SpeedCAP: An Efficient Method for Estimating Neural Activation Patterns Using Electrically-Evoked Compound Action-Potentials in Cochlear Implant Users

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Data & Code Availability

The data and code that support the findings of this study will be made available upon request from the corresponding author.

Abstract

Objectives: Electrically-Evoked Compound Action-Potentials (ECAPs) can be recorded using the electrodes in a cochlear implant (CI) and represent the synchronous responses of the electrically-stimulated auditory-nerve. ECAPs can be obtained using a forward-masking method that measures the neural response to a probe and masker electrode separately and in combination. The Panoramic ECAP (PECAP) method measures ECAPs using multiple combinations of masker and probe electrodes and uses a nonlinear optimization algorithm to estimate current spread from each electrode and neural health along the cochlea. However, the measurement of ECAPs from multiple combinations of electrodes is too time-consuming for use in clinics. This study proposes and evaluates a fast version of the PECAP measurements, SpeedCAP, that minimises recording time by exploiting redundancies between multiple ECAP measures, and that can be applied to methods where multiple ECAPs are required. **Design:** In the first study, 11 users of Cochlear Limited CIs took part. ECAPs were recorded using the forward-masking artefact-cancellation technique at the most comfortable loudness level (MCL) for every combination of masker and probe electrodes for all active electrodes in the users' MAPs, as per the standard PECAP recording paradigm. The same current levels and recording parameters were then used to collect ECAPs in the same users with the SpeedCAP method. The ECAP amplitudes were then compared between the two conditions, as were the corresponding estimates of neural health and current spread calculated using the PECAP method described by Garcia et al (2021). The second study measured SpeedCAP intra-operatively in 8 CI patients and with all maskers and probes presented at the same current level to assess feasibility. ECAPs for the subset of conditions where the masker and probe were presented on the same electrode were compared to those obtained using the slower approach leveraged by the standard clinical software. **Results:** Data collection time was reduced from 45 (PECAP) to 8 (SpeedCAP) minutes. There were no significant differences between normalized root mean squared error (RMSE) repeatability metrics for post-operative PECAP and SpeedCAP data, nor for the RMSEs calculated *between* PECAP and SpeedCAP data. When between-participant differences were removed, both the neural health ($r = 0.73$) and current spread ($r = 0.65$) estimates were significantly correlated ($p < 0.0001$, $df = 218$) between SpeedCAP and PECAP conditions across all electrodes. Valid ECAPs were obtained in all patients in the second study, demonstrating intra-operative feasibility of SpeedCAP. No significant differences in RMSEs were detectable between post- and intra-operative ECAP measurements. **Conclusions:** The improved efficiency of SpeedCAP provides time savings facilitating multi-electrode ECAP recordings in routine clinical practice. The SpeedCAP data collection is sufficiently quick to record intra-operatively, and adds no significant error to the ECAP amplitudes. Such measurements could thereafter be submitted to models such as PECAP to provide patient-specific patterns of neural activation to inform programming of clinical MAPs and/or identify causes of poor performance at the electrode-nerve interface of CI users. The speed and accuracy of these measurements also opens up a wide range of additional research questions to be addressed.

Introduction

Cochlear implants (CIs) are neuro-prosthetic devices that provide auditory sensations to profoundly deaf individuals by electrical stimulation of the auditory nerve. Many CI users understand speech well in quiet situations, but there is a lot of variability in speech performance among CI users, particularly in situations with background noise (Friesen, et al., 2001; Firszt, et al., 2004). As a result, a lot of research has been done to investigate measurements that predict CI speech performance. Many models have been developed that incorporate a myriad of behavioural and objective measurements with varying degrees of accuracy (Kim, et al., 2010; Lazard, et al., 2012; Scheperle & Abbas, 2015; Kim, et al., 2017; Schwartz-Leyzac & Pfingst, 2018; Carlyon & Goehring, 2021). However, these measurements are often summary metrics for CI users and do not provide detailed estimates of an individual user's unique pattern of neural activation at the electrode-nerve interface. This latter information may be important for optimizing efficacy of CIs and improving speech perception (Long, et al., 2014; Pfingst, et al., 2015). Obtaining multiple measurements along the length of the electrode array for a particular CI user may be sufficiently time consuming so as to prevent this being done in clinical settings, especially if utilizing behavioural techniques. Objective measurements can be faster and automatic, but they may require additional hardware. For example, Electrically-Evoked Auditory Brainstem Responses (EABRs) reflect synchronous physiological responses to electrical stimulation from various stages of the auditory pathway from the peripheral auditory nerve to the inferior colliculus (Hall III, 1992), but require additional electrodes to be placed on a patient's scalp for measurements (Brown, et al., 1994).

Electrically-Evoked Compound Action-Potentials (ECAPs) are the most practical objective measurements as they require no additional hardware and leverage the CI electrodes already inserted inside the cochlea both to stimulate and record. ECAPs measure the synchronous peripheral neural response to a current pulse delivered from an electrode in a CI, recorded with a nearby intra-cochlear electrode (Charlet de Sauvage, et al., 1983; Brown, et al., 1990). ECAPs are measured routinely in clinical practice, for example to estimate threshold (T) and comfort (C) levels, although their relevance for predicting behavioural assessments of T and C levels has been questioned (de Vos, et al., 2018). Several studies have further suggested that they can be used to estimate various aspects of neural activation patterns such as spiral-ganglion neuron survival (Prado-Guitierrez, et al., 2006; Ramekers, et al., 2014). They have also been used in more complex models to estimate neural activation patterns in individual users. Cosentino et al. (2015) described the first version of the Panoramic ECAP (PECAP) method that measured ECAPs with the forward-masking artefact-cancellation technique for all combinations of masker and probe electrodes at equal loudness levels. This measurement matrix $\mathbf{M}$ (with rows and columns corresponding to probe and masker electrodes respectively) was then processed using an algorithm that estimated underlying excitation patterns for each electrode. Biesheuvel et al. (2016) described a model using similar ECAP data at equal current levels that estimate excitation density profiles by treating them as convolutions for different electrodes. Garcia et al. (2021) presented a refinement of the PECAP method that processed $\mathbf{M}$ using a nonlinear optimization algorithm so as to estimate variation in current spread

and neural health along the electrode array in individual CI users. The PECAP method in particular shows promise for clinical use as it was able to identify localized areas of simulated reduced neural responsiveness (“dead” regions) using its neural health estimate. However, PECAP and other methods of this ilk require the measurement of many ECAPs. While individual ECAPs take only a few seconds to record, it takes approximately 45 minutes to collect ECAPs for all combinations of masker and probe electrodes in the Cochlear Limited clinical software, Custom Sound EP. This is sufficiently long to be a barrier to implementing these models in routine clinical practice, as time is already severely limited (and costly) in the clinic.

