Intraoperative and postoperative measurement of brainstem responses through electrical stimulation of the auditory nerve via implantable neurostimulators

eABR by PATH MEDICAL SENTIERO ADVANCED

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Summary

The recording of brainstem potentials is one of the most important methods currently employed in hearing diagnosis within audiological practice. Stimulation can be provided either acoustically or by means of an implanted neurostimulator, as in the case of electrically evoked auditory brainstem responses (eABR) when using neurostimulators, such as cochlear implants.

In theory, performing an eABR test is as easy as doing air conduction ABR. In practice the stimulus artifact is always a major problem. If this signal spreads too much into recording, the response waves are much more difficult to detect. This falsifies the amplitudes of the responses as well as their latency.

Postoperative examinations using eABR are very rare in everyday clinical practice. This is mainly due to the fact that a special electrically shielded room is required for the measurement, in which the measuring equipment, which is typically very large, is then installed on a trolley.

Avoiding disruptions as much as possible is extremely important, especially in an intraoperative scenario. Additional sources of interference can be present in the operating room. These interferences cannot be prevented and may also occur suddenly. Therefore, a small, portable, battery operated device provides a distinct advantage.

This report shows the practical application of such a device, the SENTIERO ADVANCED, in clinical practice, and demonstrates it to be a very valuable tool. The electrode positioning used was vertex or high forehead for the non-inverting (active (+)) electrode, contralateral mastoid for the inverting (reference (-)) electrode and lower forehead for the ground electrode. To date, 46 patients have been successfully tested and it was usually possible to perform the measurements in a simple doctor’s examination room that was not electrically shielded.

Using a small, portable, battery operated device such as the SENTIERO ADVANCED certainly eases the daily work. The portability of the device and rapid test times are a real asset in everyday clinical practice.
1. Introduction

This tutorial is designed to be an introduction to the general practice and will focus on eABR via neurostimulators. The measurement of evoked potentials (EP) is mainly based on recording the raw electroencephalography (EEG) waves, and averaging these raw waves with those triggered by a stimulus. In the field of auditory evoked potentials (AEP), the auditory brainstem response (ABR), is the most common and established method to check patients’ auditory pathway for abnormal morphologies as well as their estimated hearing threshold (acABR). For hearing patients, ABR can be performed in its classical setup using an air conduction stimulator such as a headphone. However, eABR, utilizes electrical stimulation providing clinicians with a clinical tool that offers the possibility to analyze the brainstem of hard of hearing or even deaf people. eABR makes it possible to evaluate amplitudes in addition to the absolute and relative latencies of these electrically evoked potentials similar to acABR.

In general, eABR is performed on patients that have received a cochlear implant (CI) or an auditory brainstem implant (ABI). These kinds of neurostimulators excite the auditory pathway by stimulating, respectively, the auditory nerve or the auditory brainstem through electric impulses to provide the information of sounds and speech for these patients. Besides the patients’ usage in daily life for “electric hearing”, these neurostimulators connected to an evoked potential system (EP system) can also be used to perform an eABR.

It is also possible to perform an eABR measurement in an ear with no response in acABR and where no auditory neurostimulator has been implanted (Polterauer et al., 2016; Polterauer et al., 2018). In this scenario a temporal stimulator needs to be placed by an experienced surgeon by opening the round window under local anesthesia or preoperatively by a retro-auricular approach during cochlear implant surgery. These variations of eABR preoperatively performed are currently the focus of experimental sciences for prognosis of CI performance even before an implant is placed. This allows diagnosing cases of CI candidates with uncertain prognosis more precisely than what can be achieved in most everyday clinical practices.

1.1. Application of eABR

There are two scenarios where eABR via an implanted neurostimulator is helpful. As eABR does not rely on the patient’s vigilance, it is not only possible to perform postoperative eABR on awake patients but also intraoperatively immediately after the neurostimulator has been put in place.

