When Can Stable AutoNRT Thresholds be Expected? A Clinical Implication When Fitting Young Children

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Abstract

Background: Objective measurements are important for programming cochlear implants in young children and other individuals who cannot participate in behavioral measurements. AutoNRT, the automatic method used to record responses from the auditory nerve in the Cochlear Ltd., implant system, is often used as a basis for estimating the threshold level and comfort level (C-level) for these patients. However, it has not been sufficiently established if AutoNRT measurements remain consistent over time.

Purpose: This study aimed to determine if/when AutoNRT thresholds stabilize.

Research Design: The study design was a longitudinal prospective study.

Study Sample: AutoNRT thresholds were obtained from 52 young children and 80 adults. All subjects received the same implant (CI24RE Contour Advance).

Data Collection and Analysis: AutoNRT thresholds were measured on all intracochlear electrodes during the surgery and at the initial activation. During the following year, children were measured at 1, 3, 6, and 12 months, and adults were measured at 6 and 12 months. The results were analyzed based on mean values, correlation, and absolute mean differences.

Results: There were large variations for all electrodes between the intraoperative and postoperative AutoNRT thresholds of both children and adults. For children, the thresholds were considered to be stable from 1 month. The correlations obtained between the last two measurements, 6 and 12 months, for both children and adults were generally high for all electrodes.

Conclusion: The present results demonstrate the importance of repeating the AutoNRT measurement postoperatively, at about 1 month after initial activation, to obtain reliable and stable thresholds for estimating the T- and C-level profiles.

Key Words: adults, auditory evoked potentials, AutoNRT, children, cochlear implants, deafness

Abbreviations: CI = cochlear implant; C-level = comfort level; CL = current level; ECAP = electrically evoked compound action potential; T-level = threshold level

INTRODUCTION

Recordings of the electrically evoked compound action potential (ECAP) from the auditory nerve are one of the measurements that have gained widespread use as an objective tool to estimate the appropriate cochlear implant (CI) settings for patients who are not able to participate actively in the programming process, for example, small children receiving implants. An advantage of ECAP is that it is a near-field measurement of the action potential in the auditory nerve; the implanted electrode records the response close to its source in the auditory nerve. Thus, the implanted electrode is used both to electrically

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stimulate the nerve and to record the response. The measurement can be performed during surgery and also postoperatively at any programing revisit when the patient is awake. Measurement of the ECAP threshold has been of great interest as a tool to assist researchers and clinicians in the programming of the threshold (T) and comfort (C) levels of the sound processors, that is, the lowest and highest levels of electrical stimulation assigned for each individual electrode, respectively. The T- and C-levels control the dynamic range of the stimulation and define the absolute levels of the stimulation. These levels should be set carefully because too low T-levels could deprive the CI user of auditory information and too high C-levels could lead to discomfort. The ECAP measurement also provides important information for surgeons during implantation in the form of instant verification of electrode function and placement as well as the responsiveness of the auditory nerve.

Since the introduction of the Nucleus Freedom system with the CI24RE implant in 2004, a completely automatic ECAP threshold measurement called AutoNRT has been available for CIs developed by Cochlear Ltd. Before the introduction of AutoNRT, the ECAP threshold could only be determined by visual interpretation of the ECAP response waveform or by extrapolation of the amplitude growth function using the slope of a series of suprathreshold responses to calculate at which stimulation level, the first zero amplitude response is likely to occur. Both processes can be time-consuming and require expertise to perform correctly (Gärtner et al, 2010). The AutoNRT algorithm imitates the visual identification of the ECAP threshold and also takes advantage of the much lower noise floor associated with the ECAP recordings performed with the Freedom system compared with the earlier CI24M/R implants. The recording process is also faster, as less averaging is needed. AutoNRT provides results that are equally reliable to those of an experienced observer who visually determines the thresholds. The high reliability of the AutoNRT procedure is beneficial when results must be compared between clinics, as it eliminates the subjective differences in the threshold definition that have been noted between untrained and expert observers (Van Dijk et al, 2007; Gärtner et al, 2010).