Here we present a new method, called SpeedCAP, for efficiently measuring multiple ECAPs to speed up the process of collecting the data required to implement the Panoramic ECAP method. SpeedCAP exploits various redundancies present in the ECAP recording process when using the forward-masking artefact-cancellation technique (Abbas, et al., 1999) with many combinations of masker and probe electrodes. Using the SpeedCAP method, it takes only about 8 minutes to record the measurement matrix $\mathbf{M}$ required for PECAP compared to 45 minutes when using the standard method. While the method has been applied in this study to the ECAPs required for the PECAP method using Cochlear Limited devices only, the techniques required to speed up the data collection process can also be applied to other ECAP recordings such as spread of excitation (SOE) functions (Cohen, et al., 2003), and be used in principal with other CI manufacturers’ devices. The SpeedCAP method opens up new possibilities to assess the electrode-nerve interface of individual CI users with the PECAP method in clinical environments, to provide better insights into CI stimulation patterns for optimizing fitting and improving patient outcomes.

Methods

SpeedCAP Techniques and Assumptions

Here we provide a description of the techniques used to optimize the data acquisition process for the PECAP method. The standard PECAP measurement matrix $\mathbf{M}$ described in Garcia et al (2021) is an $n \times n$ matrix that contains ECAP amplitudes obtained from every combination of probe and masker electrode, where n is the number of electrodes switched on in the patient’s MAP.

SpeedCAP combines three ways of reducing the data collection time. First, only a part of the PECAP measurement matrix $\mathbf{M}$ is recorded. Second, communication time between the testing computer and the implant processor is reduced by recording multiple ECAPs at once and transmitting them from the implant processor in batches. Third, SpeedCAP skips frames in the forward-masking artefact-cancellation technique that are repeated when recording multiple ECAPs, so as to prioritize recording of non-redundant frames and to reduce data traffic.

The first time-saving technique is the recording of only a part of $\mathbf{M}$ based on the assumption that two ECAPs are theoretically and computationally equivalent when using the forward-masking artefact-cancellation technique if the masker and probe

electrodes are swapped – that is, $\mathbf{M}$ is symmetric across its diagonal. Although this is not necessarily exactly true, we and others have modelled the ECAP in terms of the overlap between the masker and probe excitation patterns (Cosentino, et al., 2015; Biesheuvel, et al., 2016; Garcia, et al., 2021) and our previous recordings suggested that asymmetries in $\mathbf{M}$ are rather small. Indeed, PECAP initially processes the $\mathbf{M}$ to force it to become symmetric prior to processing by the nonlinear optimisation algorithm. This assumption will be evaluated below and a “raw” measurement matrix is illustrated in Figure 1 (left). For the case where the $\mathbf{M}$ matrix is recorded using all 22 electrodes and 50 sweeps are recorded for each ECAP at a rate of 80 Hz, it will take 45 minutes to record all $22 \times 22 = 484$ waveforms. We can reduce this to approximately 25 minutes in the first instance simply by skipping half of the ECAPs for which we have assumed equivalence due to symmetry of $\mathbf{M}$. This would mean recording ECAPs for the cases where the masker and probe are presented on the same electrode (referred to as the diagonal), as well as where the masker electrode is basal to the probe electrode (or vice versa), resulting in a total of 253 ECAP waveforms.

Figure 1: (left) An example of a full PECAP matrix, $\mathbf{M}_0$, from participant C35. Each cell represents the amplitude of an ECAP waveform in μV , one for each of every possible combination of masker and probe electrodes. It can be seen that the patterns of ECAP amplitudes are predominantly mirrored across the diagonal of the matrix. (right) An example of the corresponding SpeedCAP, $\mathbf{M}_S$, matrix from the same participant. It can be seen that the $\mathbf{M}_0$ and $\mathbf{M}_S$ matrices show similar ECAP patterns.

The second technique reduces the overhead communication time between the testing computer and the implant processor. With the current clinical software used to record ECAPs with Cochlear Limited devices (Custom Sound EP), it takes approximately one second for the software to send the neural response telemetry (NRT) commands to the implant processor, and approximately one additional second to deliver the recorded data from the implant processor back to the computer after recording. Using the NIC2 research software provided by Cochlear Limited (Sydney, Australia), it is possible to collect four groups of each of the four frames required to extract an ECAP

using the forward-masking artefact-cancellation technique at one time. In other words, the A, B, C, and D frames depicted in Figure 2 can be collected from the implant processor for 4 different ECAPs in a single batch. Therefore, the overhead time required to collect ECAP amplitudes can be reduced by 75% using this technique alone. For the 253 ECAPs in the reduced-sized M matrix, the approximately 8.5 minutes of overhead communication time in the 25-minute data acquisition sequence can be reduced to 2 minutes, saving a further 6.5 minutes.

	<i>Masker</i>	<i>Probe</i>	<i>Description</i>
A			Probe Alone
B			Masker and Probe
C			Masker Alone
D			System Signature
ECAP	$A - (B - C) - D$		Forward-Masking Artefact-Cancellation subtraction equation

Figure 2: Graphical representation of the four stimulation frames required to extract the neural response from the stimulus artefacts using the forward-masking artefact-cancellation technique for ECAPs.

Finally, the forward-masking artefact-cancellation technique has various redundant frames when recording ECAPs from many combinations of masker and probe electrodes. For example, when the probe remains on the same electrode and the masker is moved along the array, both the probe-alone frame (A in Figure 2) and the system-signature frame (D in Figure 2) are repeated with exactly the same recording parameters for each ECAP. In order to optimise recording time, these frames are recorded only once and then re-used to extract ECAP waveforms where the masker

is on different electrodes. Combining this technique with the batch-downloading time-saving technique described above, it is possible to record enough frames to calculate 8 ECAP waveforms at one time. This is depicted in Figure 3b, and the standard forward-masking pulse-train sequence is depicted in Figure 3a for reference. This number is limited to 8 ECAPs because the size of the NIC2 buffer only supports transfer of 19 frames of data from the implant processor to the computer at one time. One instance of this 8-ECAP recording sequence takes approximately 14.5 seconds when recording 50 sweeps.

Figure 3: **a)** example pulse-train sequence for recording 4 ECAPs using the standard forward-masking artefact-cancellation technique. Each black line on the y-axis indicates a different electrode on which the biphasic pulses are delivered, and the frame types as described in Figure 2 are labelled on the x-axis, with probe pulses indicated by solid green lines and masker pulses indicated by dashed blue lines. **b)** example pulse-train sequence for recording 8 ECAPs using the forward-masking artefact-cancellation technique and recycling the A and D frames.

Combining the three techniques described, the proposed SpeedCAP recording matrix takes only 8 minutes to record (253 50-sweep ECAPs), instead of the 45 minutes required to record the standard PECAP recording matrix (444 50-sweep ECAPs). Figure 1 (right) shows an example of a SpeedCAP matrix recorded using the techniques described above, and is from the same patient as the standard PECAP *M* matrix shown (Figure 1, left).

