

REVIEW ARTICLE

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# Electrically evoked auditory brainstem response in cochlear implantation: what you need to know (short review)

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## Abstract

**Background:** Electrically evoked auditory brainstem response (E-ABR) is an evoked potential recorded from the auditory nerve in response to electric stimulation. It is considered a short latency evoked potential. It plays a vital role, especially after the increased number of cochlear implant receivers.

**Body of abstract:** E-ABR is characterized by three positive peaks (eII, eIII, and eV) generated from the auditory nerve, cochlear nucleus, and perhaps from neurons in the lateral lemniscus or inferior colliculus. The largest is corresponding to wave V of the acoustic one. There are differences between both acoustic auditory brainstem response (A-ABR) and E-ABR. E-ABR is characterized by larger amplitudes and shorter latencies than the acoustic, and it has a steeper latency-intensity function. There are many variables affecting the E-ABR waveform, including recording-related variables, stimulus-related variables, and subject-related variables. E-ABR has potential clinical applications in cochlear implants (pre, inter, and postoperative).

**Conclusion:** After the increase in the number of cochlear implant receivers, E-ABR provides a promising new tool that can be used to evaluate auditory nerve functions. A lot of factors affect its waveform, including recording-related factors and stimulus-related and subject-related variables. E-ABR has many clinical applications, not only in post-implantation situations but also in preimplantation.

**Keywords:** Acoustic auditory brainstem response (A-ABR), Electrically evoked auditory brainstem response (E-ABR), Cochlear implant (CI)

## Background

Electrically evoked auditory brainstem response (E-ABR)—like acoustic evoked auditory brainstem response ABR (A-ABR)—is a short latency-evoked potential that occurs within 0–10 ms of abrupt stimulus onset. E-ABR is characterized by three positive peaks (eII, eIII, and eV) generated from the auditory nerve, cochlear nucleus, and perhaps from neurons in the lateral lemniscus or inferior colliculus. [1]. The standard response

waveform of E-ABR consists of two to three waves with the largest corresponding to wave V of the (A-ABR) [2]. Wave I is usually hidden by stimulus artifacts and preamplifier distortion [3].

## Electrical ABR versus acoustic ABR

### General differences between electrical and acoustic stimulations

Electrical stimulation of the auditory nerve by cochlear implants induces a pattern of activity that is different from acoustic stimulation in the normal ear.

In normal ears, acoustic stimulation generates traveling waves that progress from the base of the cochlea toward the apex. That in turn will generate receptor potential which leads to the activation of the primary

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fibers through synapses. All these processes are bypassed in electrical stimulation of the cochlea in implanted deaf individuals [4].

The auditory nerve fibers are sharply tuned to the acoustic stimuli than to the electric stimulation. Moreover, the phase-locking occurs to the acoustic sine wave to the positive phase of the acoustic stimulation, while it occurs at the peak of the negative phase with the electric stimulation but is more precise to the latter one [5, 6].

The dynamic range with electrical stimulation is much less than that induced by acoustic stimulation. The normal activation of auditory nerve fibres involves the excitation of inner hair cells; that is why it has a large dynamic range. On the other hand, with electrical stimulation, the operation is mediated through bypassing the IHC activation. Accordingly, it has a narrow dynamic range [4]. Furthermore, the maximum firing rate and the spread of excitation within the auditory nerve are much larger for electrical stimulation than for normal acoustic stimulation [4].