Although ECAP measurements are often used to predict the T- and C-levels for infants and young children, research has shown that ECAP thresholds do not correspond directly to the psychophysical thresholds; rather, they often represent the upper half of the dynamic range between the T- and C-levels (Brown et al, 2000; Smoorenburg et al, 2002; Cafarelli Dees et al, 2005; McKay et al, 2005). Studies of relationship between ECAP thresholds and T- and C-levels for individual electrodes have generally revealed results ranging from moderate to strong correlation (Brown et al, 2000; Smoorenburg et al, 2002; Cafarelli Dees et al, 2005; Lai et al, 2009). Alternative methods to use ECAP thresholds have consequently been proposed to compensate for these differences; Brown et al (2000) suggested the use of ECAP in combination with a behavioral T-level measurement of a single electrode, and more recently, Botros and Psarros (2010), in a study, successfully used the scaled ECAP threshold to set the T- and C-levels.

To use the ECAP threshold, it is important to know the variation of the neural thresholds over time, and if there is a point in time after implantation where the thresholds can be considered stable. If the ECAP thresholds used for programming vary after the programming, it likely will affect the outcome for the patient.

A previous study by Spivak et al (2011) examined the longitudinal change of AutoNRT thresholds measured with the CI24RE implant for children and adults. It compared the intraoperative measurements of five electrodes spread across the array until 3 months of use. The study showed that thresholds recorded intraoperatively are likely to be higher than those recorded at the initial activation and at the 3-month follow-up. However, it stressed that the results suggested that electrodes 11 and 16 had lower within-subject variability between the intraoperative and postoperative measurements compared with other electrodes examined and, therefore, most accurately would predict the postoperative result. Variation between the intraoperative and postoperative measurements of the manual recording procedures of the CI24RE implants have also been reported (Gordin et al, 2009). Lai et al (2009) showed stable results for the CI24RE from initial activation until 12 weeks after; this was, however, based only on group mean values which does not necessarily would yield the same results if individual differences were taken into account. For the older CI24M implant, stabilization was reported to occur between 3 and 8 months (Hughes et al, 2001). In addition, studies with the CI24M/R implants, conducted over both 4 and 8 years, have shown that once the ECAP thresholds become stable, they remain so for a substantial time (Lai et al, 2004; Brown et al, 2010).

AutoNRT has gained widespread clinical use, but there is still no study that has included results from all 22 electrodes over a sufficient period of time to determine when stable results can be expected and examine the possibility that certain electrodes stabilize more rapidly than others. The need for stable AutoNRT thresholds is most evident when they are used to program the T- and C-levels in CI's, and the use of AutoNRT thresholds for programming is most necessary for the youngest children receiving implants and other individuals who cannot participate in behavioral measurements. The primary aim of this study was to verify when the AutoNRT thresholds of young children and adults are stable and when they can be used to program the stimulation levels of the patient's CI.

MATERIALS AND METHODS

Participants

Data in this study were collected at 13 centers located in Israel, Italy, Spain, and Sweden as part of a multicenter clinical investigation. The investigation was performed according to the guidelines established by the Declaration of Helsinki; the ethics committee approved this protocol before data collection began. Informed consent was obtained from all participants and/or their guardians.

The study included 53 children (mean age at implantation, 1.8 years; range, 0–3 years) and 80 adults (mean age, 56.9 years; range, 20–83 years). All participants had bilateral severe to profound sensorineural hearing loss during a period of time that did not exceed 15 years. The hearing loss etiologies are shown in Table 1. Medical examinations, including magnetic resonance imaging, were conducted to ensure there was no cochlear abnormality or ossification that could prevent successful electrode array insertion. Subjects with signs of retrocochlear or central hearing impairment were not included in this study.

All participants received the Nucleus Freedom cochlear implant CI24RE Contour Advance with 22 electrodes and the Freedom sound processor.