Data Collection: Study 1

Participants

Eleven users of Cochlear Limited CI devices were recruited for the study. Informed consent was obtained from each participant in accordance with the International Research Code of Ethics (1990) with care to abide by international standards of ethics (i.e. the Bulletin of the Pan American Health Organization, 24, 604-621) at the MRC Cognition & Brain Sciences Unit in Cambridge, United Kingdom. Permission to conduct the study was granted by the National Research Ethics committee for the East of England (Ref No: A08225), and all participants provided their written consent to participate. They were reimbursed for their travel costs and were compensated for volunteering their time. The participants had a range of aetiologies and device types, and averaged 61 years of age (standard deviation = 13.4 years). Demographic and recording parameter information is listed in Table 1.

ID	Implanted Ear	Age	Aetiology	Device	Electrodes Assessed	ECAP recording gain (dB) / delay (μ s)	ECAP Pulse Width (μ s)	SlowCAP Recording electrode side	SpeedCAP Recording electrode side
C09	Right	69	Hereditary	CI24RE	3 – 21	50 / 98	42	Basal	Basal
C13	Right	57	Maternal rubella and ear infection	CI522	1 – 22	50 / 122	25	Apical	Basal*
C19L	Left	66	Exposure to loud sounds	CI512	1 – 20	50 / 73	42	Apical	Basal*
C26	Right	57	Hereditary	CI522	1 – 22	60 / 122	25	Basal	Basal
C27	Right	71	Progressive Sensorineural	CI512	1 – 21	60 / 98	25	Apical	Apical
C30	Right	71	Measles	CI512	1 – 22	50 / 122	25	Basal	Basal
C31	Right	27	Hereditary	CI622	3 – 22	50 / 73	37	Apical	Apical
C32	Left	66	Meningitis	CI612	1 – 22	50 / 73	37	Apical	Apical
C33	Right	56	Superficial Siderosis	CI622	3 – 22	50 / 98	50	Apical	Apical
C34	Left	70	Progressive	CI24RE	2 – 22	50 / 73	25	Apical	Apical
C35	Right	73	Meniere's Disease	CI622	1 – 22	50 / 98	37	Apical	Apical
* recording paradigm and recording electrode side confounded, and only 1 repeat of SpeedCAP available									

Table 1: Participant information for the post-operative study (Study 1)

Panoramic ECAP Measurements

The standard PECAP matrix was measured for all combinations of masker and probe electrodes active in the participant's clinical MAP at Most Comfortable Levels (MCL). These data were collected as per the methods described in detail in Garcia et al. (2021). Custom software programmed using the NIC2 platform from Cochlear Limited (Sydney, Australia) allowed for the acquisition of four measurement batches of the four frames required to extract an ECAP waveform with the forward-masking artefact-cancellation technique, each with 12 averages for a total of 48 averages (aka sweeps) per masker-probe electrode combination. The sub-sampling of measurements into batches of 12 sweeps allowed us to calculate repeatability metrics. These data, obtained with the method described in Garcia et al. (2021), will be referred to as SlowCAP and M_0 throughout the remainder of this manuscript for brevity.

SpeedCAP measurements were then additionally performed for each participant with the same recording parameters as used for the SlowCAP data (i.e. gain, delay, pulse width, recording electrode side, and current levels) for each electrode. The only exceptions to this were participants C13 and C19L for whom the recording electrode for the SpeedCAP measurements was placed 2 electrodes basal to the probe electrode, whereas for the SlowCAP measurements it was placed 2 electrodes apical to the probe electrode (see Table 1). SpeedCAP was recorded twice for each participant, both times with 50 averages for each ECAP frame, except for participants C13 and C19L from whom only one SpeedCAP recording was obtained. The SpeedCAP data will be abbreviated as M_s throughout the remainder of this manuscript.

Measurements were obtained using custom software programmed in Python (version 2.4.4, Python Software Foundation, United States of America) through the PyCharm IDE interface (Community Edition 2016.1.5, JetBrains, Czech Republic) using the NIC2 research platform (Cochlear Limited, Sydney, Australia). MATLAB R2018a (Mathworks, Natick, Massachusetts, USA) was used to visualize and analyze data using the Panoramic ECAP Method.

Data Collection: Study 2

Participants

Eight severe-to-profoundly deaf patients scheduled to receive cochlear implants from Cochlear Limited were recruited prior to undergoing surgery at Addenbrookes Hospital or the Spire Hospital through the Cambridge University Hospitals Trust. Participants were informed of the nature of the study and provided written consent to participate prior to undergoing their implant surgery. Informed consent was obtained in accordance with the International Research Code of Ethics (1990) with care to abide by international standards of ethics (i.e. Bulletin of the Pan American Health Organization, 24, 604-621). Ethical approval for the study was obtained from HRA and Health and Care Research Wales (HCRW) through University Hospitals NHS Foundations Trust and the University of Cambridge (IRAS ID: 285894, Ref No: A095798, REC Reference: 20/EM/0263). Three participants also took part in Study 1 (C32, C33, C35). Demographic and recording parameter information for these patients is included in Table 2.

ID	Implanted Ear	Age	Aetiology	Device	ECAP recording gain (dB) / delay (µs)	ECAP Pulse Width (µs)	Current Level (CUs)	SpeedCAP Recording electrode side
C32	Left	66	Meningitis	CI612	50 / 73	37	180	Apical
C33	Right	56	Superficial Siderosis	CI622	50 / 98	50	220	Apical
S4	Right	21	Congenital, Progressive	CI622	40 / 98	50	235	Apical
S5	Right	76	Congenital, Progressive	CI622	50 / 98	25	240	Apical
C35	Right	73	Meniere's Disease (L) & Infection (R)	CI622	50 / 98	37	180	Apical
S8	Left	20	Congenital, Unknown	CI622	50 / 73	37	210	Apical
S9	Left	63	Progressive, Unknown	CI522	40 / 98	50	210	Apical
S10	Left	71	Bilateral Meniere's Disease	CI622	40 / 98	37	225	Apical

Table 2: Participant Information for the intra-operative study (Study 2)

Intra-operative ECAP Measurements

After the cochlear implant electrode array was inserted into the cochlea by the surgeon, recording parameters required to elicit a valid ECAP response intra-operatively were determined using Custom Sound EP software (Cochlear Limited, Sydney, Australia). The pulse width, current level, gain, and delay settings required were noted (shown in Table 2). Custom software developed in Python (version 2.4.4, Python Software Foundation, United States of America) and compiled into a stand-alone executable programme was then used to record ECAPs using the parameters determined in Custom Sound EP with equal current level for all 22 electrodes. The first recording consisted of batches of four ECAP waveforms – each an average of 12 sweeps, resulting in 48 sweeps in total – along the diagonal of the PECAP matrix to confirm that valid ECAPs were recorded using the chosen parameters. Once this was complete, the program recorded SpeedCAP in the same manner as described in the previous section but with equal current levels for all electrodes across the implant array instead of equal loudness levels as used for the post-operative ECAPs. Recording SpeedCAP at equal loudness levels was not possible intra-operatively as the patient was under general anaesthesia for the surgical procedure. An advantage was that the current levels used, although necessarily limited by safety considerations, were not limited by the loudness that an awake patient would find comfortable. The entire intra-operative ECAP measurement procedure took approximately 10-15 minutes and was completed at the end of the surgery, prior to awakening the patient from general anaesthesia.

