0.956, *P* = 0.364, $t_{(10)}$= -0.778, *P* = 0.456 and $t_{(23)}$= 2.010, *P* = 0.056 respectively). This suggests that the duration of deafness is a possible predictor for the dip.

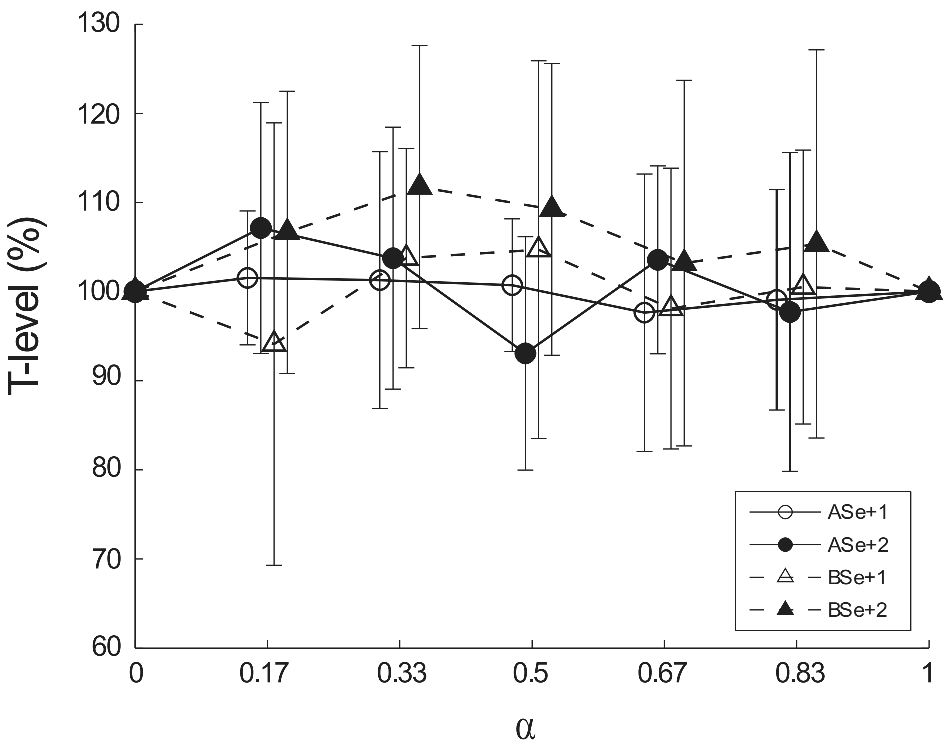

Figure 5. *The average data of the loudness balancing experiment on AS (circles) and BS (triangles) for pair e+1 (open) and pair e+2 (filled). The current was normalized on both ends, where the other percentages are calculated from Eq. 1. The symbols are plotted at staggered α-values along the x axis in order to avoid overlapping of the error bars.*

Discussion

Based on previous computational and physiological results (Bonham and Litvak 2008; Frijns et al. 2009b) it was hypothesized that current steering at TL requires a current correction in order to maintain equal loudness for all current weighting combinations between a pair of electrodes. However, TLs are not significantly influenced by the current steering coefficient, at least for adjacent and nonadjacent electrode pairs up to 2.2 mm wide. For the e+1 electrode pairs model outcomes, using TL_{1mm} as threshold criterion, were comparable to the patient data for the same condition. In the model larger distances between the contacts give rise to the need of current correction, which was not observed in the subjects.

The model showed a dip in the amount of current correction at $\alpha = 0.5$, specifically for the apical contacts, and only in the condition where the UT was degenerated but the rest of the fiber was still intact (Figure 3B2). This same effect was observed in some of the subject specific outcomes at the same location, although the effect was not large enough to reach a significant level in the whole group. With post-hoc analysis with the dip as group factor, the duration of deafness was the only parameter which showed a significant correlation with the presence of this decrease in threshold at $\alpha = 0.5$. The group with the dip had the longest mean duration of deafness (15.5 yr vs. 36.0 yr).

This observation can shed some light on the possible time course of neural degeneration in humans. The UT could be the first structure that degenerates after several years of deafness. This would imply that the majority of SG cells in subjects with a long duration of deafness still have their peripheral processes, although the UT is degenerated. In line with this hypothesis, and contrary to earlier reports (Nadol and Eddington 2006; Sly et al. 2007), Rask-Andersen et al. (2010) found that both peripheral processes and SG cells are well preserved in the apical region of the cochlea even after 28 years duration of deafness. At the same time the evidence is growing that the first part that degenerates is the UT, even before the hair cells and the nerve fiber (Kujawa and Liberman 2009; Lin et al. 2011).

As stated above, the model showed only a dip when using the fibers with intact peripheral processes without an UT, while simulations either without peripheral processes or with intact peripheral processes with UT did not exhibit such a dip. The physiological mechanism underlying this fact can be understood as follows: The UT is the unmyelinated connection between the nerve fiber and the hair cell and therefore is likely to behave as a large node of Ranvier. As a consequence, the UT is expected to possess a large electrical capacitance, which must be loaded with the intra neural potential before the fiber can fire in the peripheral process. In this case, the action potential threshold is more easily initiated in the central axon than at the peripheral process, as it must also be in cases of degeneration of the entire peripheral process. Without a UT the action potentials will be initiated in the peripheral process, as a consequence of its reduced thresholds. Additional simulations (data not shown) demonstrated that even partial preservation of peripheral processes suffices to produce this dip. The differences with respect to the location within the cochlea can be understood from the excitation site along the nerve fiber. Contacts in the more apical turns of the cochlea excite the fibers in the peripheral process, while contacts in the base directly stimulate the central axon and thus the influence of the UT is minimalized (Briaire and Frijns 2006).

It is likely, that there are other factors, like the cause of deafness, which influence the course of the degenerative process of the auditory nerve. For instance, Teufert et al. (2006) found, that subjects with idiopathic deafness had the highest residual SG cell count, while subjects with bacterial labyrinthitis had the lowest count. Unfortunately, the present group size and the known large variation in aetiology, preclude an analysis of our data along these lines.

Contrary to the model predictions, only two of the five subjects with a dip in pair AS e+2 also exhibited a dip in pair AS e+1. An explanation for this could be that the simulation conditions are extreme situations, where all the fibers exhibit the same morphological situation. The subjects probably have all three degenerative fiber conditions mixed along the cochlear partition, which may mask effects only present in one specific condition.

It is very likely that the threshold detection criterion is a patient specific parameter, which is not only determined by the situation in the cochlea (besides the number and condition of the residual nerve fibers, also tissue growth, electrode position etc.), but also by central effects. Also in the model the width and depth of the dip is influenced by the threshold criterion. As shown in Figure 3B, with TL_{0mm} the dip is completely absent, while the model predicts a much shallower dip in e+2 and an almost absent dip for e+1 if a value of 0.7mm (rather than 1mm) along the basilar membrane is used as threshold criterion (data not shown). It should be noted that the absolute value of the threshold criterion depends on the spread of excitation in the model, which, in turn, depends on various model parameters.

As stated above, both the model and the psychophysics did not show evidence for the need of current correction to maintain equal loudness for pair e+1. However, for pair e+2 the model showed a clear need for current correction at $\alpha = 0.5$, which was not seen in the psychophysical data. This discrepancy might well be caused by an underestimation of the spread of excitation (SOE) in the model. The narrower the SOE, the higher the need for current correction (Frijns et al. 2009b). The SOE in the model is not only influenced by the TL criterion (figure 3) but also by the (absence of) stochastic neural behaviour and the spatial distribution of the cell bodies in the SG.