#### Latency

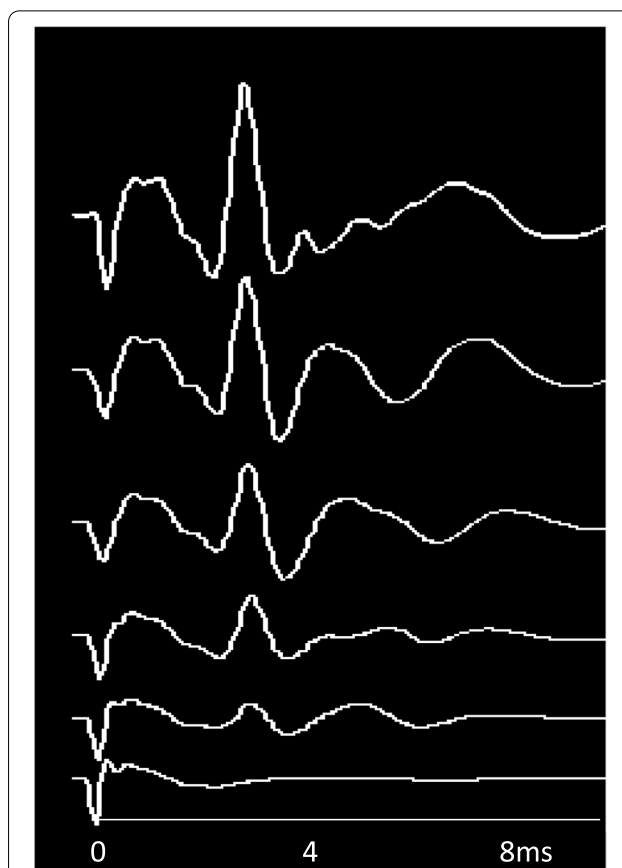
It was suggested that neural synchrony for electric-evoked potential recordings in CI patients is greater than that for acoustic stimulation in normal-hearing individuals because the auditory nerve is directly stimulated with a rapid-onset electrical pulse [7]. With the absence of delays mediated by mechanical wave propagation, sensory cell transduction, and synaptic excitation of the primary afferent neurons, E-ABR absolute wave latencies are shorter than those of A-ABR. Wang et al. reported that the absolute latencies of E-ABR were 1–2 ms shorter than the acoustic ABR latencies, while III–V intervals remained the same as that of acoustic ABR [8].

#### Latency/intensity function

The E-ABR waveform pattern is like that of A-ABRs but with a steeper latency-intensity function [8]. With A-ABR, wave latencies decrease with increasing stimulus intensity as much as 2 ms between threshold and saturation [9], while with E-ABR, latencies change slightly [10, 11] (Fig. 1).

#### Amplitude

E-ABR yields larger responses than those of A-ABR. The fibers that respond synchronously to the click stimulation are mostly from the base of the cochlea [12], whereas with electric stimulation, all excited fibers respond synchronously [10] (Fig. 1).



**Fig. 1** The E-ABR response was obtained from an apical electrode in one animal (a guinea pig) in response to a biphasic pulse. The stimulation level was lowered until the last repeatable and detectable wave (threshold) was obtained. The latency shift with the decrease in stimulation level (SL) was minimal, while the amplitude change was remarkable. Permission was taken from Nada et al. [11]

### Variables affecting E-ABR

#### Recording factors

##### *Ipsilateral versus contralateral mastoid*

E-ABR waves recorded on the same side had shifted baseline, and the artifacts were much larger than those obtained on the contralateral side [8]. So, it should be recorded from the contralateral side.

##### *Stimulus artifact*

Stimulus artifact usually affects the E-ABR recordings. This artifact is due to preamplifier distortion [2, 3]. A lot of trials were developed to overcome such complications, such as recording from the contralateral mastoid and using short biphasic pulses [13, 14]. Another possibility for this artifact is the presence of radiofrequency signals used to send information to the internal device of CI [15]. A filter for radiofrequency is often needed to successfully record target responses [2, 16, 17].

Other artifacts that can interfere with E-ABR recording involve non-auditory sensations, facial nerve stimulation, muscle artifact, and vestibular artifacts [14, 18]. In humans, facial muscle artifact has a large amplitude, grows rapidly with increased stimulus intensity, and has latency between 5 and 10 ms [14].

#### Band-pass filter

Initially, van den Honert et al. reported that the outcome of E-ABR morphology was distorted, and there was a shift in the baseline when using a bandwidth between 100 and 3 kHz. This E-ABR morphology was enhanced after setting the band-pass filter between 300 Hz and 10 kHz [14].

Later, Wang et al. [8] studied the effect of different manipulations of band-pass filter on the E-ABR. They found that the manipulation of the low cutoff frequency (100 down to 0.002 Hz) while keeping the high cutoff frequency at 3 kHz did not affect the E-ABR wave V. On the contrary, while keeping the low-frequency cutoff frequency at 100 Hz with setting the high cutoff frequency below 3 kHz, prolongation of wave V took place. While with setting the high cutoff frequency higher than 3 kHz, the wave V latency was stable. Moreover, there were more obvious noises affecting the waveform when the high cutoff frequency changed from 10 to 25 kHz [8].