Results

Study 1: Post-Operative comparison between SlowCAP and SpeedCAP

ECAP Measurement Assessment

The SlowCAP and SpeedCAP matrices ($\mathbf{M}_0$ and $\mathbf{M}_S$, respectively) were evaluated for repeatability prior to comparison. To compensate for participant-wise differences in ECAP amplitudes, the root mean squared error (RMSE) between repeat measurements of $\mathbf{M}_0$ and $\mathbf{M}_S$ were normalized by the maximum ECAP amplitude in $\mathbf{M}_0$ and $\mathbf{M}_S$ for each participant, respectively. This allowed us to compare the RMSE values between participants and meant that the RMSE metrics were reported in percentage of the maximum ECAP amplitude instead of micro-Volts (μV).

Equation (1) was used to calculate the normalized within-condition RMSE ε_S for SpeedCAP:

$$\varepsilon_S = \frac{1}{\max(\mathbf{M}_{S1}, \mathbf{M}_{S2})} \cdot \sqrt{(\mathbf{M}_{S1} - \mathbf{M}_{S2})^2} \quad (1)$$

where $\mathbf{M}_{S1}$ is the first SpeedCAP measurement taken and $\mathbf{M}_{S2}$ is the second. The $\mathbf{M}_S$ matrices are made up of full $n \times n$ matrices where n is the number of electrodes assessed for each participant. $M_{p,m}$ represents the ECAP amplitude in the cell of the $\mathbf{M}_S$ matrix that corresponds to the condition where the probe is on electrode p and the masker is on electrode m . The full $\mathbf{M}_S$ matrix is completed with $M_{p,m}$ amplitudes copied across the diagonal to the $M_{m,p}$ locations as the latter are not recorded. This is done for the error calculation because the data must be in this format prior to submission to the PECAP Algorithm.

Equation (2) was used to calculate the normalized within-condition RMSE ε_0 for SlowCAP:

$$\varepsilon_0 = \frac{1}{\sqrt{2} \cdot \max(\mathbf{M}_{0a}, \mathbf{M}_{0b})} \cdot \sqrt{(\mathbf{M}_{0a} - \mathbf{M}_{0b})^2} \quad (2)$$

where $\mathbf{M}_{0a}$ is the matrix of ECAP amplitudes calculated using sweeps 1-24 to form waveforms for each ECAP, and $\mathbf{M}_{0b}$ uses sweeps 25-48. Since halving the number of sweeps increases the measurement noise in the ECAP waveform by a factor of $\sqrt{2}$ (Underraga, et al., 2012; Stronks, et al., 2019), we incorporated this into the calculation so that ε_0 represents the noise in the 48-sweep waveform ECAP amplitudes that make up $\mathbf{M}_0$. To enable a direct comparison between ε_S and ε_0 , both $\mathbf{M}_{0a}$ and $\mathbf{M}_{0b}$ are constructed symmetrically in the same manner as described above for $\mathbf{M}_S$ matrices, including only the $M_{p,m}$ cells with the same masker and probe conditions as the $\mathbf{M}_S$ matrices for each participant. In some cases this consisted of $M_{p,m}$ conditions with the masker located basally to the probe electrode, and in others the masker was located apically to the probe electrode.

SlowCAP ($\mathbf{M}_0$) and SpeedCAP ($\mathbf{M}_S$) were then compared by calculating the normalized between-condition RMSE using equation (3):

$$\varepsilon_{0,S} = \frac{1}{\max(\mathbf{M}_0, \mathbf{M}_S)} \cdot \sqrt{(\mathbf{M}_0 - \mathbf{M}_S)^2} \quad (3)$$

where $\mathbf{M}_0$ consists only of $M_{p,m}$ cells with the same masker and probe conditions as $\mathbf{M}_S$, calculated from the full 48-sweep waveforms.

Our assumption that recording only part of the $\mathbf{M}$ matrix does not introduce significant error is additionally evaluated below using equation (4):

$$\varepsilon_{sym} = \frac{1}{\max(\mathbf{M}_{0,asym}, \mathbf{M}_{0,sym})} \cdot \sqrt{(\mathbf{M}_{0,asym} - \mathbf{M}_{0,sym})^2} \quad (4)$$

where $\mathbf{M}_{0,asym}$ is the SlowCAP ($\mathbf{M}_0$) matrix using all 48-sweep ECAP waveforms recorded from every combination of masker and probe electrode, and $\mathbf{M}_{0,sym}$ is the same SlowCAP ($\mathbf{M}_0$) made symmetric across the diagonal according to equation (5):

$$\mathbf{M}_{0,sym} = \frac{\mathbf{M}_{0,asym} + \mathbf{M}'_{0,asym}}{2} \quad (5)$$

where $\mathbf{M}'_{0,asym}$ is the transposition of $\mathbf{M}_{0,asym}$. $\mathbf{M}_{0,sym}$ is the format of the data nominally submitted to the Panoramic ECAP algorithm (Garcia, et al., 2021) and therefore ε_{sym} is of interest when considering the practical implications of implementing SpeedCAP in addition to assessing the symmetry assumption.

The ε_0 , ε_S , $\varepsilon_{0,S}$, and ε_{sym} values for each participant are shown in Table 3, as well as graphically depicted in Figure 4. Since only one $\mathbf{M}_S$ was available for participants C13 and C19L, it was not possible to calculate ε_S for them and as such they were excluded from further analysis. A one-way analysis of variance (ANOVA) was conducted using MATLAB 2018a between the four ε metrics for the remaining 9 participants. After correcting for multiple comparisons using the Bonferroni-Dunn method, neither ε_0 , ε_S , $\varepsilon_{0,S}$, nor ε_{sym} significantly differed from each other ($p = 0.131$, $df = 3$, $F = 2.02$).