Unfortunately, published literature cannot provide much additional evidence, as this is the first clinical study on current steering at threshold, while all other ones have been performed at MCL. Donaldson et al. (2005) showed that for most of the subjects no current correction was needed for creating the same loudness for e (monopolar stimulation) and e+1 with $\alpha = 0.5$. This finding was confirmed by a previous study from our group (Snel-Bongers et al. 2011), but it was demonstrated that higher current levels were required to reach MCL levels for e+x up to an excitation width of 4.4 mm (e+4).

We conclude that with present electrode arrays simultaneous dual electrode stimulation is possible at low current levels and that no current adjustment is necessary to compensate for loudness variations in most cases. The observations for apical contacts in patients with a long duration of deafness are consistent with the model predictions regarding loss of UTs. Therefore, we hypothesize that the majority of the surviving spiral ganglion cells in the cochlea in humans with a long duration of deafness still retain peripheral processes, but have lost their UTs.

In addition, these outcomes are consistent with the notion that psychophysical thresholds are not reached at excitation of the first fiber, but of a region of nerve fibers of approximately 1 mm along the basilar membrane.

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Chapter 6

Restoring speech perception with cochlear implants by spanning defective electrode contacts

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Abstract

Conclusion: Even with 6 defective contacts, spanning can largely restore speech perception with the HiRes120 speech processing strategy to the level supported by an intact electrode array. Moreover, the sound quality is not degraded.

Objectives: Previous studies have demonstrated reduced Speech Perception Scores (SPS) with defective contacts in HiRes120. The current study investigates whether replacing defective contacts by spanning, i.e. current steering on non-adjacent contacts, is able to restore speech recognition to the level supported by an intact electrode array.

Materials and methods: 10 adult cochlear implant recipients (HiRes90K, HiFocus1J) with experience with HiRes120 participated in this study. Three different defective electrode arrays were simulated (6 separate defective contacts, three pairs or two triplets). The participants received three take-home strategies and were asked to evaluate the sound quality in five pre-defined listening conditions. After 3 weeks, SPS were evaluated with monosyllabic words in quiet and in speech-shaped background noise.

Results: The participants rated the sound quality equal for all take-home strategies. SPS with background noise were equal for all conditions tested. SPS in quiet (85% phonemes correct on average with the full array) however, decreased significantly with increasing spanning distance with a 3% decrease for each spanned contact.

Introduction

The number of spectral channels in a cochlear implant (CI) created with the HiRes sound processing strategy (Advanced Bionics) is equal to the 16 intra cochlear electrode contacts. This number can be increased with either sequential (Kwon and van den Honert 2006; McDermott and McKay 1994) or simultaneous (Donaldson et al. 2005; Townshend et al. 1987) dual electrode stimulation. This is done in a more recent version of the HiRes speech processing strategy, HiRes120 (Brendel et al. 2008; Buchner et al. 2012; Buechner et al. 2008; Donaldson et al. 2011; Firszt et al. 2009), which makes use of simultaneous dual electrode stimulation ("current steering"). With this strategy, CI recipients are theoretically able to make use of 120 different spectral channels, which might lead to high levels of speech recognition in quiet and in noise in comparison with HiRes. Several studies (Brendel et al. 2008; Buchner et al. 2012; Buechner et al. 2008; Donaldson et al. 2011; Firszt et al. 2009) compared HiRes with HiRes120 and either found a small improvement in speech perception, no improvement or even deterioration, which differed per subject. However, sound and music quality was rated higher for HiRes120 by almost all users. In a European multi centre HiRes120 study some subjects from the study group had non-active electrodes in their programs. Their speech perception outcomes for the HiRes120 program were poorer than for the Hires program (Boermans et al. 2008; Buchner et al. 2012).

This can be explained by that fact that with the present implementation of HiRes120 the number of available channels will decrease by 16 with a single defective electrode contact, or by 8 if the missing contact is at either end of the array. When applying current steering on non-adjacent electrode contacts ("spanning") (Snel-Bongers et al. 2011a), such a defective electrode can be bridged and this decrease in number of channels can be compensated.

Unfortunately, current steering on non-adjacent electrode contacts, "spanning", has not the same qualities as current steering on adjacent electrode contacts, in terms of loudness and number of discriminable intermediate pitches. The number of intermediate pitches decreases when increasing the spanning distance (Snel-Bongers et al. 2011a). Furthermore, additional current is required to create equal loudness, when increasing the spanning distance, which shortens battery life. This could set a limit on the effectiveness of repairing defective contacts with spanning, and a degradation of speech perception might be expected when spanning is used in a speech coding strategy.

The purpose of the current study was to compare speech perception in quiet and in the presence of speech-spectrum shaped noise with HiRes120 using spanning to repair simulated defective (deactivated) electrode contacts. Each spanning program had 6 deactivated electrodes with various distributions. This is an extreme situation, as just 1% of all electrode contacts have been found to be non-functional (Hughes et al. 2004). However, the impact of a single deactivated contact was expected to be relatively small and might not be detectable with normal speech tests. Furthermore, a subjective sound quality rating was collected for each program under different listening conditions.

Material and Methods

Participants

The participants in this study were 9 postlingually deafened adults and 1 prelingually one who had been implanted with a HiRes90K device with HiFocus1J electrode array (Advanced Bionics, Sylmar, CA) at the LUMC. No complications were reported, either during surgery, or the rehabilitation program for any of the participants. All participants used a Harmony sound processor with a HiRes120 (also called Fidelity 120) speech coding strategy (pulse width and accordingly stimulation rates varied across implant recipients). The group consisted of three females and seven males, with an average age of 61 years (+/- 8). The average duration of implant use was 52 months (+/- 22).

The current study was approved by the Medical Ethical Committee of the LUMC (ref. P02.106.P). Written consent was obtained from each participant.

Speech coding strategies

Participants were tested with 5 different electrode array configurations as shown in Table 1. Strategy 1 (reference) was their current program, where the data from the clinical software Soundwave (Advanced Bionics, Sylmar, CA) was transferred and adapted to the research tool BEPSnet (Bionic Ear Program System, Advanced Bionics, Sylmar, CA). The BEPSnet research tool enabled us to program the participants' speech processors and the research processors with HiRes120 and with the spanning strategies.

Strategy 2 (reference 125% PW) is the same as strategy 1 except for the pulse width (PW), which was increased to 125% of the pulse width used in the clinical program. Such a broader pulse width requires a lower stimulating current, making it one of the methods proposed to conserve energy. A 125% PW was also used in the other three strategies, in which different configurations of six electrode contacts were switched off. Strategy 3 (singles) has six single deactivated contacts, strategy 4 (doubles) has three disabled pairs and strategy 5 (triplets) has two

Table 1. Five different electrode array configurations

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Reference strategy																
Reference 125% PW																
Singles				■		■		■		■		■		■		
Doubles			■	■				■	■				■	■		
Triplets			■	■	■							■	■	■		

■ *= non-active electrode*

groups of three neighboring contacts disabled, simulating various combinations of broken wires and short circuits. Each deactivated electrode contact was replaced by a spanned current steered signal (Snel-Bongers et al. 2011a). This resulted in 9 electrode pairs per strategy, as opposed to the 15 used in HiRes120. Like HiRes120 each analysis channel supported 8 current steered percepts, which resulted in 72 spectral channels along the array.