#### Monopolar versus bipolar

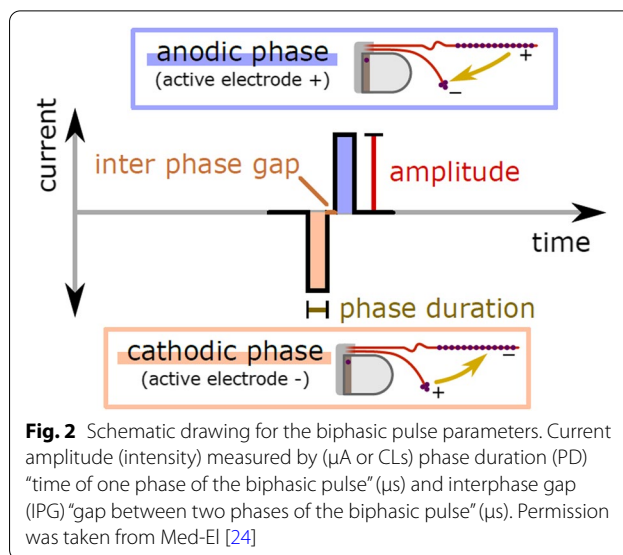
In the monopolar (MP) mode, the active electrode is an electrode on the electrode array, while the reference electrode is located on an electrode lead separated from the active electrodes and/or within the implant housing [19].

In the bipolar (BP) mode, an electrode next to the active electrode serves as the reference electrode. While the BP mode provides more focused stimulation than the MP mode, the MP mode has proven superiority mainly because the BP mode requires higher stimulation levels that slow down the stimulation rate. As the BP configuration widens, the number of stimulated channels decreases [20].

The effect of stimulation mode on the E-ABR was studied, and the results showed that thresholds tended to be lower with steeper amplitude growth function (AGF) in the case of monopolar stimulation [21, 22]. This was also proven in single nerve studies [10]. It was assumed that the steeper slope of the E-ABR growth curve in MP versus bipolar is due to encroachment of the central densely packed spiral ganglion cells (SGCs) in response to the first one [23].

#### Stimulus-related factors

Biphasic pulses are defined by the following parameters: current amplitude, phase duration (PD) for each phase of



**Fig. 2** Schematic drawing for the biphasic pulse parameters. Current amplitude (intensity) measured by ( $\mu\text{A}$  or CLs) phase duration (PD) "time of one phase of the biphasic pulse" ( $\mu\text{s}$ ) and interphase gap (IPG) "gap between two phases of the biphasic pulse" ( $\mu\text{s}$ ). Permission was taken from Med-EI [24]

the pulse, and interphase gap (IPG) as illustrated in Fig. 2 [24].

#### Intensity

E-ABR is affected by the changes in stimulus intensity. An increase in the stimulation level (SL) enhances the amplitudes of the waves. Wave V is the last to disappear with decreased SL, although its latency does not change significantly [11]. The latency decreases slightly with increasing SL (Fig. 1). However, the extent of latency changes determined in E-ABR is less than in acoustic stimulation [21]. A lot of studies in the E-ABR field reported the same results [25–27].

#### Phase duration (PD)

Magnifying PD leads to augmented excitability. The amount of applied charges toward the electrode increases proportionally with the total phase area (PD  $\times$  current level) [28]. Biphasic pulses with longer duration require smaller currents than shorter pulses to evoke an E-ABR of a given intensity [29]. Studies on humans revealed that increasing the PD resulted in shortening in the III–V latencies [30–32]. The increase in PD yields an increase in wave V amplitudes [33] and lower thresholds [22]. Also, in an animal study, it was noticed that the slope of the AGF became steeper with increasing the PD [23].

#### Inter-phase gap duration (IPG)

IPG represents the zero-current interval between the two phases of a biphasic stimulus [29] (Fig. 2). Animal studies revealed that the increase in the IPG duration would lead to large E-ABR amplitudes and lower thresholds [28, 29].

Also, the increase in IPG duration would result in lower psychophysical detection thresholds and improved loudness perception in CI recipients [34]. One explanation for this effect is increased IPG that delays the beginning of the second phase (hyperpolarization) of the current stimulus away from the first phase. In this way, spike probability is raised [35–37]. Recently, it is reported that while elevating IPGs from 10 to 30  $\mu$ s, the E-ABR waves showed an increase in amplitude and decrease in the threshold with a steeper slope of AGT (Fig. 3) [11, 25]. A similar effect of increasing IPGs and PDs on E-ABR slopes was observed by Prado-Guitierrez et al. [29].