Both scenarios allow response evaluation of the auditory pathway. For wave I, it is currently unclear whether eABR can show it or not. Early research results show that special placement of the CI causing almost no stimulation artifact could elicit a wave I (Polterauer, 2018). Wave II, III and wave complex IV/V on the other hand can be clearly found in eABR in most cases (Gordon et al., 2006, p. 17; Firszt et al., 2002, p. 505; Hey et al., 2007, p. 44-47). Wave II is a response of the hearing nerve and wave III a response of the nucleus cochlearis. Waves IV and V like acABR is a wave complex. This wave complex IV/V is often dominated by one wave, mainly wave V. Therefore, a differentiation between wave IV and V can be challenging and almost impossible. In doubtful cases, it is recommended to mark the complex with the wave V marker.

In general, eABR has lower latencies than acABR (Gordon et al., 2006, p. 20). This seems to be caused by presenting an electrical stimulus directly into the cochlea, and higher electrical stimulation to the structure leading to the auditory nerve. In contrast, abnormal late absolute latencies can be found in patients with lower myelination of the hearing nerve. This might also affect the relative latencies. Low hearing path maturation or retrocochlear disorder often lead to a high relative latency between wave III and V (Eggermont, 1988; Gordon et al., 2006, p. 8-16; Steffens, 2018; Rosenhall et al., 2003).
The different electrodes on the array placed in the cochlea after implantation of an auditory neurostimulators also affect the eABR results. In the apex, the neural elements are narrower than the stimulating electrode on the array. This results in higher amplitude of response waves, lower threshold and a lower latency of wave V compared to stimulation in the basal area of the cochlea (Minami et al., 2015, p. 1012 - 1013; Gordon et al., 2004; Firszt et al., 2002, p. 503-505; MED-EL, 2015, p. 6).

2. Material and Methods

2.1. Equipment and Parameters

To synchronize the external stimulator in eABR with the EP system both need to be connected by means of a trigger cable. The SENTIERO ADVANCED device offers a trigger input for eABR measurements. Following the easy to use color code, the trigger cable is connected to the red socket, while the electrode cable is connected to the white socket (Figure 1).

![Figure 1: Sentiero Advanced device (left) sockets, trigger cable (middle) and shielded electrode cable (right)](image1)

The 3.5mm stereo jack plug of the trigger cable is plugged into the programming box when testing patients who have been implanted with a CI or ABI made e.g. by MED-EL, Advanced Bionics or Cochlear®.

For MED-EL a stimulation coil directly connects the programming box to the patient’s neurostimulator (see Figure 2: 1<sup>st</sup> and 2<sup>nd</sup> from left).

For Cochlear®, a behind-the-ear processor is to be connected via programming cable to the programming box (Figure 2: 3<sup>rd</sup> and 4<sup>th</sup> from left). As of June 2020, the latest processor cannot be used for eABR due to pending software development. So, you may use an older one from your clinical storage.

![Figure 2: MED-EL programming box and stimulation coil (1<sup>st</sup> and 2<sup>nd</sup> from left; image sources: MED-EL (2019) and own photography); Cochlear® programming coil and latest eABR compatible speech processor (3<sup>rd</sup> and 4<sup>th</sup> from left; image sources: CI Shop (2019) and Cochlear (2019))](image2)
Currently, patients with a CI from Advanced Bionics cannot be tested as easily. In this case, you must use an old pocket processor controlled by the former programming box (Figure 3). In addition, you cannot use the current clinical software but the old Clarion® SCLIN on for Microsoft® Windows® XP and older. As today's computers do not have serial ports anymore, you will have to use an adapter cable making it possible to connect via USB.

Figure 3: Former Advanced Bionics programming box besides laptop (left; image source: Kessler, D. K. (1999)) and pocket processor (right; image source: Childress, T. (2013, p. 6))

The eABR task in the software of each CI manufacturer offers at least the option to set the stimulus rate and amplitude. The units for amplitude of stimulation vary from manufacturer to manufacturer and thus the values are not comparable among different systems. For a general testing, it is recommended to start with a stimulus rate of 34 Hz. If you run into problems, it is advisable to use a lower rate such as 19 Hz. If possible, the amplitude must be set to the maximum comfort level. This way you get high response amplitudes and the stimulus intensity is still within levels acceptable to the patient. Do not forget to also set the stimulation polarity to alternating polarity, as this will significantly reduce stimulus artifact. Other parameters like the pulse width depend on the CI manufacturer or even the CI model itself. For pulse width, you should avoid values above 50 µs or at least stay below 100 µs. Pulse width over 100 µs will result in very broad stimulus artifacts that can even mask the eABR waveform completely.