The ability to perceive multiple percepts using current steering is described by the Just Noticeable Difference of the corrected α (JNDα_c) (Snel-Bongers et al. 2011a) or, more grossly the associated number of discrete percepts which can be perceived along the array (Firszt et al. 2007; Koch et al. 2007). For every participant a JNDα_c was determined and the total number of discrete percepts calculated for each spanning condition

Sound quality rating

The participants made use of three speech processors during the testing period. On speech processor 1 and 2, the five different strategies were programmed in a randomized order, three strategies on processor 1 and two on processor 2. Three (the maximum capacity of the processor) of the five strategies (ref. 125% PW, singles and doubles) were programmed into speech processor 3, a research Harmony sound processor for the take home part of the study.

On the first appointment the current correction coefficient found to maintain equal loudness for spanning, found by Snel-Bongers et al. (Snel-Bongers et al. 2011a), was applied for all spanning strategies. This coefficient gives the average factor by which the total amount of current on the electrode pair has to be increased for α=0.5 to obtain a percept with equal loudness to the apical electrode. For intermediate values of α, a linear interpolation was applied.

If a participant reported poor sound quality when the different programs were evaluated, the levels of the programs were manually adjusted as is done in clinical practice.

A single blind randomized controlled trial was used to determine whether there was a difference between these strategies in home situations. The participants used speech processor 3, with strategy 2, 3 and 4. The triplets were omitted, because this represented an extreme situation and was not believed appropriate for take home use. The participants were blinded for the strategies, but the researchers were not, since the programming had to be done manually. The participants were asked to use each strategy at home in five different situations (speech understanding in silence, with background noise, with ambient sound and with multiple speakers at the same time and, listening to music), and to use each strategy for at least 1 complete day. Over a three week period the sound quality of the three strategies relative to each other was rated on a Visual Analogue Scale (VAS).

Speech perception

After three weeks the participants were seen again for their second appointment. They handed in their VAS scores of the five different situations in home situations. Further, speech perception in quiet and with background noise was investigated during this appointment, using the standard Dutch monosyllabic (CVC) word test on a Decos Audiology Workstation (Decos systems B.V., Noordwijk, the Netherlands) with speech processor 1 and 2 (all five strategies). The results are expressed as the percentage of phonemes perceived correctly. The different strategies were tested in random order, counterbalanced across participants. Four runs, each containing 11 words, for a total of 132 phonemes were administered to each participant. Words were presented in free field at 65 dB SPL. Participants were familiar with this test method, as it is used routinely in the clinical setting. The experiment started by determining the Speech Reception Threshold (SRT), the signal-to-noise ratio (SNR) at which 50% of phonemes were perceived correctly using the participant's own HiRes120 program. The signal, as well as the competing speech-spectrum-shaped background noise, was delivered from a loudspeaker placed 1 meter in front of the participant. The signal level was maintained at 65 dB SPL. The noise level was increased until the participant was able to understand around 50% of the phonemes. The SNR found was then used to test speech reception with the other strategies for this participant.

Results

Sound quality rating

The VAS ratings of the participants, obtained in the take-home period of three weeks, for the five different situations described before (silence, background noise, appreciation of music, ambient sound and, multiple speakers at the same time) are shown in Figure 1 in a box plot. The median with quartiles range is shown and the

outliers are indicated with a dot. Each situation demonstrates a large variation between subjects in sound quality score, particularly the appreciation of music and listening to multiple speakers. The group mean scores however, are not significantly different between the three strategies tested (2, 3 and 4) for any of the five situations ($p = 0.385$), as determined with a linear mixed model.

Speech perception

The box plot in Figure 2 shows the phoneme scores for the five different strategies in quiet and with speech-spectrum-shaped background noise, obtained at the second appointment. In quiet the average score is around 80%, and by intent the scores in noise at SRT are around 50% (indicated by the dashed line). As expected on the basis of Figure 2 no difference was found between group mean scores for the normal pulse width and the125% pulse width, with a Wilcoxon Signed Rank test in quiet (82.7% vs. 84.7%; $p = 0.475$) and with a paired Student's T-test at SRT noise level (47.5% vs. 47.9%; $p = 0.875$).

When using a linear mixed model, no significant difference ($p = 0.06$) was found between the speech perception scores in quiet and in noise between the strategies with the 125% pulse widths (strategy 2, 3, 4 and 5). Since there was a difference between phoneme scores in quiet and in noise, the strategies were also compared for the two situations separately. In Figure 2 a negative trend can be observed for the results in quiet; strategy 2, an intact electrode array with a pulse width of

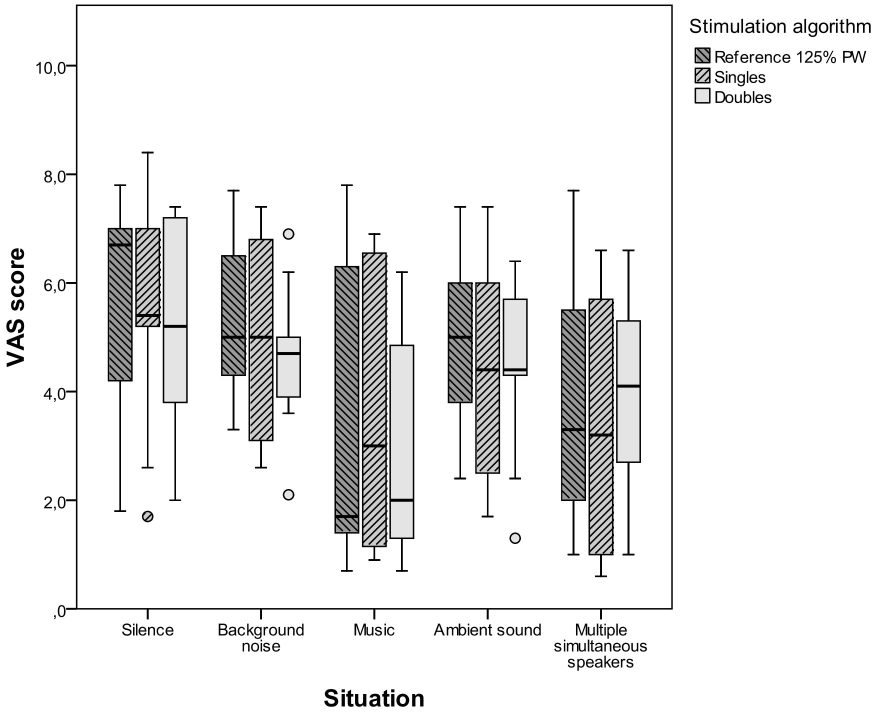

Figure 1. *The VAS-ratings (on the y axis) for the appreciation of the sound of three strategies (ref. 125% PW, Singles and Doubles) in 5 different situations (silence, background noise, appreciation of music, ambient sound and, multiple speakers at the same time) on the x-axis demonstrated with a box plot.*

125%, had a phoneme score of 84.7%, while strategy 5 (two spanned triplet gaps) had a score of 75.2%. Analyzing these data with a linear mixed model gave a significant decrease ($p < 0.001$) in speech perception with approximately 3% per extra spanned contact. No effect of the different strategies on speech perception was found when testing with speech-spectrum-shaped background noise ($p = 0.258$).

