Neural Response Imaging: Measuring Auditory-Nerve Responses from the Cochlea with the HiResolution™ Bionic Ear System

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Neural Response Imaging (NRI) is the method by which one can measure responses from the auditory nerve using the HiResolution™ Bionic Ear System. In short, one contact of the HiFocus® electrode is used to stimulate surviving nerve fibers, and another contact is used to measure the resulting electrical activity. The ability to measure neural responses is highly dependent upon how much neural tissue remains, the stimulus used, and the recording technique.

What is being measured with NRI?

In a normal ear, a single auditory nerve fiber generates an action potential when the cell's membrane is depolarized to a threshold value, after which a spike occurs. (Though not detailed here, sodium ions entering the cell make the inside of the cell more positive, that is, depolarized. Injected current will depolarize a nerve cell.) It is like taking a photograph by pressing the shutter button on a camera. Pressing on the button has no effect until it crosses a threshold pressure, and then "click"—the shutter opens and the film is exposed. In the same way, depolarizing a neuron has no effect until it reaches a threshold, and then—all at once—an action potential is generated.

Moreover, as long as the neuron remains depolarized beyond its threshold level, action potentials, or spikes, will continue to occur. The firing rate (spikes per second) is dependent on the magnitude of the depolarizing current—the greater the current, the faster the spike rate. However, there is a limit to the rate at which action potentials can be generated. The maximum rate is about 1000 spikes per second. In other words, once a spike occurs, it is impossible to generate another one for about 1 millisecond. That time is called the *absolute refractory period*.

One can measure individual action potentials only by placing a microelectrode inside the nerve cell. Nonetheless, it is possible to measure the electrical activity of neurons using electrodes placed outside of the cells. However, these relatively large electrodes can measure only the voltages that represent the complex sum of spike activity across a large number of nerve fibers. The summed responses of many fibers are termed the *compound action potential* or CAP.

In order to have enough voltage to measure a CAP, the measuring electrode must be fairly close to the nerve tissue, a sufficient number of neurons must be firing, and the spikes must occur closely in time. Thus, the ability to measure a CAP is highly influenced by how many nerve fibers are available to respond, whether those fibers fire synchronously or are in refractory periods, and the fibers' location with respect to the measuring electrode.

What does the electrical CAP look like?

A typical electrically elicited CAP (ECAP) consists of a triphasic waveform with a small positive peak (P1) followed by a negative trough (N1) followed by a positive peak (P2) (Figure 1). The latency of the CAP—the time between stimulus onset and the onset of P1—is about 100-300 µsec. The amplitude of the ECAP is defined as the absolute difference (in µvolts) between N1 and P2. This amplitude usually increases with the magnitude of the stimulating current because more nerve fibers are contributing to the response as the stimulus level is increased.

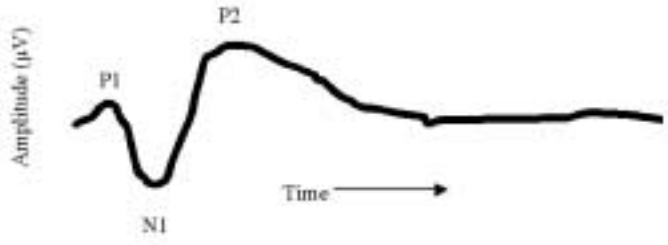

Figure 1. Typical ECAP waveform. The amplitude of the ECAP is defined as the voltage difference between N1 and P2.

How does NRI elicit and measure the ECAP?

The NRI software uses biphasic pulses to elicit the ECAP. However, one of the technical problems associated with measuring CAPs or ECAPs is that the stimulus artifact is much bigger than—and overlaps—the responses. In order to reduce that artifact, NRI delivers the stimulus pulses in alternating polarity. When the responses to many stimulus presentations are averaged, the stimulus artifact cancels out (because the alternating positive and negative pulses sum to zero) and the ECAP responses are enhanced. In contrast, neural response telemetry (NRT) software uses a masker-probe technique to cancel the stimulus artifact. That method requires collecting more averages and, because the amplifier has a slower recovery time, the amplifier parameters must be set for each response desired.