2.2. Patient preparation

A very important point in AEP recording is always the preparation of the patient’s skin and the choice of recording electrodes. The first step is to clean the skin using a skin antiseptic (Figure 4: Left). This removes any oil, dirt or moisture from the patient’s skin. Secondly, the skin’s non-conductive layer must be removed. Therefore, I recommend an abrasive tape (Figure 4: Middle) that lowers the recording impedance of recording electrodes. Finally, recording electrodes are attached. Surface electrodes such as the ones used in acABR are suitable for eABR recording (Figure 4: Right). There is almost no difference to needle electrodes in eABR testing. Therefore, skin preparation and electrode montage should not pose a problem for experienced examiners.

Figure 4: Example of a skin antiseptic (left; image source: Bode Chemie (2019)), an abrasion tape (middle, image source: 3M (2019)) and a surface electrode (right, image source: Ambu (2019)).
In our hospital we use the following electrode montage for eABR recording that has proven to yield good results: Ground electrode is placed on the lower forehead. Non-inverting electrode is placed on the vertex or if not possible to the higher forehead. Inverting electrode is placed on the contralateral mastoid. Response amplitudes may be lower when the inverting electrode is placed on the contralateral mastoid, however the stimulus artifact is much lower, too, compared to placing the inverting electrode on the ipsilateral mastoid. Using the ipsilateral mastoid may result in a better quality of earlier waveforms in eABR. Optimal recording impedances are $\leq 2\, \text{k}\Omega$ with a $< 1\, \text{k}\Omega$ difference. Electrode impedances about $\leq 4\, \text{k}\Omega$ with a $\leq 2\, \text{k}\Omega$ difference will provide acceptable responses.

The connection cables from the electrodes to the preamplifier of the EP system must be as short as possible and as far away as possible from the stimulation cable (Cochlear, 1999, p. 8.16). Since the SENTIERO ADVANCED electrode cable is shielded up to the clips it is more robust against interference from surrounding electrical sources.

For the recording EP system, a special eABR setting is needed. In SENTIERO ADVANCED the following settings shown in Table 1 are used.

The optimal settings may differ in other devices. PATH MEDICAL’s SENTIERO ADVANCED uses weighted averaging there is no need to manually set rejection thresholds. If you get interferences over time, try to reduce the number of averages per waveform recorded.

Table 1: Recommended parameters for eABR

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Bandpass filter</td>
<td>30Hz to 2000Hz</td>
</tr>
<tr>
<td>Analysis time</td>
<td>-1ms to 10ms</td>
</tr>
<tr>
<td>Recording time</td>
<td>-1ms to 16ms</td>
</tr>
<tr>
<td>Averages</td>
<td>2-3x 1000 for clinical practice, up to 4000 for research</td>
</tr>
</tbody>
</table>

3. Results

3.1. Workflow with SENTIERO ADVANCED

Up to now, 46 patients have successfully been tested and it was usually possible to perform reliable measurements in a simple doctor's examination room that was not electrically shielded.

In general, the operation is straightforward. Once the SENTIERO ADVANCED and the CI programming box are correctly connected and the patient is ready as recommended in the last section, you can start eABR recording. The device can be operated as standalone, independent of a computer. It offers patient management and all measurement functions to be operated directly from its touch screen. For viewing the measurement progress on a computer, the display content can be mirrored via USB to a computer (PATH MEDICAL, 2020, Quick Guide #21). A PC based patient and result management software is available, too. PATH MEDICAL’s PC software may be used as standalone or
Figure 5: SENTIERO ADVANCED main menu (left), patient selection menu (middle) and patient creation dialog (right)

...integrated in hospital information system e.g. by using GDT (see PATH MEDICAL (2020, Guide #34)) or NOAH (see PATH MEDICAL (2020, Quick Guide #28)). When using Mira as standalone software there is the possibility to create new patient records and transfer them to the device.