Number of discriminable percepts

On average the total number of discrete percepts found along the array for neighboring contacts, or spanning a single, double or triple contact gap was 28, 24, 22 or 17 percepts, respectively in the present study group. The number of intermediate pitches decreased significantly ($p = 0.040$) with increasing spanning distance. In a post hoc analysis with a linear mixed model, speech perceptions scores were compared with JNDα_c, in order to investigate whether JNDα_c can be used as a predictor for speech perception scores for the different spanning conditions. However no association could be demonstrated between a high JNDα_c and low speech perception score for the different spanning pairs (p = 0.789). Two of the participants showed a larger increase in JNDα_c than the rest, namely up till 2, when increasing the spanning pair's separation. Leaving these subjects out the analysis of speech perception did not change the outcome of this analysis.

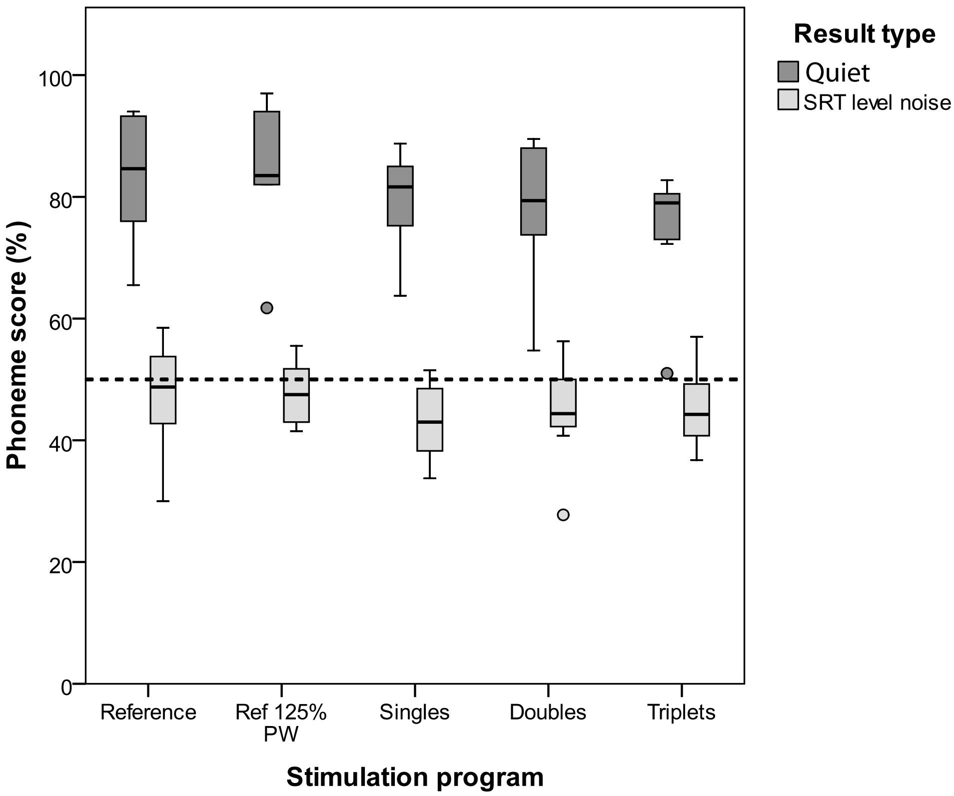

Figure 2. *Box plot of the speech perception data in quiet (dark grey) and with SRT level noise (light grey). The strategies (reference, ref 125% pw, Singels, Doubels and Triplets) are denoted on the x axis and the phoneme scores expressed in percentages on the y axis.*

Discussion

Earlier research concluded that spanning has reduced specificity with increasing distance, yet is a potentially useful mechanism to bridge a defective electrode contact in a speech coding strategy (Snel-Bongers et al. 2011b). To test the effectiveness of spanning in a real life situation, rather than in controlled psychophysical experiments, implementation of the spanning methodology in a speech coding strategy is required and comparative tests need to be performed. This study showed that HiRes120 with spanning yields on average the same scores as HiRes120 with current steering on adjacent contacts. However, the speech perception score measured in quiet showed degradation when increasing the spanning distance. In the European HiRes120 multicentre study of Buechner et al, participants with non-active contacts on their electrode arrays experienced major reductions in the number of analysis channels and had poorer speech perceptions scores (9; Boermans et al. 2008). One option could be to replace the HiRes120 strategy in such cases by a HiRes program, for which it is well-known, that even with 8 contacts good speech perception can be achieved (Frijns et al. 2003). The present study, however, indicated that such implant recipients would also benefit from implementation of spanning, which would enable them to continue using the HiRes120 speech strategy, especially because the non-active electrode contacts were always single contacts flanked by active electrode contacts.

Our participants used the various strategies (2, 3 and 4) in different situations at home and indicated that the sound quality of these different speech programs was the same. As expected, no overall difference between the five listening situations was found. Listening to music showed a diverse response from the participants, but no difference was found between the different strategies.

All the strategies were fitted individually, because even with the loudness correction from Snel-Bongers et al. (Snel-Bongers et al. 2011a), the participants were not content with the quality and loudness of their program. However, no significant difference was found between the levels of the different strategies. This indicates that individual fitting is still necessary to optimize listening and speech perception for bridged contacts, and thus that the Snel-Bongers et al. (Snel-Bongers et al. 2011a) correction may not be relied upon as a definitive fitting method. An easy solution would be to implement fitting the M-levels for the bridged virtual contacts just like the ones for the physical contacts in the clinical fitting software.

In line with previous research (Snel-Bongers et al. 2011a) the number of intermediate pitches decreased significantly ($p = 0.040$) with increasing spanning distance. Since no association could be demonstrated between a high JNDα_c and low speech perception score for the different spanning pairs the number of intermediate pitches cannot be used to predict whether a participant will benefit in terms of speech perception from spanning when the electrode array contains one or more defective electrode contacts.

In the HiRes120 speech strategy, each of the 15 electrode pairs supports 8 spectral channels, resulting in 120 spectral channels. In this study we made use of 9 electrode pairs. With 8 spectral channels per pair, this led to a total of 72 spectral channels, resulting in a tonotopic reorganization and a change in rate compared to the participant's own program. The take-home experience was used to allow acclimatization to this new frequency distribution along the array, before the speech perception tests were performed. In future implementations this reduction in number of spectral analysis channels can be compensated by replacing a defective electrode contact with a spanned signal containing two new virtual pairs, each pair generating 8 spectral channels. This will also keep tonotopy and stimulation rate between defective and non-defective electrode arrays constant. As the number of perceived intermediate pitches decreased for several participants with increasing spanning distance, it would be of extra interest to test this new strategy in a follow-up study to determine the influence on speech perception, especially for larger spanning distances.

This more sophisticated approach is promising, as the present study already demonstrated that spanning defective electrode contacts in a HiRes120 speech coding strategy largely restores speech recognition scores in quiet and in noise to the level of an intact electrode array, while preserving the sound quality.

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Chapter 7

General discussion and concluding remarks

Dual electrode stimulation (DES) is a method that is used to encode the spectral fine structure, by enhancing the number of perceived pitches beyond the number of physical contacts. If DES indeed can be used to improve tonotopical resolution, this could result in improved speech perception in general and possibly in improved speech perception in noise and better music perception. This thesis firstly investigates the fundamental principles underlying current steering and phantom stimulation with respect to loudness variation, number of perceived percepts and the spread of excitation. These evaluations were made using psychophysics and computational modeling of the implanted cochlea. Finally, in the last study these fundamental findings are verified by implementing spanning in a speech coding strategy. In a group of test subjects it was shown that spanning can preserve the speech perception scores in patients with defective electrodes.