With NRI, the stimulus pulse width is 32 µsec and the pulses are delivered at a rate of 30 pulses per second. Clearly, that pulse width is wider than the pulses typically delivered with HiRes, and the stimulation rate is orders of magnitude slower. Why the differences? First, the pulse width is longer because the pulse must be long enough to elicit synchronous neural firing, yet shorter than the response latency (100-300 µsec). The stimulation rate is much slower because, as the rate increases, nerve fibers will enter their refractory periods. Consequently, the neurons will fire less synchronously and the ECAP will be much smaller, or not measurable at all.

Note the difference. It is important that the nerve fibers fire synchronously in order to elicit a measurable ECAP. Therefore, a SLOW stimulation rate is used with NRI. On the other hand, it is not desirable for the fibers to fire synchronously during live sound processing because with very high rates 1) the listener's dynamic range may be widened and (2) neurons will be able to follow temporal information in the signal. Therefore, a HIGH stimulation rate is used with HiResolution™ Sound (HiRes™) processing.

During an NRI evaluation, an input-output function is generated. That is, the neurons are stimulated with different pulse amplitudes and the N1-P2 amplitude is measured. Typically, the responses to 32 stimulus presentations are measured and averaged. If the resulting ECAP amplitude is plotted as a function of stimulus intensity, an input-output curve, or neural growth function, is generated (Figure 2).

There are two NRI responses currently used to compare across electrodes or time, or to compare to HiRes program levels. The first is termed the "1st NRI". The 1st NRI is defined as a stimulus level that elicits a response having an N1-P2 amplitude between 20 and 50 µvolts. Typically, that amplitude range is the smallest ECAP that can be detected visually. The other NRI response is called the "tNRI." If one draws a line through the input-output function and extrapolates down to the stimulus level that would elicit a threshold ECAP response, that level is the

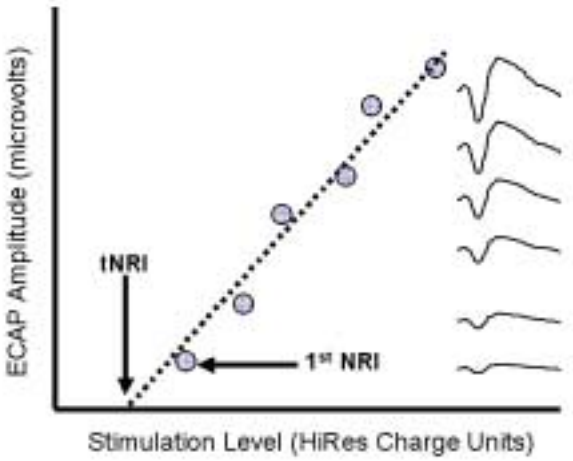

Figure 2. ECAP input-output function, also called the neural growth function (response waveforms at right). The 1st NRI is defined as the lowest stimulus level that elicits an observable ECAP response. The tNRI is defined as the stimulus-level x-intercept created by fitting a regression line to the input-output function.

tNRI (Figure 2). Note that the true threshold cannot really be measured because it falls below the noise floor.

By converting the 1st NRI and tNRI stimulus levels to HiRes charge units, a HiRes stimulus with the same current density can be determined. The conversion equation is:

HiRes charge units = pulse width x pulse amplitude x 0.0128447

The relationships between ECAP amplitude and HiRes loudness perception using stimuli with comparable current densities then can be explored.

Are NRI levels comparable to M levels?

Figure 3 shows the average 1st NRI and tNRI levels in comparison to the average M levels from 19 patients that participated in the HiRes clinical trial. If one were to average across all electrodes, the average 1st NRI was at 85% of M whereas the average tNRI was at 65% of M. Note that these are averages and may not be applicable to individual patients. Nonetheless, the relationships can be used as ballpark guides when no behavioral data are available.

Interestingly, the relationships between neural responses and program levels for patients in other studies are quite similar to the HiRes patients (Figure 4). In order to make comparisons across the different pulse widths and amplitudes used by other devices, data from other studies were converted into HiRes charge units. Not only are the average levels required to elicit an ECAP similar but the standard deviations (as indicated by the error bars) also are similar across studies. These data reflect the fact that neural responses to electrical stimulation are, on average, comparable across devices.