AutoNRT

The AutoNRT measurements were conducted using Custom Sound software. The same ECAP analysis algorithm was used for all versions of the software in this study. The software uses two protocols to measure ECAP thresholds, one for intraoperative and one for postoperative measurements. The intraoperative measurement protocol uses a 250-Hz stimulation rate and begins the stimulation at a current level (CL) of 170; it also uses conditioning pulses at 230 CL to reduce intraoperative artifacts associated with the high impedance present immediately after electrode insertion. The intraoperative protocol is primarily designed to minimize the test time and is not used if the patient is not under general anesthesia. The postoperative protocol uses an 80-Hz stimulation rate that starts at 100 CL and does not use conditioning pulses. The postoperative protocol is intended for use in awake patients and was devised to avoid stimulations that may cause patient discomfort. As a result, it requires more time than the intraoperative protocol because of the slower stimulation rate and the lower starting point of the stimulation. In-depth descriptions of the decision tree analysis and AutoNRT algorithm have been previously described Botros et al (2007). The stimulation rates used by the two protocols were determined to not significantly affect the threshold response (Spivak et al, 2011).

AutoNRT was performed to record the ECAP thresholds from all intracochlear electrodes of both children and adult subjects. Data were collected at six time points for children: intraoperatively, at the initial activation, and at 1, 3, 6, and 12 months after the initial activation. For adults, measurements were performed at four time points: intraoperatively, at the initial activation, and at 6 and 12 months after activation.

Statistical Analysis

To compare AutoNRT thresholds between time points, the Pearson correlation coefficient and the absolute mean difference was calculated by comparing a single electrode threshold from one time point to the subsequent measurement. This was carried out by comparing the thresholds for each individual electrode. All statistical analyses were performed with IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY).

RESULTS

Mean Variation in AutoNRT Thresholds over Time

The mean of the AutoNRT thresholds demonstrated, on group level, that for both children and adults, the intraoperative measurement deviated compared with the postoperative measurements, whereas the postoperative mean results showed consistency over time

Table 1. Causes of Deafness

Etiology	Children (n)	Adults (n)
Familial	19	12
Meniere's Disease	0	9
Meningitis	1	0
Noise exposure	0	1
Otosclerosis	0	2
Ototoxic drug	1	3
Trauma	0	1
Unknown	31	42
Viral	1	0
Total	53	80

(Figure 1). The children's intraoperative measurements seemed to be closer to their postoperative results than the measurements of the adults, for some electrodes. However, the AutoNRT threshold profile was not consistent between the intra- and the postoperative measurements. The intraoperative thresholds showed a general gradual increase in CL toward the electrode 1, whereas the postoperative measurements showed a different profile (see Figure 1A). Worth pointing out is that a mean result overlap is not necessarily caused by good individual consistency over time between measurements.

In contrast to the children, the adults' results showed similar threshold profiles at all time points. However, the intraoperative result revealed higher AutoNRT thresholds than the postoperative ones.

Correlation of AutoNRT Thresholds When Subsequent Measurements Were Compared

Subsequent measurements were compared on an electrode-per-electrode basis for each measurement to make the individual variation visible. The scatter plots in Figures 2 and 3 show the variation in the individual thresholds for each electrode between subsequent measurements. The results revealed considerable variation between the intraoperative and initial activation measurements, and the difference between the following measurements gradually decreased. The correlation in the children increased during the first 3 months after implantation, and remained high ($r = 0.91$) from 3 months onward. There was a higher correlation between the intraoperative and initial activation measurements of the adults ($r = 0.72$) than those of the children ($r = 0.58$) (Figures 3 and 2, respectively). There was also a high correlation ($r = 0.93$) between the last two measurements (6 and 12 months) of the adult subjects.

The results showed that there was a higher variation between postoperative measurements than could be seen using the mean values in Figure 1. The children's results showed consistently high correlation ($r = 0.89$) beginning 1 month after activation. The adults were not measured at 1 and 3 months. However, the measurements taken at 6 and 12 months after activation had a high correlation ($r = 0.93$).

Comparison of Each Electrode

The previously described mean AutoNRT threshold of the children indicated that electrodes in the middle of the array are more stable over time than those near the apical and basal ends of the array. To examine this phenomenon, we calculated the mean of the absolute difference between the subsequent measurements of each electrode and the correlation between each electrode and its subsequent measurement.

