CLINICAL APPLICATIONS OF NUCLEUS® NRT™ (NEURAL RESPONSE TELEMETRY)

INTRODUCTION

NRT™ (Neural Response Telemetry) of the Nucleus® 24 cochlear implant system is a quick and non-invasive way of recording the electrically evoked compound action potential (ECAP) of the peripheral auditory nerves in-situ. It gives clinicians valuable information for programming the T- and C-levels of the recipient’s speech processor MAP, and records the neural responses to electrical stimulation at discrete sites along the electrode array.

The Nucleus 24 cochlear implant is the first implant system with the capability of recording the ECAP using NRT. The NRT software was developed at the University of Zurich, Switzerland, in collaboration with Cochlear in 1995. The first NRT responses were recorded with a recipient of the Nucleus 24 implant in August 1996. Now NRT has been used with thousands of adults and children. The reported success rate is over 95% (Cafarella Dees et al, 2001; Brown et al, 2000). NRT has proved to be a valuable tool for clinicians, and this review describes some of the recent clinical advances in the application of Nucleus® NRT™.

ECAP: The electrically evoked compound action potential.

T-NRT: The ECAP threshold as measured using Neural Response Telemetry.
WHAT IS THE PERIPHERAL NEURAL RESPONSE AND HOW IS IT MEASURED?

The ECAP is the synchronized response of peripheral auditory nerves to electric current pulses delivered by an intracochlear electrode. The ECAP waveform typically consists of an initial negative peak followed by a positive peak, labelled N1 and P1 respectively (Figure 1). These peaks have relatively short latencies, 0.2 to 0.5 ms for N1 and 0.5 to 1.0 ms for P1 (Cafarelli Dees et al, 2001; Lai, 1999).

![Figure 1: The ECAP waveform showing the negative (N1) and positive (P1) peaks.](image1)

The bidirectional telemetry system of the Nucleus 24 implant is used to measure the ECAP. The NRT software communicates with the implant via the SPrint™ speech processor and headset. Biphasic current pulses are delivered to a single intracochlear electrode typically using a pulse rate of 80 pulses/s. The next NRT software release will have enhanced features which allow for higher stimulating pulse rates up to 400 pulses/s. The resulting ECAP is measured from a neighboring electrode, amplified, encoded and sent back to the speech processor via the headset coil. The data is then analyzed using the SPrint processor and the NRT software. The NRT software presents the results in a way that is easily interpreted by the clinician. The stimulating and recording options available in the NRT software assist clinicians in obtaining clear waveforms (Lai, 1999).

The N1 and P1 amplitudes of the ECAP waveform vary with stimulating current (Figure 2). The amplitude growth function can be used to estimate the ECAP threshold, also known as the NRT threshold (T-NRT), and to quantify how the response changes with stimulus intensity.

![Figure 2: Changes in ECAP as a function of stimulus current level. The amplitudes of N1 and P1 increase with increases in stimulating current level.](image2)
ARE THERE DIFFERENT TYPES OF NRT WAVEFORMS?

Two basic types of NRT waveforms have been recorded (Figure 3). The most common waveform consists of N1 followed by a single P1 positive peak, and is found in the majority of cases. A rarer waveform has two positive peaks, P1 and P2. The latencies of P1 and P2 are 0.4-0.5 ms and 0.6-0.7 ms respectively (Lai and Dillier, 2000a), and this P1 latency tends to be less than that found in the more typical NRT waveform with a single P1 peak, which is 0.5-1.0 ms. The double positive peak waveform was found in only 3% of cases in a multicentre European trial with 170 adult recipients (Cafarelli Dees et al, 2000). The P1 and P2 waveform was mainly found on apical electrodes, and may be related to the activity of both the peripheral dendrites and the more central axons (Stypulkowski and van den Honert, 1984; Lai and Dillier, 2000a).

WHAT ARE THE CLINICALLY RELEVANT NRT MEASURES?

The most clinically relevant measures are the ECAP threshold (T-NRT) and the amplitude growth function. These can be easily obtained using the automated amplitude growth series option of the NRT software. Typically, a series of NRT waveforms are recorded for a series of current levels below the recipient’s Loudest Acceptable Presentation Level (LAPL).

The ECAP amplitude is used to determine the T-NRT and amplitude growth function. The ECAP amplitude is the difference (in µV) between the N1 and P1 amplitudes. The location of N1 and P1 is set manually or by using the peak-picking function of the NRT software.

T-NRT may be estimated visually by reviewing the amplitude growth series and selecting the electric stimulation level which produces the smallest repeatable N1 and P1 peaks in the waveform. Alternatively, the analysis function of the software can extrapolate T-NRT from the amplitude growth function. The amplitude growth function is a plot of ECAP amplitudes as a function of stimulus current levels. A linear regression line can be fitted to the data to extrapolate the T-NRT and to define the slope of the function (Figure 4).