General Information on how to enter patients and operate ABR measurements can be found here: PATH MEDICAL (2020, Quick Guide #17)

If you need to create a patient on the SENTIERO ADVANCED itself, just click on the green button on the bottom of the main menu (see Figure 5 left) and then “New Patient” in the patient selection menu (see Figure 5 middle). Now fill in the patient’s data and click on save (see Figure 5 right). If the patient already exists on the SENTIERO ADVANCED just select it after clicking on the green button on the bottom of the main menu (see Figure 5 right). Return to the main menu, select “E-ABR” from “AEP” menu. Select the ear you want to perform eABR on. (see Figure 6 left). Then impedances are checked on the next screen (see Figure 6 right).

Figure 6: Ear selection (left) and impedance pre-check (right) on the SENTIERO ADVANCED
The device will show the exact impedance values and save them automatically. Two separate impedance values for inverting as well as the non-inverting electrode will be recorded. Depending on the impedance values the text color will change. There are three ranges categorizing impedances as “Optimal”, “Good”, and “Fair” (see Table 2).

Table 2: Impedance ratings by absolute impedance (R) and relative difference (ΔR)

<table>
<thead>
<tr>
<th>Impedance rating</th>
<th>R</th>
<th>ΔR</th>
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<tbody>
<tr>
<td>Optimal</td>
<td>≤ 4 kΩ</td>
<td>≤ 2 kΩ</td>
</tr>
<tr>
<td>Good</td>
<td>≤ 6 kΩ</td>
<td>≤ 3 kΩ</td>
</tr>
<tr>
<td>Fair</td>
<td>≤ 12 kΩ</td>
<td>≤ 6 kΩ</td>
</tr>
</tbody>
</table>

As written in the previous section it is recommended to stay within the “Optimal” impedance values for eABR testing. If you wish to perform eABR with higher impedance values click on the play button on the bottom center (see Figure 6 right). It is not possible to perform an eABR test with values higher than “Fair”.

As eABR is measured you will see live averaging on the SENTIERO ADVANCED (see Figure 7 left). During the test, markers can be placed on recorded traces. Once test progress is finished you can record further waveforms by clicking on the play button on the bottom center. Up to 15 waveforms may be collected per test session. Clicking on the stop button in the bottom left corner will allow you to start a new eABR session later, and record more waveforms. Waveform markers may be placed directly on the device or on your computer after exporting the data to Mira software.

To position the markers on the SENTIERO ADVANCED, enter the peak edit mode by swiping from right to left until the appropriate screen is shown (Fig. 7).
As soon as the measurement has been finished, the eABR data can be exported to your computer. Click on “Receive” button in the “Your Patient” menu tab (see Figure 8) and follow the steps indicated by the import assistant.

To place or change the wave markers, select the patient and the eABR measurement from the list. On the right you will find the eABR waveforms for this measurement (see Figure 8).

In the eABR viewer (Fig. 8), simply drag and move the markers as required. A right click of the mouse confirms the marker, which changes to green. Finally, all results can be put into a report selecting the eABR session(s) (hold “Ctrl” to select more than one measurement or tick the checkmarks). Then click on “Print” in the “Your Patient” menu tab and select your preferred report style.

![Figure 8: eABR results shown in Mira software including markers](image)

### 3.2. Postoperative eABR

Postoperative eABRs are measured while patients are laying down in a relaxed position. In most cases postoperative eABR measurements can also be performed on patients sitting on a chair. As in cochlear implant fitting sessions, patients are already sitting and clinicians can directly integrate the eABR in such an appointment. This way an eABR becomes almost as easy as the measurement of ECAPs. The eABR data in this study was collected from CI patients while sitting to evaluate a scenario as close to clinical practice as possible.