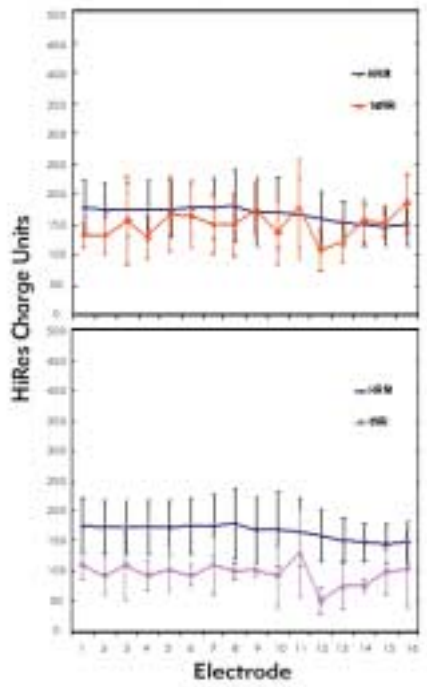

Figure 3. Average 1st NRI, tNRI, and HiRes M levels for 19 patients who participated in the HiRes clinical trial.

It is important to note that the data in Figure 4 are from patients where the ECAP could be recorded. In other words, there is a selection bias in the data. So one might ask what the real hit-rate is for NRI. As of February 2003, the HiRes data set (including patients not in the HiRes clinical trial) indicates that a neural response could be verified in 96% of the cochleae tested. Furthermore, of the 349 electrodes tested, neural responses could be identified in 74% of the cases at or below a "most comfortable" psychophysical level for the NRI stimulus. If the maximal comfort level for the NRI stimulus was used as the criterion, then neural responses could be seen in 91% of the electrodes tested. It should be noted that this is still a small data set and may or may not reflect the demographics of the general implanted population. The NRI field trial currently underway will provide more information for determining hit rates in the real world.

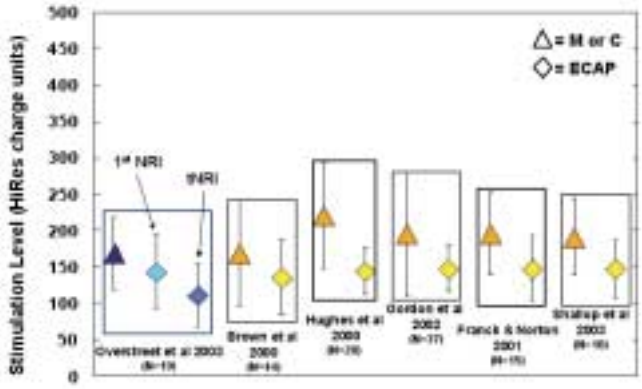

Figure 4. tECAP levels and behavioral M or C levels for HiRes patients and for patients using the Nucleus device. All stimulus levels were converted to HiRes charge units for comparison.

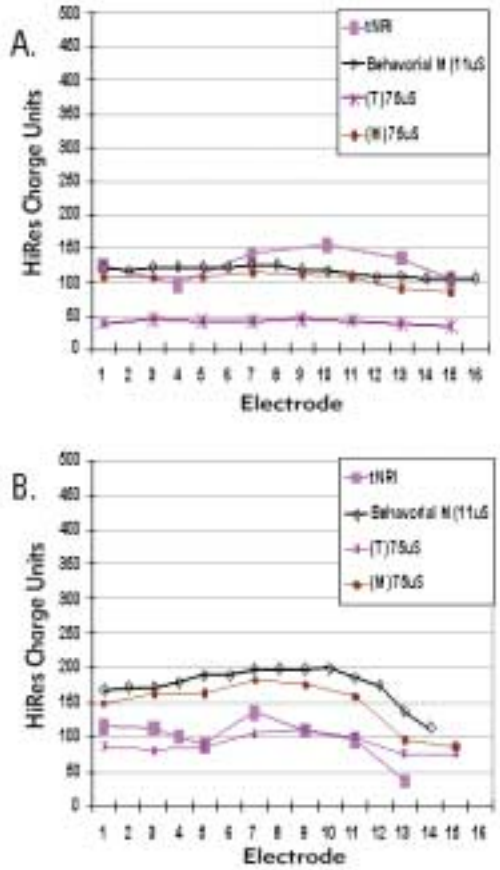

Figure 5. tNRI levels, behavioral speech M levels, and single-channel T and M levels for two HiRes patients.