FIGURE 3: The upper graph (A) shows the typical ECAP waveform consisting of the N1 and P1 peaks. The lower graph (B) shows the rarer ECAP waveform consisting of the P1 and P2 double peak.

FIGURE 4: The ECAP growth function and the estimate of the T-NRT, using linear regression, shown by the red square.
Further research is being conducted to more fully explore clinical applications of the amplitude growth function. Preliminary research at the Cooperative Research Centre in Melbourne, Australia (Cohen et al., 2001) suggests that the amplitude growth function may correlate with the perceptual loudness growth function (Figure 5). This information may be helpful for improved loudness mapping in speech processors. Research in the experimental animal has also shown that the ECAP amplitude growth function significantly correlated with spiral ganglion survival (Hall, 1990). The growth function might therefore be used to estimate differences in residual nerve survival.

CAN NRT BE USED TO PREDICT T- AND C-LEVELS FOR THE RECIPIENT’S MAP?

The clinical value of NRT is backed by research from several clinical trials which have shown several important relationships between the current levels of the post-operative T-NRT and those of the behavioural T- and C-levels in the recipients’ MAPs (Cafarelli Dees et al., 2000, 2001; Brown et al., 2000; Lai and Dillier, 2000b; Hughes et al., 2000; Murray et al., 2000a; Thai Van et al., 2000). The major findings were:

- The T-NRT levels significantly correlate with the behavioural T- and C-levels.
- However, the T-NRT levels are not equal to either the T- or C-levels. The T-NRT levels typically lie between the T- and C-levels, on average at about 70% of the dynamic range (Figure 6). T-NRT is typically audible to the recipient.
- The profile of the T-NRT levels as a function of electrode number resembles the profiles of the T-levels, and to a lesser extent the C-levels (Figure 7).

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The relationship between the T-NRT and behavioural T-levels is influenced by several factors. The number of auditory neurons contributing to a visible neural response may be greater than the number of responding neurons for a perceptual hearing threshold. The T-NRT levels would therefore be higher than those of the behavioural T-levels. Also, different pulse rates and pulse trains have been used to measure T-NRT and the behavioural T-levels. It is known that temporal summation will affect the behavioural T- and C-levels (Murray et al., 2000b), and may therefore also affect the correlations. NRT stimuli so far have typically used a pulse rate of 80 pulses/s. The behavioural T- and C-levels for the SPEAK strategy are measured using a pulse rate of 250 pulses/s and the recommended default rate for the ACE™ and CIS strategies is 900 and 1200 pulses/s. Hearing thresholds tend to be lower for the higher pulse rates. Even though the pulse rates used in the behavioural measures vary, the profile of T-NRT closely follows the profile of the T-levels and the T-NRT values significantly correlate with the behavioural T-levels for rates between 35 and 1200 pulses/s (Murray et al., 2000a). The option to record NRT at stimulation rates up to 400 pulses/s will be available in the NRT Version 3.0 software, and it would be expected that the correlations between the T-NRT and the behavioural measures will improve because of the more similar pulse rates.

It has also been shown that the correlations between T-NRT and the behavioural T- and C-levels improve over time in children (Thai Van et al., 2000). This improvement could reflect the improved accuracy in setting the T- and C-levels as the children become more familiar with the auditory signal and are better able to respond appropriately. For instance, perceptual markers of the comfortable listening level could be absent in the congenitally deaf child with no prior auditory experience, and these markers possibly develop over time with experience.

These relationships between the objective T-NRT and the behavioural T- and C-levels have led to the development of formulae to predict the T- and C-levels using NRT together with a reduced amount of information from behavioural measures. Brown et al. (2000) reported significant correlations of \( r = 0.83 \) for the T-level and \( r = 0.77 \) for the C-level between the predicted and behavioural levels in a study with 44 adult recipients. The predicted levels were calculated using behavioural measures on a single electrode in the middle of the array and the T-NRT levels for a series of electrodes. Similarly in a group of 20 children high correlations were found between the behavioural T- and C-levels and those predicted using the same procedure (Hughes et al., 2000).

Several research studies have investigated speech understanding by recipients using MAPs calculated from T-NRT formulae and limited behavioural results (Murray et al., 2000b; Smoorenburg et al., 2001). As shown in Figure 8, NRT based MAPs can provide significant speech information to recipients. This encouraging finding clearly indicates that NRT based MAPs would be particularly helpful for difficult-to-test recipients. However, because there can be some variability in the relationship between the behavioural T- and C-levels and T-NRT across the array (Lai and Dillier, 2000b) these predictive methods of setting the T- and C-levels of MAPs to be used by recipients are still being refined.