Loudness

When using DES in a speech coding strategy, the patient must be able to hear the signal. The loudness of a Single Electrode Stimulation (SES) signal depends on the amount of current given on a single electrode contact. With DES the current normally used on one electrode is now divided over two electrodes. When simultaneous DES is applied on adjacent electrode contacts with 1.1 mm spacing at the Most Comfortable Loudness (MCL) level, very little adjustment of that current level is needed to maintain equal loudness in comparison with SES (Chapter 4) (Donaldson et al. 2005), due to electric field summation (Frijns et al. 2009b). Also when stimulating on low stimulation levels (TL), no correction is needed with current steering (Chapter 5). However, when increasing the spanning distance, a current correction is needed on MCL and TL, presumably due to less overlap between the regions of neural excitation produced by the two stimulating contacts (Chapter 4 and 5). In comparison, also non-simultaneous DES requires a current correction to maintain equal loudness due to attenuation of the electrical field. There is no direct electric field interaction, but only interaction on neural level, which results in two separate regions of excitation (Frijns et al. 2009b).

In chapter 4 the adjustment of the current required to maintain equal loudness for various spanning distances was measured, this relation was used in the study of chapter 6. Unfortunately, individual fitting of the virtual channels in the speech coding strategies was still necessary, because the patients were not content with the loudness after implementing the current correction. Also with phantom stimulation, when two electrode contacts are stimulated with non-equal pulses in opposite-polarity, a current correction is needed when increasing σ (the ratio between amplitudes of the two stimulated contacts) (Chapter 3). Phantom stimulation on low stimulation levels is not even possible. The computational model of the cochlea shows that the initial increase in current needed to achieve 4 mm excitation (considered the equivalent of most comfortable loudness level) is caused by the negative stimulus (see Figure 10, chapter 3, page 82). The negative stimulus is counteracting some of the current spread of the positive stimulus. This makes it more difficult for the electrical current to reach the neurons and overall more current is needed to reach 4 mm excitation.

The required current corrections for spanning and for phantom stimulation when actually used in a speech processors can have for example detrimental consequences for battery life. Increase in current can also lead to overstimulation of other structures in the region of the cochlea, for instance the facial nerve (Frijns et al. 2009a). Also stimulation of auditory nerve fibers in another turn of the cochlea can take place, so called cross-turn stimulation. This can lead to perception of another frequency or distortion of sound. Although none of the patients had complains about these topics in the study of chapter 6, where spanning was implemented in a speech coding strategy, this can become a problem when implementing phantom stimulation in a speech coding strategy, because the current levels are much higher here. However, when this correction is not applied, a subject would not be able to hear the created signal.

Spectral channels

As mentioned above, DES can be used to enhance the number of perceived pitches. With simultaneous DES on adjacent or non-adjacent electrodes these pitches are created intermediate to the stimulated electrode contacts, while with phantom stimulation these pitches are created more apical than the stimulated electrode contacts. The number of created pitches differs per subject and per method. However, if patients are able to discriminate between pitches created with current steering, they are also able to discriminate between pitches created with phantom stimulation (Chapter 3). The amount of pitches decreases when increasing the spanning distance (Chapter 4), which can have a negative influence on performance when spanning is used for instance in future devices to decrease the number of physical contacts in an array. On the other hand, additional signal channels are provided, which is a better solution for patients with a defective contact on their already implanted array than nothing.

At the present time, the principle of DES is implemented commercially in the Advanced Bionics Harmony system, using the HiRes 120 speech coding strategy. Instead of 16 spectral channels generated using the physical electrode contacts, 8 intermediate or virtual channels are available per electrode contact pair, giving a total of 120 different pitches. The number of possibly created intermediate pitches with DES, however, differs per subject and has a positive correlation with their speech perception score with monopolar stimulation (Chapter 2). There are subjects who are not able to distinguish between two contacts, which are up till 4 mm apart from each other (Chapter 4) and there are subjects who are able to distinguish more than 40 extra percepts between adjacent electrode contacts (Firszt et al. 2007; Koch et al. 2007). For subjects who are not able to discriminate available spectral channels, virtual channels will probably not be beneficial when used in a speech processor and potentially even detrimental. It is possible that each patient needs an individual adjustment of his or her HiRes program. For example, the patient who is not able to discriminate between two adjacent contacts will maybe reach his or her highest speech perception scores with 8 different pitches, which will give for example a new HiRes program, denoted as HiRes8, instead of HiRes120. While the patient who can differentiate about 20 percepts, will reach his or her highest speech perception score with 300 different pitches and will get a HiRes300 program. Unfortunately, we have not found a parameter that can predict the number of intermediate pitches (Chapter 2). This means that the just noticeable difference of α (JNDα), which can be used to calculate the number of possible intermediate pitches, must be determined individually, which is time-consuming, after which each HiRes program must be individually adjusted. It would be of interest to investigate whether speech perception scores can be increased when each patient will get their individually adjusted HiRes program with DES based on their JNDα.

Another improvement could be to use an “n of m” strategy in HiRes120. In the current implementation of HiRes 120 the stimulation place of the peaks in the spectrum are positioned more accurately. The channels without a peak in their spectral band are, however, stimulated at the edges of the channel on the slope of the peak of the neighboring channel. These stimulations can lead to larger spread of excitation and lower pitch discrimination. The ‘n of m’ addition would only select the channels with a peak that can be steered to the correct excitation place. This will probably reduce the problem of the high interactions between the spectral channels, because of the close proximity of the stimulation areas.

Place of stimulation

When using DES in a speech coding strategy the place or site of stimulation (X) is of interest. This can either be investigated with a psychophysical experiment or with an objective measurement. The X of current steering for $\alpha = 0.5$ was found exactly between the two stimulating contacts with an eCAP forward-masking curve, an objective measure. X appeared to follow a linear pattern up till 4.4 mm for spanning, investigated with a pitch matching experiment, which is a psychophysical experiment. The X of phantom stimulation was determined psychophysically by comparing it with a current steering signal also in a pitch matching experiment. The maximum pitch shift found for phantom stimulation was about 1 electrode contact spacing in the apical direction.

For future investigation, the question arises whether eCAP forward-masking curves will give the same results for spanning and phantom stimulation as found for current steering. Preliminary data of spanning show promising results, however the initial experiment must be extended in future research for better comparison. For example, with taking several different locations of the recording electrode into account. The recording electrode in the eCap experiments, described in Chapter 2, was always at the same position, 2 electrode contacts closer to apical than the stimulated electrode contact. This can be of influence on the determined place of stimulation (van der Beek et al. 2012). Further, the preliminary data of phantom stimulation were not usable, because the used program was not able to implement the required high current correction. New adjustments of the program will make it hopefully possible to determine X of phantom stimulation in the future objectively.