#### Polarity sensitivity and type of pulse waves

Polarity sensitivity means the difference in responses to positive (anodic) and negative (cathodic) electrical currents (Fig. 2) [38]. Better sensitivity to anodic polarity than to cathodic polarity may denote peripheral process degeneration or demyelination [39–41]. Preference to one polarity is thought to reflect differences in the site of spike initiation in response to anodic and cathodic pulse shapes [38]. Undurraga et al. compared different pulses of E-ABR. They found that anodic stimulations for all pulses caused lower threshold and higher amplitudes than cathodic stimulation [42].

Several physiological and modeling studies have shown that monophasic stimuli yield a lower threshold than biphasic pulse [28, 43, 44]. Monophasic pulses could not be used in humans due to safety issues. So, it was necessary to develop a balanced pulse (biphasic, triphasic, and pseudomonophasic) [43]. Pseudomonophasic pulses are biphasic pulses whose 2nd pulse has different duration and amplitude [44]. Triphasic pulses provide a benefit over the biphasic pulse. Artifacts are more minimized

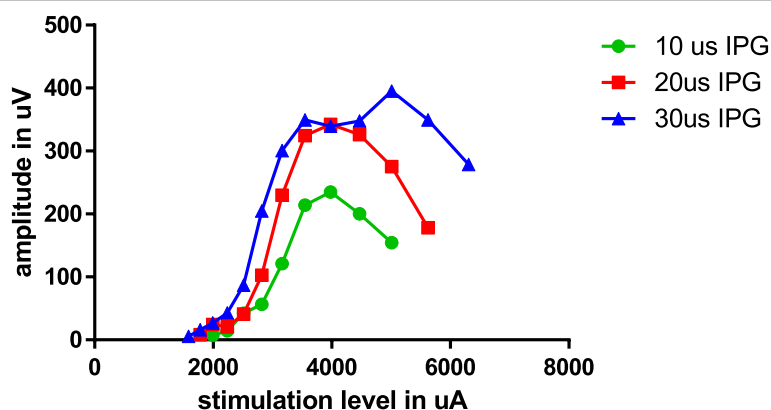
by restoring the neural membrane to its resting potential faster than in biphasic pulses [45]. However, another research group compared triphasic and biphasic pulses in evoking E-ABR. On the contrary, they found that biphasic pulses had better detectability [46]. More studies are required to compare the effect of different pulse shapes on E-ABR detectability.

#### Variables related to the CI electrodes

##### Electrode style or configuration

The response amplitude profile reflects both the spread of excitation across fibers and the spread of the response fields from each active neuron to the recording electrode [47]. The design of the electrode (being straight or curved) largely affects E-ABR. E-ABR thresholds were much lower in the animals implanted with the curved electrode [48]. This is so far accepted due to the proximity of the electrode arrays to the stimulated SGCs. Most of the current literature evaluating the effects of charge on array type reported that peri-modiolar placements resulted in lower E-ABR thresholds and larger suprathreshold wave V amplitude [49, 50]. The latter study reported that removal of the stylet with the Nucleus 24 Contour array results in decreased threshold and increased suprathreshold amplitude, consistent with more medial electrode placement.

A most recent study has compared the effect of the slim modular electrode with pull-back maneuver and the conventional perimodiolar electrode on the electrically evoked compound action potential (ECAP). The authors reported significantly lower thresholds for the 1st. The pull-back maneuver led to better modiolar proximity. However, more research should be done to study the effect on the E-ABR recordings also [51].



**Fig. 3** The E-ABR response obtained from an apical electrode of CI in one animal to biphasic pulse. E-ABR input/output curves represent responses to the three different stimuli with different IPGs (10, 20, 30  $\mu$ s). Notice that the larger the IPG, the greater the suprathreshold amplitude of the amplitude growth curve (AGC), the steeper the slope of the (AGC), and the further the shift of the amplitude growth curve (AGC) to the left. Permission was taken from Nada et al. [11]

### **Electrode (full band versus half band)**

The full band electrode is believed to deliver more current to the stimulated SGCs than the half band electrode. One study investigated the differences between the full band and the half bands on E-ABR recordings. Furthermore, they compared E-ABR when stimulating the inner half of the half band versus the outer half. The E-ABR had significantly lower amplitudes, and significantly higher CLs were required to elicit threshold responses when stimulation was delivered through outer half band electrodes than when delivered through either the inner half band or full band electrode. However, the stimulation level delivered through both full band electrodes and half band inner side necessary to evoke E-ABR threshold did not significantly differ [52].