Participant	RMSE (%)			
	SlowCAP (ε_0)	SpeedCAP (ε_S)	Comparison ($\varepsilon_{0,S}$)	SlowCAP Symmetry (ε_{sym})
C09	1.96	1.72	2.26	5.00
C13	5.46	n/a	7.71	3.91
C19L	3.38	n/a	7.37	3.64
C26	6.07	9.04	8.73	4.54
C27	4.76	5.52	7.54	4.06
C30	6.07	6.61	6.61	4.15
C31	1.71	2.32	7.02	2.82
C32	1.82	2.61	4.89	3.75
C33	5.63	8.78	20.75	7.56
C34	1.32	2.21	4.00	3.20
C35	2.35	2.15	2.87	2.84
Across	3.52 ± 1.60	4.55 ± 2.29	7.19 ± 4.25	4.12 ± 1.12

Table 3: RMSEs for post-operative SlowCAP (M_0) and SpeedCAP (M_S), calculated as described in equations (1), (2), (3), and (4). The ‘Across’ metrics are the means of the RMSEs for all participants except C13 and C19L, $\pm$ 95% confidence intervals. (n/a = not applicable)

95% confidence intervals were calculated for the mean difference in RMSE between each of the four ε metrics, resulting in six overall comparisons. After correcting for multiple comparisons, the highest upper 95% confidence limit was 8.23% and resulted from the comparison between $\varepsilon_{0,S}$ and ε_0 . This indicates that while the ANOVA showed no evidence for statistically significant differences between ε_0 , ε_S , $\varepsilon_{0,S}$, nor ε_{sym} , the data suggests that in 95% of future cases, differences between any of the metrics would be smaller than 8.23%. Therefore it can be concluded that replacing SlowCAP with the SpeedCAP method of measuring ECAPs introduces no more than 8.23% error in ECAP amplitudes.

Figure 4: RMSEs for repeatability of SlowCAP (ϵ_0) and SpeedCAP (ϵ_s) data, as well as for the comparison of the two ECAP recording paradigms ($\epsilon_{0,s}$) and the symmetry assumption (ϵ_{sym}). The right-most column shows the across-participant means for each of the four error metrics for each of the 9 participants included in the ANOVA (this excludes C13 and C19L), none of which are statistically significant from each other. The error bars indicate 95% confidence intervals around the mean.

Neural Activation Patterns Assessment

SlowCAP (M_0) and SpeedCAP (M_s) data were then submitted to the PECAP algorithm described in Garcia et al. (2021). Note that for this analysis, M_0 is the symmetric version of SlowCAP ($M_{0,sym}$) obtained using equation (5) and that is nominally submitted to the PECAP algorithm. This section therefore evaluates the practical implications on the PECAP algorithm of replacing SlowCAP with the SpeedCAP method. Estimates of current spread and neural health along the cochlea were calculated for each participant using either M_0 or M_s . The results of the PECAP algorithm are shown in Figure 5 for each of the 11 participants, with the dashed black lines representing the current spread (σ) and neural health (η) estimates when M_0 was submitted to the PECAP algorithm, and the solid blue lines representing the estimates when M_s was submitted to the PECAP algorithm. With the exception of C33, the patterns of the current spread and neural health estimates generally agree between the two conditions.

Figure 5: Current Spread (σ) and Neural Health (η) estimates from the PECAP algorithm using SlowCAP (M_0) measurements indicated by the dashed black lines, and SpeedCAP (M_S) measurements indicated by the solid blue lines.

Across-electrode, within-participant correlations between neural health estimates for M_0 vs M_S were significant in 10 of 11 cases with pearson r-values ranging from 0.59 to 0.97. There was only one case, participant C33, for whom there was no significant for the neural health estimate. Across-electrode, within participant correlations between current spread estimates for M_0 vs M_S were significant in 8 of 11 cases with pearson r-values ranging from 0.51 to 0.96. There were no significant correlations for the current spread estimates for participants C31, C33, and C34. Across all electrodes with between-participant differences removed, both the neural health ($r = 0.73$, $p < 0.0001$, $df = 218$) and current spread ($r = 0.65$, $p < 0.0001$, $df = 218$) estimates were significantly correlated between the SlowCAP and SpeedCAP conditions. Table 4 contains details of correlation coefficients and p-values for all within- and across-participant comparisons, and Figure 6 shows the correlations for the neural health and the current spread estimates between M_0 vs M_S across all electrodes.

Subject	Current Spread (σ)		Neural Health (η)	
	<i>r-value</i>	<i>p-value</i>	<i>r-value</i>	<i>p-value</i>
C09	0.51	0.026	0.81	***
C13	0.96	***	0.91	***
C19L	0.96	***	0.83	***
C26	0.90	***	0.59	0.004
C27	0.55	0.009	0.70	**
C30	0.98	***	0.81	***
C31	0.26	0.26	0.98	***
C32	0.61	0.003	0.90	***
C33	0.08	0.75	-0.15	0.52
C34	0.19	0.42	0.96	***
C35	0.53	0.011	0.92	***
ALL	0.65	***	0.73	***

Table 4: Correlation coefficients and p-values for the current spread (σ) and neural health (η) estimates from PECAP between the M_0 and M_S data. Significant r-values are shown in **bold**. (**p<0.001, ***p<0.0001)

Figure 6: Across-electrode correlations for the (left) current spread (σ) and (right) neural health (η) estimates from PECAP between the M_0 and M_S data with between-participant differences removed.

In addition to the correlation analysis between the SlowCAP and SpeedCAP conditions, the average signed error was calculated for the current spread (σ) and neural health (η) estimates to investigate whether there were trends of over- or under-estimation when using SpeedCAP as opposed to SlowCAP data. The results can be seen in Figure 7. The across-participant mean signed differences were not statistically significant from 0 for current spread ($p = 0.29$, $df = 1$, $F = 1.18$) nor for neural health ($p = 0.52$, $df = 1$, $F = 0.43$), providing no evidence to support the hypothesis that SpeedCAP data either over- or under-estimated ECAP neural activation estimates compared to SlowCAP data.

Figure 7: Mean signed differences for the (top) current spread (σ) and (bottom) neural health (η) estimates from PECAP between the M_0 and M_S data. The error bars represent the 95% confidence intervals around the means. For both metrics, positive values indicate $\sigma_0 > \sigma_S$ or $\eta_0 > \eta_S$ where σ_0 and η_0 are the current spread and neural health estimates from the PECAP algorithm using SlowCAP (M_0) data, and σ_S and η_S are the current spread and neural health estimates from the PECAP algorithm using SpeedCAP (M_S) data.

Study 2: Intra-Operative SpeedCAP Robustness

Diagonal ECAP Measurement Assessment

The limited time available during surgery made it impossible to collect multiple M_S datasets intra-operatively. However, repeat measures of the ECAPs along the diagonal of the PECAP matrix could be collected. Therefore, it was possible to calculate ε_0 and $\varepsilon_{0,S}$ for the intra-operative data using only ECAPs from conditions where the probe and masker used the same electrode (the diagonal of the PECAP matrix). The intra-operative ECAP measurements along the diagonal will be referred to as D_0 , and the diagonal of the intra-operative SpeedCAP data will be referred to as D_S . Due to the reduced number of ECAPs available to calculate the repeatability and reliability metrics for the intra-operative dataset, a subscript ε_d is used to indicate that only the diagonal and not the entirety of the PECAP matrix was included.