#### 3.2.1. Recording impedances

The SENTIERO ADVANCED automatically measures and saves the recording impedances. The resulting values were statistically analyzed recording their change over time. Three measurements where done per session and patient. The change over time in both impedance values (white = vertex electrode and red = mastoid electrode) in reference to the black electrode is illustrated in Figure 9. The mean white impedance before the first eABR recording increased slightly from 1.65 ± 0.87 kOhm (n = 46) to 1.77 ± 0.85 kOhm (n = 32) before the third eABR recording. For the red impedance, the mean value decreased slightly from 1.83 ± 1.23 kOhm (n = 46) to 1.50 ± 1.17 kOhm (n = 32).
3.2.2. Residual noise

The SENTIERO ADVANCED also automatically measures and saves residual noise values. For apical stimulation, a mean value of $170.25 \pm 56.66$ nV ($n = 46$) was calculated. For medial stimulation, a mean value of $180.00 \pm 58.61$ nV ($n = 46$) was calculated. For basal stimulation, a mean value of $186.00 \pm 57.20$ nV ($n = 32$) was calculated. All three parameters are illustrated in Figure 10.

3.2.3. Case reports

With amplitudes varying amongst patients it was decided to analyze single cases. In Figure 11 three typical cases are shown. The blue waveform represents a clear eABR with a low latency. The brown waveform shows an eABR with slightly prolonged latencies. Both waveforms feature acceptable quality and amplitude. Both patients had good performance in speech tests. These two examples show the variability within normal eABRs without an impact on speech performance (Gibson et al., 2009; Guevara et al., 2016; Song et al., 2010).
Figure 11: Examples of different patients. Blue: clear eABR with short latency. Brown: Clear eABR with longer latency. Green: Good eABR followed by light facial nerve response around 5.5ms.

Longer latencies especially for eV around 5ms must be classified as a late response. These eABRs are mostly recorded in patients with low speech performance or on recently implanted second sides in bilateral CI users (Gallego et al., 1998; Lammers et al., 2015b).

The green waveform is an example of a myogenic artifact influencing the eABR result. Around 5.5ms a large response can be noted. This response is generated by the facial nerve as a side effect of electrical stimulation inside the cochlea. Facial nerve responses in eABR show up at a latency of circa 6 to 7ms (Cushing et al., 2006). This myogenic response is often even larger than typical eABR responses of the auditory pathway like eV. Therefore, this example shows a small facial nerve response. Higher responses mostly cause eye twitching or a tickling on the ipsilateral side of the face. In summary, eABR offers the opportunity to analyze facial nerve side stimulations in CI patients even if you cannot observe it in the patient’s face or the patient is not aware of it.

3.2.4. Grand average and means

As a reference waveform, the grand average of the newest present eABR was calculated for stimulation on the most apical electrode (see Figure 12). All typically waveform markers could be identified: eII peak (green), eIII peak + trough (red) and eV peak + trough (blue). Latencies for the peak markers of a single curve are ~1.4ms for eII, ~2.0ms for eIII and ~3.8ms for eV.

To show the variability in latencies across all included patients, the latencies of eIII and eV were analyzed. These mean latencies are documented in Table 3 for apical, medial, and basal stimulation.
Figure 12: Grand average of first measurement over all tested patients at apical stimulation (i.e. electrode 1). Peak markers of waves (circle): eII (green), eIII (red) and eV (blue). Trough markers of waves (triangle): eIII (red) and eV (blue). Grand average latency: 1.38ms @ eII, 1.95 @ eIII and 3.83 @ eV. Grand average amplitude: 157.15nV @ eIII and 150.4nV @ eV.