![FIGURE 8: Scores for open set CNC words in quiet from seven adults using NRT based MAPs and behaviourally established MAPs (Murray et al., 2000b). The NRT based MAPs provided significant speech information to the recipients. There were no significant differences between the two MAPs.](image-url)
HOW NRT CAN HELP CLINICIANS – THREE CASE STUDIES

1. Programming the multiple-handicapped child

This case concerns a six year old multiple-handicapped child (Figure 9) who received a Nucleus 24 implant. Before implantation she had limited gestural as no oral communication, but did have eye blinking responses to visual stimulation.
Post-operatively in the MAP fitting sessions, the stimulation levels were increased slowly until there was an eye-blink response indicating auditory stimulation. The initial programming sessions were carried out with extreme caution to avoid any adverse reactions. The clinicians used the available T-NRT data to reassure themselves and the family that the psychophysical measures were appropriate. For this recipient the T-NRT levels were recorded at about 33% of the dynamic range.

2. Programming an adult with a long duration of deafness and hearing aid use

Post-operative NRT can also be helpful in optimizing the MAP for adults. This 42 year old woman had a severe-to-profound hearing loss and had worn hearing aids for many years prior to receiving the Nucleus 24 implant. She had considerable experience in hearing assessment and her responses in speech processor programming were consistent and reliable.

However, she was not making good progress with the implant and she began to report headaches after wearing her speech processor for several hours. Her clinician decided to investigate a new NRT based MAP. NRT measures were taken on three electrodes and an extrapolated MAP was created. The C-levels were set at the T-NRT + 10 current levels, and the T-levels remained at the previous psychophysical levels. When the NRT based MAP was tested the recipient reported that speech was much clearer and she no longer complained of headaches.

The NRT based MAP had lower C-levels. The recipient had been accustomed to the high powered low frequency range of her acoustic hearing aids and had some difficulty finding a suitable level for the high frequencies she was now receiving from her implant. NRT assisted the clinician in finding comfortable levels for the C-levels, especially for the basal electrodes which code high frequencies.

3. The difficult-to-condition child

The intra-operative NRT measures can be a helpful guide for setting the current levels at the first and subsequent MAP fitting sessions. In this case, a two and a half year old congenitally deaf child was very difficult to condition. In the MAP fitting sessions, the intra-operative T-NRT measures assisted the clinicians in setting arbitrary T- and C-levels. The clinicians used the intra-operative T-NRT levels, which were audible to the child, as a starting point for conditioning behavioural responses (Figure 10). By two months post-activation, a stable MAP was achieved and the child was responding more consistently to sound. Without the information from the intra-operative NRT, it would have taken considerably more clinical time to achieve a stable MAP. The family were also reassured that their child was being stimulated during the first few months of using the implant.

![Figure 9: Behavioural T- and C-levels and T- NRT levels at five and nine months after surgery in a multiple-handicapped child who was implanted at six years of age. The T-NRT levels confirmed that the behavioural responses were appropriate.](image)

![Figure 10: A series of T- and C-levels over time and the intra-operative T-NRT levels in a difficult to condition child who was implanted at two and a half years of age. The upper graph (A) shows the initial T- and C-levels, and the lower graph (B) shows the subsequent T- and C-levels at later MAP fittings. The intra-operative T-NRT levels guided the clinicians in fitting the MAP.](image)
IN SUMMARY

- Nucleus NRT is a valuable clinical tool of the Nucleus cochlear implant system, providing information about the integrity of the implant and the status of the peripheral auditory nerves.
- NRT can be readily recorded in most recipients of the Nucleus 24 implant system, with post-operative success rates in the order of 95%.
- NRT can be quickly measured soon after the device has been surgically implanted and before the recipient leaves the operating theatre, providing direct evidence of the auditory nerve's responsiveness.
- At any time, NRT can clearly indicate whether the residual auditory nerves are being stimulated, reassuring surgeons, clinicians and families that the implant recipient will be able to benefit from the device.
- NRT can be particularly helpful in guiding the clinician in setting the MAP levels of young children and recipients who are difficult to test.
- NRT shows considerable promise in providing information for predicting the appropriate T- and C-levels to be used in the MAPs of recipients where there is very limited behavioural information.

Research is continuing into the benefits of NRT. The roles of the ECAP amplitude growth and refractory recovery functions are being investigated in several on-going research studies. Cochlear is committed to further development of the Nucleus NRT software and advances in implant telemetry so that NRT can be even more useful for clinicians and cochlear implant recipients.

REFERENCES