Computational model

To supplement clinical data, simulations of DES excitation were performed using a computational model of the implanted human cochlea developed at Leiden University Medical Center. The computational model consists of two parts, a volume conduction part simulating the current flow through an implanted cochlea and a neural part simulating the response of the nerve fibers (Briaire and Frijns 2000; Briaire and Frijns 2005; Briaire and Frijns 2006; Frijns et al. 2001; Frijns et al. 2009a; Frijns et al. 2009b). As shown in chapter 5, the model can be used to understand and explain the result of the psychophysical experiments. Here three different cochlea models were used based on different stages in the degeneration process. After comparing the clinical data with the predictions of the computational model, a new insight in the neural degeneration process of the auditory nerve became apparent. Patients with a long duration of deafness were best compared with the graphs of nerve fiber, which still exhibited a peripheral process, but no unmyelinated terminal (UT), while patient with a significantly shorter duration of deafness were better compared with the graph where an UT was still present. This observation suggested that degeneration of auditory nerve fibers in humans involves loss of UTs rather than loss of complete peripheral processes.

The predictions made by the model in this thesis were comparable with the results of the clinical experiments. This implicates that the model can be used in future studies, but also that it probably can be used in the future for composing an individual speech coding strategy for each cochlear implant user. Here the CT-scan can be used to create an individual model of the cochlea per subject and place the electrode array in the exact same position as in the patient.

Assessment of electrode position with CT scan

As a new element, we selected the tested electrode contacts based on their location in the cochlea, instead of selecting based on their rank number on the electrode array. The main reasons for this choice were the differences between subjects regarding insertion angle, size of the cochlea and electrode position. To locate the exact position of the electrode array, and thereby the individual electrode contacts, we used postoperative high resolution CT-scans. A system of coordinates (Verbist et al. 2005), was used and the angles were calculated from the round window, the 0° reference, according to an international consensus (Verbist et al. 2010). We prefer this approach since it is a reliable and standardized method and allows comparison of comparable parts of cochleae across subjects and across electrode designs. We recommend using it in all future clinical cochlear implant studies. A detrimental effect is caused by the radiation dose of a high resolution CT-scan, especially when making for each cochlear implant patient a pre- and post-operative CT-scan. Fortunately, it is nowadays possible to make use of low dose temporal bone CT-scanning. Nauer et al. (2011) showed that in a comparable study between low-dose versus standard high-dose CT-scans, that the image quality of the new low-dose protocol remains diagnostic for assessing the middle and inner ear anatomy despite a 3- to 8-fold dose reduction. Also Niu et al. (2012) showed that the radiation dose reduces up till 50%, while maintaining diagnostic image quality. Nevertheless, Nauer et al. (2011) pointed out that the image quality of small structures is critical and may be perceived as insufficient.

Next to this, one upcoming dose-saving technique with a high resolution is the cone beam CT. The cone beam CT offers several advantages over the traditional high resolution CT; namely lower radiation dose, reduced flaring from electrode artifacts and lower cost (Faccioli et al. 2009; Ruivo et al. 2009; Trieger et al. 2011). Although the cone beam CT allows relatively safe evaluation of the electrode in the basal turn, a disadvantage is that it is not really a useful tool with deep insertions (Guldner et al. 2012). Cone Beam CT also did not demonstrate adequate resolution to detect reversal of the electrode contacts or basilar membrane rupture (Cushing et al. 2012).

Future perspectives

In this thesis we have shown how fundamental research can help to successfully implement a speech coding strategy, in this case dual electrode stimulation. Phantom stimulation has only been investigated on fundamental grounds, so the next step should be to implement it in a speech coding strategy. Before phantom stimulation can be implemented, two issues must be considered. First impractically high currents may be required to achieve audibility, and this can have a negative influence on battery life, and lead to overstimulation of other structures in the region of the cochlea or to cross-turn stimulation, which can lead to perception of another frequency or distortion of sound. Also the fact that phantom stimulation is not possible on low current levels, limits its clinical applicability. A solution could be, to only use the phantom channels when the energy of the signal is high enough and omitting the low energy signals, like the “n of m” strategy. Secondly, not every patient will be able to distinguish several percepts, which is comparable with current steering. Fortunately, each patient was able to perceive a pitch percept induced to the apical side of the reference contact. However, the patients involved in the study were good performers with a speech perception score above 70%, which can be of influence on their ability to discriminate an extra percept. Possibly, poor performers will be able to perceive a pitch more to apical, but will be unable to discriminate this percept from a monopolar stimulus on the apical contact.

Next to enhancing the number of pitches with DES to improve speech perception scores, it might be possible to improve these scores by limiting the large current spreads in the cochlea of monopolar stimulation. With less current spread, the population of activated neurons would narrow, which would therefore presumably reduce channel interaction across electrode contacts. This should in theory improve spectral resolution and possibly enhance the number of independent channels. As mentioned in chapter 1, phased array, multipole stimulation, is in theory a method that possibly can reduce current spread. According to Frijns et al. (2011), the excitation profiles, computed with the computational model of the cochlea, were broader for monopolar stimulation than for phased array stimulation. This would mean that speech perception could improve. Of concern are, however the high currents needed to achieve audibility, which was also the case in tripolar stimulation. One of the problems with tripolar stimulation was that the large current amplitudes were not physically achievable due to the compliance limits of the device (Litvak et al. 2007). High current levels could, however, also have negative influence on battery life, lead to overstimulation of surrounding structures or to cross-turn stimulation equal to phantom stimulation. This will only become apparent when phased array will be implemented in a speech coding strategy. Preliminary data from our research group (Vellinga et al., KNO vergadering april 2013), however, show that each patient is able to reach MCL with phased array, which is a positive result.

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Summary

The Dutch population counts about 12,000 adults and children with a severe to profound hearing loss. Cochlear implantation is an established technique to improve the ability to understand speech, and therefore nowadays a paramount opportunity of rehabilitation. Since the 1980's, manufacturers develop multi-channel cochlear implants with even more advanced speech coding strategies, in conjunction with the continuous evolution of the electrode arrays, which improved the speech perception scores significantly over the years. The newest developments on speech coding strategies are based on spectral and temporal fine structures cues, which potentially result in better speech perception in background noise and better appreciation of music. Fidelity 120 is one of these strategies based on simultaneous dual electrode stimulation (DES), the subject of the translational study in this thesis. The mechanism of DES is investigated both psychophysically and in a computational model of the cochlea, followed by a clinical implementation of DES, which aims to correct for defective electrode contracts.

Chapter 1 presents the basic principles of a cochlear implant and a short historical overview of the development of this device. Next, a historical overview of the development of the speech coding strategies is given from the basic principles to the currently used strategies and strategies under development. This chapter ends with an outline of this thesis.

Objective of **Chapter 2** was to establish how DES can be optimized and whether it has the same qualities as single electrode stimulation (SES), enabling its use in a CIS (Continuous Interleave Sampling) like strategy. The comparison of DES with SES was investigated with respect to the site of stimulation in the cochlea, the spread of excitation (SOE) and sequential channel interactions. Because it is relevant to be able to determine in advance to what extent a patient is able to discriminate extra pitches created with DES, it was investigated whether the number of intermediate pitches created with DES can be predicted from SOE, channel interaction measures, current distribution in the cochlea, or distance of the electrode to the medial wall. It turned out there was no significant difference between dual and single electrode stimulation for the SOE curves and sequential channel interaction. This led to the hypothesis that dual electrode stimulation can be used in CIS like strategies without degradation of speech perception. Furthermore, the displacement found, the excitation site of dual electrode stimulation relative to the region of excitation induced by the neighboring single electrode contact, was in line with expectations. Unfortunately, only the sequential channel interaction index showed a significant correlation with the number of intermediate pitches created with DES along the array on a per-patient basis. Therefore, it could be concluded that no clinically useful predictor for the number of intermediate pitches was found.