Table 3: Mean latencies for apical, medial and basal stimulation for waves eIII and eV

<table>
<thead>
<tr>
<th></th>
<th>Latency eIII</th>
<th>Latency eV</th>
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<tbody>
<tr>
<td>Apical stimulation</td>
<td>2.45 ± 0.37 ms (n = 46)</td>
<td>3.88 ± 0.25 ms (n = 46)</td>
</tr>
<tr>
<td>Medial simulation</td>
<td>2.45 ± 0.37 ms (n = 46)</td>
<td>3.98 ± 0.24 ms (n = 46)</td>
</tr>
<tr>
<td>Basal stimulation</td>
<td>2.57 ± 0.35 ms (n = 32)</td>
<td>4.03 ± 0.21 ms (n = 32)</td>
</tr>
</tbody>
</table>

3.2.5. Further applications of postoperative eABR

The use of eABR results in CI patients in the field of objective CI fitting is still a subject under debate. Several scientific papers found correlations between eABR parameters and the main fitting parameters while other researchers couldn’t verify them (Kubo, et al., 2002, S. 107-109; Raghunandhan et al., 2014; Guenser et al., 2015; Gaufman et al., 2014; Brown et al., 2000; Truy et al., 1997; Brown et al., 1994; Lopes-Fontanelli et al., 2014). However, clinical practice showed that a smoothly decreasing amplitude of eV and slightly increasing latency of eV can be measured at maximum comfortable stimulation level. This way the currently set map on the patient’s speech processor can be verified.
3.3. Intraoperative eABR

As artifacts from muscle contraction can interfere with eABR recording, intraoperative eABRs are easily to perform. Intraoperative measurements need to be as fast as possible to minimize the duration of narcosis. Therefore, the stimulation rate can be increased, resulting in longer latencies (Marcrum & Steffens, 2014).

eABR can be used for monitoring auditory nerve preservation during tumor removal and checking eABR in general in doubtful CI performance (Lundin et al., 2015). In addition, it is possible to recognize a tip fold-over or buckling of the cochlear implant electrode array (Gibson & Sanli, 2008, S. 63-67).

The convenient portability of the SENTIERO ADVANCED, provides a clear advantage compared to other established EP systems. In addition to the fact that no laptop or even monitor is required, the SENTIERO ADVANCED can be positioned next to the stimulation system. Surgical staff do not need to deal with a large trolley in the operating theater. Other EP systems mostly have to be connected to an external isolating transformer, but the SENTIERO ADVANCED is battery operated and so there is no need for an external transformer in this scenario.

Another important advantage of the SENTIERO ADVANCED’s size is the ease of portability to the surgical area. EP systems are usually located in the measurement rooms inside the clinic. Therefore, the technical staff need to transport the EP system for eABR measurement to the operating theater each time a measurement is needed. If the need for eABR is identified later in the process, you save a lot of time using a portable system compared to the standard EP systems that need to be placed on an additional trolley.

In intraoperative measurements in general, you can experience several different interferences that cannot be identified quickly. Therefore, the standalone system with no wiring to a computer, or a monitor, saves time that would be spent looking for interferences that hinder a clear eABR recording with traditional EP systems. The SENTIERO ADVANCED offers fast and easy recording of eABR in intraoperative scenarios and has clear advantages in comparison to classical EP systems especially regarding unplanned eABR measurements.

Summary

eABR is quick and easy to perform. In the majority of cases, the response waveforms are clearly identified. As the auditory brainstem is also active in sleep or even narcosis an intraoperative eABR is also an option. This offers information for the CI surgeon about the integration of the implanted device and the patient’s auditory pathway. This intraoperative scenario reveals the initial CI stimulation processing. Postoperative eABR can support CI fitting by checking sufficient stimulation via response amplitude, facial nerve side stimulation and abnormal signal processing along the auditory pathway mainly by prolonged eV latencies.

To date, 46 patients have been tested, and with the majority of cases measurements were conducted in a simple doctor's examination room that was not electrically shielded.

To conclude, using a small, portable, battery operated device such as the SENTIERO ADVANCED by PATH MEDICAL certainly improves and eases the daily work routine. The portability of the device and rapid test times are a real asset in everyday clinical practice.
4. Literature


MED-EL (2015), eABR Guide.


eABR by PATH MEDICAL SENTIERO ADVANCED, Polterauer