The mean absolute difference in the children (Supplemental Table S1, available with the online version of this article) showed that the intraoperative and the initial activation measurements of all electrodes varied considerably; the mean ranged from 13 to 24 CL. However, between the two final measurements, the mean absolute difference ranged from 3 to 9 CL. The correlation when the intraoperative and initial activation were compared varied between $r = 0.19$ and $r = 0.76$. At 6 and 12 months after activation, r was between 0.77 and 0.97, respectively. Electrode 1 was distinguished in all comparisons regarding the children, as it had both a high absolute mean value (9–24 CL) and a low correlation ($r = 0.57$–0.88) compared with the other electrodes.

The results of the adult subjects (Supplemental Table S2, available with the online version of this article) showed a mean absolute difference of the intraoperative and initial activation for each electrode of 16–21 CL, which decreased to 3–6 CL when the 6- and 12-month measurements were compared. The correlation in the adults varied between $r = 0.54$

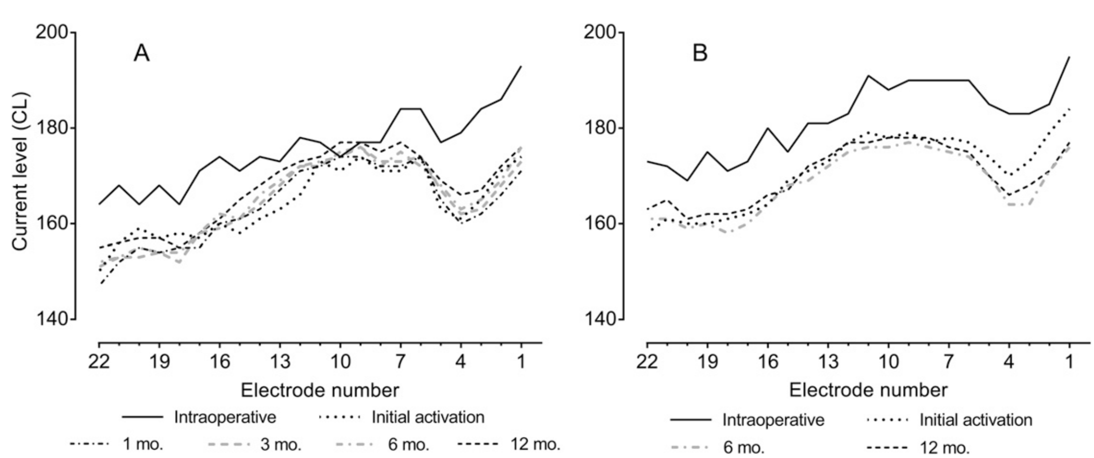

Figure 1. Mean AutoNRT thresholds of (A) 53 children aged 0–3 years and (B) 80 adults aged 20–83 years, recorded at different time points from surgical insertion of the CI electrode until 12 months after the initial activation. The standard error was 1.9–4.3 for children and 1.3–3.7 for adults.