With Phantom stimulation, a pulse with opposite-polarity on the basal electrode contact of the pair of DES is used to create a pitch beyond the electrode array in the apical direction. This pitch is than shifted away from the apical electrode and therefore is lower in pitch than the one of the apical electrode contact with SES. This phantom stimulation was explored in **chapter 3** by using psychophysical experiments and computational modeling of the cochlea. It turned out, that phantom stimulation was effective in all patients tested. Next, it was demonstrated that phantom stimulation indeed needed more current and that a current correction was necessary to maintain equal loudness with varying pitch shifts. In this respect, the psychophysical data was comparable with the computational modeling data. Finally, the place of stimulation of phantom stimulation was explored. Each patient was able to perceive a lower pitch in the apical region, with a maximum pitch shift of approximately 1.1 mm along the basilar membrane. The model showed a smaller overall pitch shift and predicted that the shift is larger with an electrode array in a lateral position in the scala tympani than in a medial position.

The last three chapters further explored the possibilities and qualities of simultaneous DES. In **chapter 4** the possibility is explored to bridge defective electrode contacts with DES applied on non-adjacent electrode contacts (spanning). With psychophysical experiments spanning was compared with DES on adjacent electrode contacts in terms of the number of intermediate pitches, loudness effects and linearity of the current weighting coefficient with respect to the perceived pitch. Data showed that spanning is feasible up till 4.4 mm, but that with increasing distance between the electrodes, a gradual increase in loudness adjustment and decrease in pitch discrimination precision occurs. The pitch distribution is linear with α, where α is denoted as the proportion of the total current directed to the more basal contact of the dual electrode contact pair. This coefficient varies from $\alpha = 0$, where all current is directed to the apical electrode to $\alpha = 1$, where all current is directed to the basal electrode. Further was shown that the data were not influenced by the apical to basal location of electrode contacts in the cochlea.

The experiments in all former chapters were performed on Most Comfortable Loudness (MCL) level. When DES will be used in a speech coding strategy, it is also of interest to know what happens at Threshold Level (TL). In the clinical fitting procedure, TL is the level where the patient indicates that the signal is just audible. **Chapter 5** describes the efficiency of DES at lower levels, with the focus on the requirements to correct for threshold variations along the array. TLs were determined both psychophysically and with computational modeling, where the computational model utilized three different neural morphologies with different stages of degeneration. We concluded that with present electrode arrays DES is possible at low current levels and no current adjustment is necessary to compensate for loudness variations in most cases. Furthermore, comparison of the psychophysical data with the data from the computational model led to the hypothesis that degeneration of apical auditory nerve fibers in humans mainly involves loss of unmyelinated terminals rather than loss of complete peripheral processes.

After fundamental experiments with DES, the challenge remained if implementation of spanning in a speech coding strategy would be possible and would not decrease the performance and the quality of sound. In **chapter 6** three different speech coding strategies were designed, with 1, 2 or 3 defective electrode contacts next to each other. Each of the programs simulated to have a total of 6 defective electrode contacts. Patients were asked to use these different strategies in five different home situations and indicated no difference in sound perception between these situations. Further, speech perception scores were measured in quiet and with speech-weighted background noise. No significant difference was found between the strategies. However, in quiet an increasing spanning distance showed a small but significant decrease in speech perception scores (from 84.7% to 75.2%).

Chapter 7 presents an overall discussion of the major results and conclusions of the studies described in this thesis. Furthermore, implications for clinical practice and areas of future research are discussed.

Samenvatting

De bevolking van Nederland telt ongeveer 12.000 volwassenen en kinderen met ernstig tot zeer ernstig gehoorsverlies. Cochleaire implantatie is een alom erkende techniek om spraakverstaan permanent te verbeteren, en daarom een doorslaggevende mogelijkheid tot revalidatie. Sinds de tachtiger jaren van de vorige eeuw ontwikkelen fabrikanten cochleaire implantaten met meerdere kanalen met geavanceerde spraakcodering strategieën. Dat in combinatie met de voortdurende evolutie van de elektrode array heeft het spraakverstaan significant verbeterd over de jaren heen. De nieuwste ontwikkelingen op het gebied van spraakcodering strategie zijn gebaseerd op spectraal en temporeel "fine structure cues". Dit leidt mogelijk tot beter spraakverstaan bij achtergrondruis en tot betere waardering van muziek. Fidelity 120 is een van de strategieën die gebaseerd is op simultane "dual electrode stimulation" (DES), het onderwerp van het onderzoek beschreven in dit proefschrift. Het mechanisme van DES is zowel psychofysisch onderzocht als in een computermodel van de cochlea, gevolgd door een klinische implementatie van DES, met als belangrijkste doel om te corrigeren voor defecte elektrodecontacten.

Hoofdstuk 1 presenteert de basisprincipes van een cochleair implantaat en geeft een kort historisch overzicht van de ontwikkeling hiervan. Vervolgens wordt een historisch overzicht van de ontwikkeling van spraakcodering strategieën gegeven, vanaf het basis principe tot de meest recent gebruikte strategieën en de strategieën in ontwikkeling. Dit hoofdstuk eindigt met een overzicht van dit proefschrift.

De doelstelling van **hoofdstuk 2** was om vast te stellen hoe DES kan worden geoptimaliseerd en of het dezelfde kwaliteiten heeft als "single electrode stimulation" (SES) om het vervolgens mogelijk te maken in een CIS (Continuous Interleaved Sampling) strategie. De overeenkomsten en verschillen tussen DES en SES werden geanalyseerd kijkend naar de plaats van stimulatie in de cochlea, de excitatie spreiding en sequentiële kanaal interactie. Omdat het is belangrijk om op voorhand te kunnen bepalen of een patiënt in staat is om te discrimineren tussen extra gecreëerde toonhoogtes gegenereerd bij DES, werd onderzocht of het aantal tussenliggende toonhoogtes gecreëerd met DES voorspeld kan worden met de excitatie spreiding, met sequentiële kanaalinteractie, met stroomspreiding in de cochlea of met de afstand van de elektrode tot de mediale wand. Het bleek dat er geen significant verschil was tussen DES en SES voor excitatie spreiding en de sequentiële kanaalinteractie. Dit leidde tot de hypothese dat DES gebruikt kan worden in één van de CIS strategieën zonder degradatie van spraakverstaan. Bovendien was de gevonden verplaatsing, dit is de plaats van excitatie van DES ten opzichte van het excitatie gebied geïnduceerd door het naast gelegen enkele elektrodecontact, in lijn met de verwachtingen. Helaas liet alleen de sequentiële kanaalinteractie index een significant correlatie zien met het aantal extra gecreëerde kanalen met DES langs de array voor individuele patiënten. Daarom kan worden geconcludeerd, dat er geen klinisch bruikbare voorspeller voor het aantal verschillende tussenliggende toonhoogtes is gevonden.