The equation to calculate the error for the intra-operative SlowCAP diagonal (D_0) is displayed in equation (6):

$$\varepsilon_{d0} = \frac{1}{\sqrt{2} \cdot \max(D_{0a}, D_{0b})} \cdot \sqrt{(D_{0a} - D_{0b})^2} \quad (6)$$

where D_{0a} is a vector of ECAP amplitudes along the diagonal calculated using sweeps 1-24 of each ECAP, and D_{0b} using sweeps 25-48 of each ECAP. Data were not available to calculate the ε_{dS} metric corresponding to the post-operative ε_S (equation 1), but the equation for the between-condition RMSE for the intra-operative data using both D_0 and D_S is displayed in equation (7):

$$\varepsilon_{d0,s} = \frac{1}{\max(D_0, D_S)} \cdot \sqrt{(D_0 - D_S)^2} \quad (7)$$

where D_0 and D_S ECAP amplitudes are calculated using the full 48-sweep waveforms.

The ε_{d0} and $\varepsilon_{d0,s}$ values for each intra-operative participant are included in Table 5, as well as graphically depicted in Figure 8. A paired-sample t-test was conducted using MATLAB 2018a between the two metrics and did not reveal a significant difference ($p = 0.174$, $t\text{-stat} = 1.52$, $df = 7$, $95\% \text{ CI} = -4.46$ to 20.29).

Figure 8: ε_{d0} and $\varepsilon_{d0,s}$ for intra-operative datasets, calculated using the Diagonal of the ECAP matrices only. The right-most column shows the across-participant means for each of the two ε metrics. No significant difference was detectable between the two groups. The error bars indicate 95% confidence intervals around the mean.

Participant	RMSE (%)	
	SlowCAP (ε_{d0})	Comparison ($\varepsilon_{d0,s}$)
C32	2.82	14.00
C33	8.53	51.38
S4	11.76	7.52
S5	1.60	5.43
C35	0.66	2.59
S8	0.76	6.69
S9	2.17	2.95
S10	2.76	3.81
Across	3.88 ± 3.40	11.80 ± 13.72

Table 5: ε_{d0} and $\varepsilon_{d0,s}$ for intra-operative datasets, calculated using the Diagonal of the ECAP matrices only (D_0 and D_S for SlowCAP and SpeedCAP, respectively). The 'Across' metrics are the means of the RMSEs for all participants, $\pm$ 95% confidence intervals.

Post-Operative vs Intra-Operative ECAP Errors

A further analysis was done to compare the ε_0 and $\varepsilon_{0,S}$ for the post-operative datasets to the corresponding ε_{d0} and $\varepsilon_{d0,S}$ for the intra-operative datasets. The motivation for this comparison was to determine whether reliability of the D_S and D_0 data was significantly lower intra-operatively compared to the post-operative M_S and M_0 data.

Neither of the comparable error metrics were significantly different from each other intra- vs post-operatively. A one-way ANOVA was performed between ε_0 and ε_{d0} and resulted in a non-significant result ($p = 0.89$, $df = 1$, $F = 0.02$, $n_1 = 11$, $n_2 = 8$). A second one-way ANOVA was performed between $\varepsilon_{0,S}$ and $\varepsilon_{d0,S}$ and also resulted in a non-significant result ($p = 0.39$, $df = 1$, $F = 0.76$, $n_1 = 11$, $n_2 = 8$).

However, as these were across-participant as opposed to within-participant analyses, these two comparisons had relatively low statistical power compared to the other statistical tests calculated in these studies. Using G*Power software (version 3.1.9.2, Aichach, Germany), it was determined that the data had 80% power to detect an effect size of a Cohen's d equal to 1.2. Therefore, while no evidence was available to suggest that there were significant differences in the ε metrics intra- vs post-operatively, the data only had power to detect differences larger than 3.5% RMSEs for the ε_0 metrics and 13.3% RMSEs for the $\varepsilon_{0,S}$ metrics.

Discussion

Robustness of SpeedCAP as an ECAP Recording Technique

The analysis of variance in the SpeedCAP recording technique in comparison to the standard ECAP recording paradigm for the Panoramic ECAP measurement methods showed no evidence for a difference in repeatability of the ECAP amplitudes calculated from SpeedCAP data compared to the standard recording paradigm. This suggests that for this group of participants the reliability and repeatability of ECAP amplitudes using the SpeedCAP method is, practically speaking, equivalent to (or no more than 8.23% different from) the standard recording paradigm for most purposes. The analysis also showed no evidence for a difference between the repeatability metrics for either SpeedCAP (ε_S) or SlowCAP (ε_0) and the comparison metric ($\varepsilon_{0,S}$). This suggests that no statistically significant error in ECAP amplitudes is incorporated when replacing the standard ECAP recording paradigm with the faster SpeedCAP method. In addition to this, the analysis showed no evidence for a difference between either of the repeatability metrics (ε_S , ε_0) nor the comparison metrics $\varepsilon_{0,S}$ and the error incorporated when the standard SlowCAP data is made symmetrical for submission to the Panoramic ECAP algorithm (ε_{sym}). Therefore, replacing SlowCAP with SpeedCAP introduces no more error to the ECAP amplitudes than this standard symmetricalization of M_0 already implemented by Garcia et al (2021) for estimation of neural health and current spread using the PECAP algorithm.

There was one participant in the dataset for whom the $\varepsilon_{0,S}$ metric visually appeared to be an outlier. For this participant, C33, the repeatability metrics for both SpeedCAP

(ε_s) and SlowCAP (ε_0) did *not* appear to be outliers, suggesting that significant, reliable differences in the ECAP amplitudes *would* be present between SpeedCAP and SlowCAP. It's possible that this difference could be due to C33's particular aetiology; superficial siderosis is a rare condition in which hemosiderin is deposited on the pial surface of the brain. This condition presents commonly with atrophy of neural tissue, and could mean that the peripheral auditory nerves take longer to recover from stimulation than with normal hearing or other hearing-related conditions (Kumar, 2007). The primary difference in stimulation patterns between SlowCAP and SpeedCAP is that SpeedCAP stimulates more areas of neural tissue along the length of the cochlea in quicker succession than in SlowCAP. The stimulation rate of 80 pulses per second (pps) for both SlowCAP and SpeedCAP allows the stimulated areas of neural tissue to recover from a refractory state between successive ECAP recording frames under normal circumstances, but in the presence of siderosis there may be other longer-term temporal properties of the neural tissue that elongate refractory periods or mean they may need longer to fully recover between successive stimulation for other reasons. There are other conditions, such as cochlear nerve deficiency (CND), where the pulse rate is often slowed down to 15-20 pps from the standard 80 pps for ECAP recording in order to allow the neural tissue more time to recover between stimulation frames due to longer absolute refractory periods (He, et. al., 2016; Xu, et al., 2020; Zhan, et al., 2021). In such cases and with other hearing pathologies that elongate the temporal recovery properties of the auditory nerve, SpeedCAP may not be practically equivalent to standard recording techniques for ECAPs.