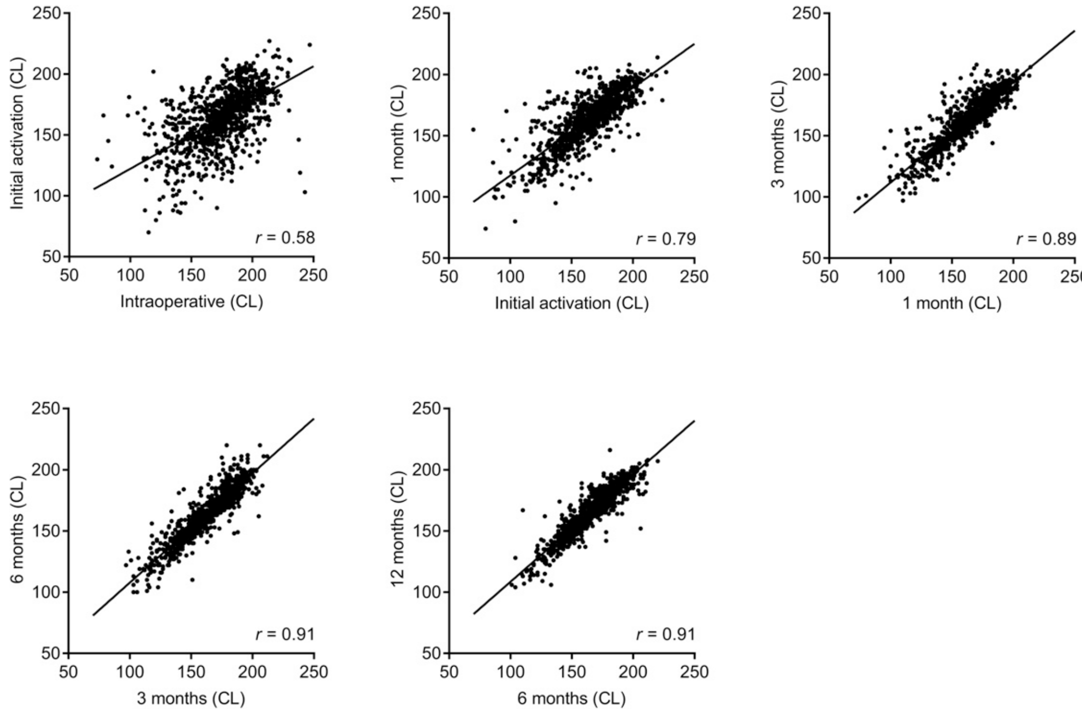

Figure 2. Scatter plot comparing the AutoNRT measurements of all 22 electrodes from the intraoperative time point until 12 months after the initial activation of CIs in children. The Pearson correlation coefficient r was calculated for each comparison.

and $r = 0.83$ when the intraoperative and initial activation measurements were compared, and between 6 and 12 months, it increased to between 0.81 and 0.96, respectively. The results of the adult measurements did not indicate any single electrode to be less stable than the others.

The variation between measurements decreased over time in both children and adults. The results did not reveal any electrode/s or region of the electrode array that was more stable over time for either group.

DISCUSSION

Correlation of AutoNRT Thresholds When Subsequent Measurements Are Compared

We investigated the changes in the AutoNRT thresholds during the first year after CI in adults (20–83 years) and young children (0–3 years) on all 22 electrodes. Our results showed that the postoperatively recorded AutoNRT thresholds clearly deviated from those intraoperatively recorded and that no specific electrode's threshold was more stable over time. Stable threshold results were seen in children at 1 month after activation and later. Our results showed that the thresholds in adults were stable at 6 months.

The thresholds of the adults in this study were measured at fewer time points, which made it difficult to compare the results between the two groups. Based on the comparisons of the same time points between groups, the correlations observed in the adult subjects were similar or even slightly better than those of the children. Therefore, it could be that the adults also would have shown stable results at 1 month, if it would have been measured.

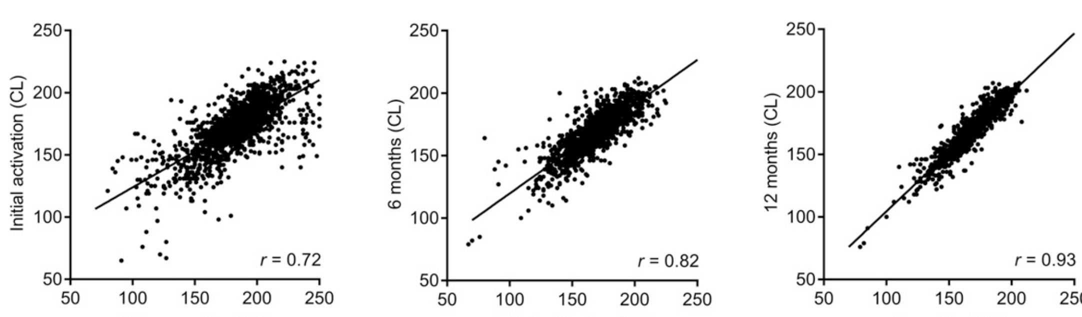

Figure 3. Scatter plot comparing the AutoNRT measurements of all 22 electrodes from the intraoperative time point until 12 months after the initial activation of CIs in adults. The Pearson correlation coefficient r was calculated for each comparison.