Met fantoomstimulatie, wordt een puls met tegengestelde polariteit op het basale contact van het DES paar gebruikt om een toonhoogte buiten de elektrode array te creëren in de apicale richting. Deze toonhoogte wordt van het apicale contact weg bewogen en is lager in toonhoogte dan de toonhoogte van het apicale contact met SES. Deze fantoomstimulatie werd onderzocht in **hoofdstuk 3** met behulp van psychofysische experimenten en een computermodel van de cochlea. Het bleek dat fantoomstimulatie bij alle geteste patiënten effectief was. Vervolgens werd aangetoond dat fantoomstimulatie inderdaad meer stroom nodig heeft en dat een stroomcorrectie nodig is om gelijke luidheid te behouden met het variëren van de toonhoogtes. In dit opzicht was de psychofysische data vergelijkbaar met de data van het computermodel. Tenslotte werd de plaats van stimulatie van fantoom stimulatie bepaald. Elke patiënt was in staat om een lagere toonhoogte te ontvangen in de apicale regio, met een maximale toonhoogte verschuiving van ongeveer 1.1 mm langs het basilair membraan. Het computermodel liet over het algemeen een kleinere verschuiving in toonhoogte zien en voorspelde dat de verschuiving met een elektrode in laterale positie in de scala tympani groter is dan in mediale positie.

In de laatste drie hoofdstukken worden de mogelijkheden en kwaliteiten van simultane DES verder onderzocht. In **hoofdstuk 4** wordt de mogelijkheid om defecte elektrodecontacten te overbruggen met DES op niet naast elkaar gelegen elektrodecontacten onderzocht ("spanning"). Met psychofysische experimenten werd "spanning" vergeleken met DES op naast elkaar gelegen elektrodecontacten in termen van het aantal gecreëerde tussenliggende toonhoogtes, geluidsterkte effecten en de lineariteit van de huidige wegingcoëfficiënt ten opzichte van de ontvangen toonhoogte. De data lieten zien dat "spanning" uitvoerbaar is tot op 4.4 mm, maar dat met vergroten van de afstand tussen de elektrodecontacten, een geleidelijke toename van geluidsterkte correctie optreedt en een afname in het aantal te discrimineren toonhoogtes. De toonhoogte spreiding is lineair met α, waarbij α wordt aangeduid als het percentage van de totale stroom gericht op het meest basale contact van de twee gebruikte contacten. Deze coëfficiënt varieert van $\alpha = 0$, waar alle stroom gericht is op het apicale contact tot $\alpha = 1$, waar alle stroom gericht is op het basale contact. Verder werd aangetoond dat de data niet beïnvloed werden door de apicale-basale locatie van de elektrodecontacten in de cochlea.

De experimenten in alle vorige hoofdstukken werden uitgevoerd op "Most Comfortable Loudness" (MCL) niveau. Wanneer DES gebruikt gaat worden in een spraakcoderingstrategie, is het ook interessant om te weten wat er gebeurt op "Threshold level" (TL). In de klinische fitting procedure is TL het niveau waarop de patiënt aangeeft dat het signaal net te horen is. **Hoofdstuk 5** beschrijft de effectiviteit van DES op lagere niveaus, met de focus op de noodzakelijkheid om te corrigeren voor drempel variaties langs de array. TL's werden zowel psychofysisch als met het computermodel van de cochlea bepaald, waarbij het computermodel gebruik maakte van drie verschillende neurologische morfologieën met verschillende stadia van degeneratie. We konden concluderen dat met de huidige elektrode arrays DES mogelijk is op lage stroomniveaus en dat het niet nodig is om de stroom aan te passen om te compenseren voor geluidsterkte variaties in de meeste situaties. Bovendien, leidde vergelijkingen van psychofysische gegevens met de gegevens van het computermodel tot de hypothese, dat degeneratie van de apicale gehoorzenuwvezels in de mens vooral gepaard gaat met het verlies van "unmyelinated terminals" in plaats van compleet verlies van perifere uitlopers.

Na fundamentele experimenten met DES, bleef de uitdaging over of het implementeren van "spanning" in een spraakverwerking strategie mogelijk was en of hiermee het spraakverstaan en kwaliteit van muziek niet zou afnemen. In **hoofdstuk 6** werden drie verschillende spraakcodering strategieën ontworpen, met 1, 2 of 3 defecte elektrodecontacten naast elkaar. Elk programma simuleerde in totaal 6 defecte elektrodecontacten. Patiënten werden gevraagd om deze verschillende strategieën in vijf verschillende thuissituaties te gebruiken en gaven geen verschil in geluidsperceptie aan tussen deze situaties. Verder werden spraakverstaan scores gemeten in stilte en met spraak-gewogen achtergrondruis. Er werd geen significant verschil gevonden tussen de strategieën. Echter, in stilte toonde een toegenomen "spanning" afstand een kleine, maar significante daling in spraakverstaan scores (84,7% naar 75,2%).

Hoofdstuk 7 geeft een algemene discussie van de belangrijkste resultaten en conclusies van de studies beschreven in dit proefschrift. Daarnaast worden implicatie voor de klinische praktijk en gebieden van toekomstig onderzoek besproken.

Curriculum Vitae

Jorien Snel-Bongers was born on the 19th of January 1983 in the city of Leiderdorp. During her secondary education at "het stedelijk Gymnasium" of Leiden she was a fanatic waterpolo player and attended the national championships four times. This resulted the third time in winning the national title. After completing her secondary education (VWO) in 2001, she started her medical studies at the University of Leiden. During this period she followed a pathology course at the Karolinska institute of Stockholm, Sweden. She obtained medical qualification in 2007, after which she started research for this thesis as a research-resident at the department of Otorhinolaryngology, Head and Neck surgery of the Leiden University Medical Centre under the supervision of Prof. Dr. ir. J.H.M. Frijns. Under his supervision she is also trained to become an otorhinolaryngologist since 2009. Part of this training took place at the Medisch Centrum Haaglanden, location Westeinde in The Hague (supervisor: Dr. H.P. Verschuur) and at Rijnland hospital, locations Leiderdorp and Alphen a/d Rijn (supervisor: Dr. M.L. Sassen).
Jorien is married with Frans Snel. Together they have a son Twan (2009) and a daughter Ymke (2012)

Curriculum Vitae

Jorien Snel-Bongers werd op 19 januari 1983 geboren in Leiderdorp. Tijdens haar middelbare school aan het stedelijk Gymnasium te Leiden, was ze een fanatiek waterpolo speler en heeft ze vier keer deelgenomen aan de Nederlandse kampioenschappen. De derde keer resulteerde dit in het winnen van de Nederlandse titel. Na het afronden van de middelbare school (VWO) in 2001, begon ze met haar studie geneeskunde aan de universiteit van Leiden. Tijdens deze periode, volgde ze een pathologie cursus aan het karolinska instituut in Stockholm, Zweden. Ze behaalde haar arts examen in 2007, waarna ze begon met het onderzoek dat ten grondslag ligt aan dit proefschrift bij de afdeling Keel-, Neus-, en Oorheelkunde in het Leids Universitair medisch centrum onder de supervisie van Prof. Dr. Ir. J.H.M. Frijns. Onder zijn supervisie wordt ze ook sinds 2009 opgeleid tot KNO-arts. Delen van deze opleiding werden genoten in het Medisch Centrum Haaglanden, locatie Westeinde in Den Haag (opleider: Dr. H.P. Verschuur) en in het Rijnland ziekenhuis, locaties Leiderdorp en Alphen a/d Rijn (opleider: Dr. M.L. Sassen).

Jorien is getrouwd met Frans Snel. Samen hebben ze een zoon Twan (2009) en een dochter Ymke (2012).