Use of SpeedCAP for Estimating Neural Activation Patterns

High and significant correlations for the neural health (η) and current spread (σ) estimates between the SpeedCAP (M_s) and SlowCAP (M_0) conditions suggest that similar neural activation patterns can be estimated using the Panoramic ECAP Method described by Garcia et al (2021) when using the SpeedCAP method for collecting these data instead of the standard recording paradigm. More of the individual participant correlations were significant between conditions for the neural health estimate (10 of 11 participants) than for the current spread estimate (8 of 11 participants), suggesting that employing the faster data-collection procedure may slightly sacrifice accuracy in current-spread estimates. One participant showed no significant correlation for the neural health nor current spread estimates between the SpeedCAP and SlowCAP methods, providing an exception to our general conclusion that SpeedCAP is a suitable method for measuring neural activation patterns in CI patients. However, it can be seen that the patterns of neural health and current spread appear to be quite similar for SpeedCAP and SlowCAP for the other participants, suggesting that in most cases, SpeedCAP data can be used to estimate neural activation patterns in cochlear implant users using the Garcia et al (2021) method.

Feasibility of Intra-Operative SpeedCAP

The second study showed that it was feasible to record viable ECAPs using SpeedCAP intra-operatively, after the electrode array was in place in the cochlea, prior to awakening the patient from general anaesthesia. No evidence was found for a difference between the repeatability of the intra-operative SlowCAP measures of the diagonal (ε_{d0}) and the comparison metric between these data and the diagonal of the intra-operative SpeedCAP measures ($\varepsilon_{d0,S}$), consistent with the post-operative analysis in the first study. The data also show that if a difference did exist it would be below 20.29% RMSE. This suggests that the assumption that no practical difference exists between SlowCAP and SpeedCAP measures holds true for intra-operative measurements in addition to post-operative ones.

There was also no evidence that recording SlowCAP or SpeedCAP intra-operatively led to any difference in repeatability or comparison metrics compared to post-operative data, further supporting reliability and feasibility of intra-operative SpeedCAP measurements. However, future work investigating intra- vs post-operative SpeedCAP data is underway and will investigate any potential differences with greater statistical power in order to assess feasibility of estimating neural activation patterns using intra-operative SpeedCAP data and transform the Panoramic ECAP method into a fully-objective tool.

Clinical Implications

The time savings involved with the SpeedCAP method for recording ECAPs compared to SlowCAP has substantial implications for the clinical viability of the Panoramic ECAP method. In many scientific fields, speeding up the process of collecting data is a 'nice-to-have' aspect of the research methods. However, time is of the essence for the clinical application of new techniques, and resources are both costly and limited in the clinic. Therefore, long measurements such as the 45 minutes that were previously required to collect data for the Panoramic ECAP Method are prohibitively long to be a viable diagnostic tool that could be used in routine clinical practice. The 8-minute SpeedCAP data collection method is sufficiently quick such that these data can now be collected in the clinic without requiring additional resources, and can be collected intra-operatively without adding significant time to the surgical procedures. This transforms the Panoramic ECAP method from a research-exclusive tool into a method ready for use in clinical environments, and opens up new possibilities for assessing the CI electrode-nerve interface and for applying precision medicine approaches such as PECAP to cochlear implant healthcare.

In addition to transforming PECAP into a clinically-viable tool, similar principles to SpeedCAP for obtaining quicker recordings of otherwise uncollectable data due to time-constraints could be applied to other measurement procedures. For example, any research study that utilizes intra-operative ECAP measures (e.g. Söderqvist et al., 2021) could benefit from collecting all Spread of Excitation functions of interest instead of being restricted in their data collection by limited time in the operating theatre. Of course this is not limited to the operating theatre; even in research settings where

multiple hours are available for data collection from cochlear implant research volunteers, collecting ECAP data in a more efficient way allows for more conditions to be evaluated without extending research time.

Conclusion

SpeedCAP, a new, more efficient method for measuring multiple ECAPs using the forward-masking artefact-cancellation technique, has been presented and validated against the standard ECAP recording paradigm. This method takes only 8 minutes to record in Cochlear Limited cochlear implant devices instead of 45 minutes, and transforms the Panoramic ECAP method for estimating patient-specific neural activation patterns from a research laboratory method into a clinically viable tool. While further work is required to establish this transition, practically speaking, SpeedCAP appears to be broadly-equivalent to the standard recording paradigm for calculating ECAP amplitudes and estimating patient-specific neural activation patterns. The quality of these data recorded intra-operatively was similar to post-operative data. As well as providing methods that open up more possibilities in clinical environments to assess neural responsiveness using ECAPs and ask more detailed research questions, this is a step forward in development of clinically-viable diagnostic tools for precision medicine in cochlear implant healthcare, and may lead to better insights into stimulation patterns for optimizing fitting and CI patient outcomes.

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Author Contribution

The primary bulk of the work done for this study was carried out by primary author, Charlotte Garcia, including the methodological approaches and experiment programming for the methods, the data collection, analysis, and the majority of the writing for the manuscript. John M Deeks provided training and input for experimental programming, collected the data for a few of the intra-operative datasets, and provided comments on the manuscript. Tobias Goehring provided analysis advice and comments on the manuscript. Daniele Borsetto and Manohar Bance were instrumental with patient recruitment and facilitating intra-operative data collection for Study 2. Robert P Carlyon guided and directed study design and statistical analysis, as well as providing major contributions to the manuscript.