### **The electrode position**

Thresholds, amplitudes, and waveform morphologies have been observed to differ across subjects and within individual subjects for different electrodes [2, 53]. Wave V latencies were longer for more basal electrodes (e.g., 4.20 ms) and shortest for electrodes in an apical position (e.g., 3.82 ms) [53, 54].

The effect of stimulus current level and the electrode site on E-ABR was studied in patients using CI, and the authors concluded that the apical electrode had better responses with respect to latency, amplitude, and morphology compared with the basal one [2]. This was also mentioned in other study [3]. It has been suggested that this difference in latency, amplitude, and morphology might occur due to the differences in the population and pattern of surviving (SGCs) within the apical region and the better neurophysiology “phase locking” of these apical fibers [3].

The closer the electrode array is to the stimulated SGCs (as it is at the apical region), the more influence on the threshold there is, i.e., lower threshold compared to the basal region [49].

### **Variables related to subjects**

#### **Surviving spiral ganglia cells**

E-ABR responses (thresholds, AGF, and slope) are affected by the underlying SGCs. Some studies have reported poor predictive relationships between response measures and SGC survival [55, 56], while others reported the contrary [29, 57–60].

Miller et al. observed a significant correlation between spiral ganglion neuron counts and E-ABR threshold [58]. Other studies reported a “strikingly good correlation” between both input/output function slope and maximum peak-to-peak amplitude with neural survival [59–61]. In another study done on guinea pigs injected with stem cells, the authors reported that E-ABR recorded from animals (with stem cells)—which expressed a larger

amount of surviving SGCs—had larger amplitudes and lower thresholds with steeper AGF [25].

Moreover, intra-subject variability in the E-ABR waveform can be correlated with the surviving SGCs within the same cochlea. Several studies reported that E-ABR latencies follow a decreasing gradient from the base to the apex of the array, associated with increasing amplitudes of E-ABR waveforms [2, 53].

### **Auditory plasticity and E-ABR**

Gordon et al. evaluated the effect of auditory plasticity on E-ABR recorded from 50 children with CI over a period of 1 year [62]. All the children were pre-lingual and had severe to profound hearing loss. The age of implantation ranged from 1 to 17 years. E-ABR was assessed immediately after activation of their CIs. Over the year, it was noticed that latencies of the peaks significantly decreased, and amplitudes significantly increased. The authors proposed that improvements in synaptic efficacy or even increased myelination happened due to the repeated stimulation of the neural pathways [63].

Furthermore, Gordon et al. evaluated E-ABRs in three groups of children. All were implanted at younger than 3 years old. The first group was with bilateral simultaneous implants, the second and third groups received their second ear implant after a short interval (< 1 year) and a long interval (> 2 years), respectively [64]. The E-ABRs were recorded immediately after CI activation, then 3 and 9 months later. The results revealed no differences in E-ABRs between the ears in the children in the first group with simultaneous CI implants. However, for sequentially implanted children, the ears with later implantation showed prolonged latencies compared to the 1st implanted ears [64]. In a recent work performed on an animal model of guinea pigs [25], E-ABR was recorded over a period of 2 months post-implantation. Thresholds shifted to lower values and amplitude to higher values over this period in both study and control groups. Changes in the excitable elements or the current path to the excitable tissue were proposed as potential mechanisms [65]. Another study also reported a highly significant negative correlation between wave III latency and threshold and duration of implant use [3].

### **The age factor**

The age of the CI candidate does not affect the E-ABR recording. In one study done on children with CIs with an age range of 10 months to 5 years, no correlation was found between E-ABR wave latencies and the age of the candidates [66]. In another study aimed to compare children's E-ABR responses with adult E-ABR responses, there was not any statistically significant difference between both groups as regards E-ABR threshold or latency [3].



### **Effect of anesthesia**

Only one study was found to record the effect of anesthesia. It was found that there was not much change in E-ABR morphology recorded under general anesthesia “intraoperative” and under sedation “post-operative” for the same pediatric patients. Authors concluded that anesthesia did not have a large effect on E-ABR recording [67].