The results presented here indicate that AutoNRT is a reliable and stable measurement when performed at the correct time. Compared with the results by Tavartkiladze et al (2015), this study show only slightly lower correlation for a long-term follow-up period (3 and 6 months).

The difference between the intraoperative and postoperative measurements agrees with the AutoNRT results by Spivak et al (2011). They also correspond to other studies that examined the manually recorded ECAP thresholds (Hughes et al, 2001; Gordin et al, 2009). The variation between intraoperative and postoperative measurements may be due to several contributing factors. The insertion of the electrode array affects the composition of the cochlear fluids, and may cause damage to the cochlear walls, causing the need of higher stimulation levels intraoperatively before returning to a normal state. In addition, Hughes et al (2001) suggest that the fibrous tissue, which encapsulates the array over time, affects the electrical transmission from the electrodes to the auditory nerve.

Spivak et al (2011) stated that the intraoperative measurements for electrodes 11 and 16 were closer to the postoperative measurements. However, careful examination of the results of all 22 electrodes revealed that the thresholds of adjacent electrodes can vary substantially. A comparison of the results of all electrodes showed that the intraoperative results were more random than the postoperative results. If only a subset of the electrodes in each part of the array is examined, this randomness could remain undetected. Therefore, when considering all electrodes, we cannot state that electrodes in certain regions are generally more stable over time. This seems to be true for all electrodes, with the exception of electrode 1 in children. Considering the variability and relatively high mean results of electrode 1, it is advisable to take additional caution when using the AutoNRT results of this electrode to program the implant. The higher and more fluctuating results of electrode 1 is likely reflecting the electrode's basal placement in the cochlea and close proximity to the insertion point of the electrode array. Based on our clinical experience, it may in many cases be better to deactivate this electrode from the map.

The present results showed large variations between the AutoNRT thresholds measured intraoperatively and at initial activation. The AutoNRT thresholds should therefore be remeasured postoperatively to ensure they are stable enough to be used as a basis for setting the T- and C-level profiles.

Mean Result of AutoNRT Thresholds over Time

There appeared to be a robust AutoNRT threshold profile visible in all postoperative measurements for both children and adults; they all show a very similar relative difference between electrodes across the array. There was an increase in the CL from the apical end, with a well-defined decrease from approximately electrode 7 to electrode 4, which increased again near electrode 1 at the basal end of the array. Similar threshold profiles have been presented in other studies (Botros and Psarros, 2010; Tavartkiladze et al, 2015). This result indicates that there is a greater need to record the thresholds of neighboring electrodes in the basal section of the array than in the middle or apical sections because these thresholds more accurately can be interpolated.

Limitations and Future Directions

The implant CI24RE was used in this study; however, the results should also be valid for the newer precurved implant type, CI512, which has an updated housing, but still uses the same electrode array as the CI24RE. In addition, newer implants from Cochlear Ltd., use similar amplifiers for the ECAP recording as the CI24RE. However, this does not ensure that the results presented here are applicable to other types of implants. The development of thinner electrode arrays could lead to different results, especially regarding the intraoperative result, if it has a decreased effect on the internal physical structure of the cochlea during insertion. Studies on other electrode types are, therefore, required.

Although, our results have shown that AutoNRT thresholds are stable from 1 month for children, further validation of AutoNRT as the main basis for setting the T- and C-levels on children is needed.

CONCLUSIONS

We have demonstrated that there are large differences between the AutoNRT thresholds recorded intraoperatively and those recorded postoperatively, that the thresholds in children are stable from 1 month after initial activation, and that the thresholds in adults are stable from at least 6 months after initial activation. We have also shown that AutoNRT thresholds obtained after this stabilization period are reliable and that there is no specific electrode that generates more reliable results than others. For clinicians, who program CIs, we have shown the importance of repeating the AutoNRT measurements postoperatively, at least at about 1 month after activation, to obtain reliable and stable results to serve as a basis for setting the T- and C-level profiles. However, the accuracy of AutoNRT-based map profiles requires further validation.

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