Bibliography

- Abbas, P., Brown, C., Shalloo, J., Friszt, J., Hughes, M., Hong, S., & Staller, S. (1999). Summary of results using the nucleus CI24M implant to record the electrically evoked compound action potential. *Ear & Hearing*, 45-59.
- Biesheuvel, J., Briare, J., & Frijns, J. (2016). A novel algorithm to derive spread of excitation based on deconvolution. *Ear & Hearing*, 572-581.
- Brown, C., Abbas, P., & Gantz, B. (1990). Electrically evoked whole-nerve action potentials: Data from human cochlear implant users. *Journal of the Acoustical Society of America*, 2205-2210.
- Brown, C., Abbas, P., Fryauf-Bertschy, H., Kelsay, D., & Gantz, B. (1994). Intraoperative and postoperative electrically evoked auditory brain stem responses in nucleus cochlear implant users: implications for the fitting process. *Ear & Hearing*, 168-176.
- Carlyon, R. P., & Goehring, T. (2021). Cochlear Implant Research and Development in the Twenty-first Century: A Critical Update. *Journal of the Association for Research in Otolaryngology*. doi:10.1007/s10162-021-00811-5
- Charlet de Sauvage, R., Cazals, Y., Erre, J.-P., & Aran, J.-M. (1983). Acoustically derived auditory nerve action potential evoked by electrical stimulation: An estimation of the waveform of a single unit contribution. *Journal of the Acoustical Society of America*, 616-627.
- Cohen, L., Richardson, L., Saunders, E., & Cowan, R. (2003). Spatial spread of neural excitation in cochlear implant recipients: comparison of improved ECAP method and psychophysical forward masking. *Hearing Research*, 72-87.
- Cosentino, S., Gaudrain, E., Deeks, J., & Carlyon, R. (2015). Multistage nonlinear optimization to recover neural activation patterns from evoked compound action potentials of cochlear implant users. *IEEE Transactions on Biomedical Engineering*, 833-840.
- de Vos, J. J., Biesheuvel, J. D., Briare, J. J., Boot, P. S., van Gendt, M. J., Dekkers, O. M., . . . Frijns, J. H. (2018). Use of Electrically Evoked Compound Action Potentials for Cochlear Implant Fitting: A Systematic Review. *Ear & Hearing*, 39(3), 401-411.
- Friszt, J., Holden, L., Skinner, M., Tobey, E., Peterson, A., Gaggl, W., & Wackym, P. (2004). Recognition of speech presented at soft to loud levels by adult cochlear implant recipients of three cochlear implant systems. *Ear & Hearing*, 375-387.
- Friesen, L., Shannon, R., Baskent, D., & Wang, X. (2001). Speech recognition in noise as a function of the number of spectral channels: Comparison of acoustic hearing and cochlear implants. *Journal of the Acoustical Society of America*, 1150-1163.
- Garcia, C., Goehring, T., Cosentino, S., Turner, R., Deeks, J., Brochier, T., . . . Carlyon, R. (2021). The Panoramic ECAP Method: Estimating Patient-Specific Patterns of Current Spread and Neural Health in Cochlear Implant Users. *Journal of the Association for Research in Otolaryngology*.
- Hall III, J. (1992). *Handbook of auditory evoked responses*. Boston, MA: Allyn and Bacon.
- He, S., Abbas, P. J., Doyle, D. V., McFayden, T. C., & Mulherin, S. (2016). Temporal Response Properties of the Auditory Nerve in Implanted Children with Auditory Neuropathy Spectrum Disorder and Implanted Children with Sensorineural Hearing Loss. *Ear & Hearing*, 37(4), 397-411.

- Kim, J.-R., Abbas, P. J., Brown, C. J., Etler, C. P., O'Brien, S., & Kim, L.-S. (2010). The Relationship Between Electrically Evoked Compound Action Potential and Speech Perception: A Study in Cochlear Implant Users With Short Electrode Array. *Otology & Neurotology*, 1041-1048.
- Kim, J.-R., Tejani, V. D., Abbas, P. J., & Brown, C. J. (2017). Intracochlear Recordings of Acoustically and Electrically Evoked Potentials in Nucleus Hybrid L24 Cochlear Implant Users and Their Relationship to Speech Perception. *Frontiers in Neuroscience*, 11.
- Kumar, N. (2007). Superficial Siderosis. *Journal of the American Medical Association Neurology*, 64, 491-496.
- Lazard, D. S., Vincent, C., Venail, F., Van de Heyning, P., Truy, E., Sterkers, O., . . . Blamey, P. J. (2012). Pre-, Per- and Postoperative Factors Affecting Performance of Postlingually Deaf Adults Using Cochlear Implants: A New Conceptual Model over Time. *PLOS One*, 7(11).
- Long, C., Holden, T., McClelland, G., Parkinson, W., Shelton, C., Kendall, D., & Smith, Z. (2014). Examining the electro-neural interface of cochlear implant users using psychophysics, CT scans, and speech understanding. *Journal of the Association for Research in Otolaryngology*, 293-304.
- Pfingst, B., Zhou, N., Colsea, D., Watts, M. S., Garadat, S., & Zwolan, T. (2015). Importance of cochlear implant health for implant function. *Hearing Research*, 77-88.
- Prado-Guitierrez, P., Fewster, L., Heasman, J., McKay, C., & Shepherd, R. (2006). Effect of interphase gap and pulse duration on electrically evoked potentials is correlated with auditory nerve survival. *Hearing Research*, 47-55.
- Ramekers, D., Versnel, H., Strahl, S., Smeets, E., Klis, S., & Grolman, W. (2014). Auditory-nerve responses to varied inter-phase gap and phase duration of the electric pulse stimulus as predictors for neuronal degeneration. *Journal of the Association for Research in Otolaryngology*, 187-222.
- Scheperle, R. A., & Abbas, P. J. (2015). Relationships Among Perihelical and Central Electrophysiological Measures of Spatial and Spectral Selectivity and Speech Perception in Cochlear Implant Users. *Ear & Hearing*, 36(4), 441-453.
- Schwartz-Leyzac, K. C., & Pfingst, B. E. (2018). Assessing the Relationship Between the Electrically Evoked Compound Action Potential and Speech Recognition Abilities in Bilateral Cochlear Implant Recipients. *Ear & Hearing*, 39(2), 344-358.
- Söderqvist, S., Lamminmäki, S., Aarnisalo, A., Hirvonen, T., Sinkkonen, S. T., & Sivonen, V. (2021). Intraoperative transimpedance and spread of excitation profile correlations with a lateral-wall cochlear implant electrode array. *Hearing Research*, 405, 108235. doi:<https://doi.org/10.1016/j.heares.2021.108235>
- Stronks, H., Biesheuvel, J., de Vos, J., Boot, M., Briare, J., & Frijns, J. (2019). Test/Retest Variability of the eCAP Threshold in Advanced Bionics Cochlear Implant Users. *Ear & Hearing*, 1457-1466.
- Underraga, J., Carlyon, R., Wouters, J., & van Wieringen, A. (2012). Evaluating the noise in the electrically evoked compound action potential measurements in cochlear implants. *IEEE Transactions in Biomedical Engineering*, 1912-1923.
- Xu, L., Skidmore, J., Luo, J., Chao, X., Wang, R., Wang, H., & He, S. (2020). The effect of pulse polarity on neural response of the electrically-stimulated cochlear nerve in children with cochlear

nerve deficiency and children with normal-sized cochlear nerves. *Ear & Hearing*, 41(5), 1306-1319.

Zhan, K. Y., Adunka, O. F., Eshraghi, A., Riggs, W. J., Prentiss, S. M., Yan, D., . . . He, S. (2021). Electrophysiology and genetic testing in the precision medicine of congenital deafness: A review. *Journal of Otology*, 16, 40-46.