## **Clinical applications of E-ABR**

### **Preoperative**

Electric excitability is established by the minimally invasive transtympanic (E-ABR) test. E-ABR will be accomplished either by direct round window stimulation or transtympanic promontory stimulation without significant differences in signal delivery [68, 69].

As stated in a previous section, a lot of studies have reported that E-ABR measurements correlated with SGCs [29, 44, 57, 59, 60] and may serve as an objective indicator of the ability of the auditory pathway to respond to electric stimulation. Lower promontory E-ABR thresholds were found in patients with normal cochlear anatomy compared with those with cochlear ossification. This was possibly due to reduced SGCs together with the inefficient electric stimulus delivery to the cochlear nerve because of the ossification [68].

More recently, one study conducted on children with different inner ear malformations, it was reported that those children had elevated threshold E-ABR compared to the control group. SL had to be increased in order to provoke a good E-ABR waveform [70]. So, E-ABR monitoring seems to be a useful tool to further predict the outcome of CI surgery cases with inner ear malformations [69, 71].

### **Intraoperative**

The E-ABR recordings can be obtained at the end of the surgery after the surgical insertion of all the active electrodes into the cochlea. Testing can be done while the surgeon is suturing the skin flap, thus minimizing the need to extend the time the patient is with general anesthesia. The surgeon can use a gas-sterilized transmitting coil, including a magnet, over the internal device to start averaging [53]. In this way, the electrode placement and functionality of CI can be checked [15, 69].

### **Postoperative**

#### **Confirming auditory function in special populations of children**

Auditory brainstem responses can be variable in children with hypoplastic auditory nerves [72]. While responses provide evidence of the auditory nerve response to the CI, these responses are different according to the severity

of the underlying malformation [72]. Also, in children with ANSD, it can be argued that the presence of E-ABR or other electrically evoked responses is the most important initial measure to confirm CI's usefulness in such patients. The presence of E-ABR proved that synchronous brainstem function has been restored. Indeed, those children with ANSD exhibiting normal E-ABR showed better speech perception outcomes than their peers with absent/abnormal E-ABR [73, 74]. Moreover, it was found that children with ANSD that is associated with cochlear nerve deficiency had higher rates of abnormal E-ABR than those with ANSD but with normal cochlear nerves [73].

#### **Evaluation of auditory brainstem development and plasticity**

For most implant recipients, with 1st introduction of electrical stimulation to a cochlear implant, we can get a clear E-ABR response. Therefore, the E-ABR test can be used in the functional evaluation of the auditory system between the time of initial implant activation and after chronic cochlear implant use [8].

The quality of the E-ABR waveform appears to correlate well with postoperative speech perception [75, 76]. Hence, the E-ABR can be used as a successful tool to measure the developed and enhanced central auditory plasticity which occurs because of delivering chronic electric stimulation [77].

#### **Programming or mapping of the implanted device**

E-ABR can be used as an objective measure for CI programming, especially in children. The E-ABR detection threshold can be used to estimate a patient's T levels [78–80]. Also, Mittal et al. (2015) conducted a study on 75 children and found that eABR thresholds were correlated with T levels than with C [79]. Electric ABR threshold was always between T and C levels. Furthermore, earlier studies found the same results regarding eABR detection threshold being more correlated, however, not so strong, with T level [21, 80]. However, future studies need to be done on a large sample size to confirm whether the E-ABR threshold is more correlated with the C or T level.

## **Conclusion**

Electric ABR measurement provides a valuable tool to assess auditory nerve functions. Getting E-ABRs with good morphology is a challenge. Multiple factors affect the quality of the E-ABR, including stimulus-related parameters, recordings parameters, and subject-related variables. E-ABR has potential clinical uses in the preoperative, intraoperative, or postoperative setting for patients who are candidates for cochlear implantation.

### Abbreviations

A-ABR: Acoustic auditory brainstem response; AGF: Amplitude growth function; BP: Bipolar; CI: Cochlear implant; E-ABR: Electrically evoked auditory brainstem response; IPG: Interphase gap; MP: Monopolar; PD: Phase duration; SGCs: Spiral ganglion cells; SL: Stimulation level.

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### Authors' contributions

TE: proposed the idea, and contributed to reviewing and editing the article. NN: collected, interpreted the data, and wrote the original draft. EK and PS: contributed to reviewing and editing. All authors have read and approved the manuscript.

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### Declarations

#### Ethics approval and consent to participate

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#### Consent for publication

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#### Competing interests

The authors declare that they have no competing interests.

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