The data in Figures 3 and 4 are averaged data, and it is important to realize that individual data may be much more variable. Figure 5 shows data from two patients where the NRI levels fell at different extremes of their dynamic ranges (both patients were using conventional strategies with a 75 µsec pulse width). For the patient in panel A, the tNRI levels were always above the M levels, although the contours were similar across electrodes. For the patient in panel B, the tNRI levels were substantially lower than the M levels. In fact, the tNRI levels were closer to this patient's T levels.

These individual variations are encountered frequently in the clinic, sometimes across an electrode array in the same patient. It is important to remember that the level required to elicit the ECAP is not the same as the level that elicits a perception of "loudness." In other words, "loudness" is determined centrally rather than in the cochlea. Thus, without behavioral responses, it is impossible to determine the "loudness" of a stimulus based only upon the output of the cochlea. Nonetheless, the ECAP will be elicited by a stimulus that is audible. However, the ECAP will not tell us where this audible level falls within an individual patient's dynamic range. Interestingly, the contour of the ECAP thresholds across electrodes often will follow the contour of the behavioral measures of M levels. Therefore, when no other behavioral information is

available, it is not unreasonable to create a program that follows the NRI contour.

Can NRI be used to troubleshoot?

Based upon clinical experience to date, there are several situations where NRI may be helpful in troubleshooting. One situation is to use the NRI as an electrode integrity test. If the NRI response is substantially different on one electrode compared to its neighbors (and there is no artifact problem), then one might try removing the channel from the program.

The other situation is when an NRI response cannot be recorded at all. On one hand, if the patient can hear the stimulus and no NRI is recordable, even at uncomfortably loud levels, the behavioral response determines how the program is set. More specifically, if the M level is below 250-300 HiRes units and no NRI can be recorded, there is no cause for concern. On the other hand, if the stimulus level is high and the patient cannot hear the stimulus AND no NRI can be recorded, a more serious problem may exist. To examine this issue, a study of the relationship between M levels and speech perception is underway. Figure 6 shows three-month CNC scores as a function of average M levels for the 51 patients in the HiRes clinical trial. Notably, even though some "poor" performers may have low M levels, there are no "good" performers who have high M levels in this group of patients. If, in fact, M levels are related to ECAP thresholds, then a high M may indicate that there is poor neural survival, thereby suggesting a poor prognosis for benefit from the implant.

Bear in mind that the data in Figure 6 are from postlingually deafened adults in the clinical trial and may not reflect the real distribution of M levels seen in the average clinic. For example, patients who have deformed cochleae or have had meningitis may show substantially different M levels compared to patients with normal cochleae. Studies are ongoing to define "normal" program levels in the broader population of implant users and how those levels correlate with outcome/performance in both pediatric and adult patients. The goal is to understand how to better identify and optimize program settings for poor-performing patients.

Limitations of Existing Neural-Response Measurement Techniques

There are limitations to using available neural-response measurement techniques to evaluate neural survival or to predict HiRes program levels. For example, the exact cochlear or modiolar location from which the responding neurons originate is unknown. All that is known is that an unspecified population of neurons has responded to current delivered at a particular electrode contact. There is no way to determine whether current delivered at one contact stimulates a different population from current delivered at another contact, or the amount and extent of overlap.

One also cannot make direct comparisons between the amplitude of the ECAP and an individual's perception of loudness. In normal ears, there is no direct relationship between the number of neural spikes and loudness judgments because loudness is a central auditory phenomenon. Even if some clear relationship did exist in normal listeners, it likely would be disrupted in ears with significant neural degeneration.

Future NRI Developments

In spite of these limitations, the neural responses measured using NRI may be helpful in estimating other program parameters in HiRes users. In addition to the programming suggestions discussed above, further research is aimed at using NRI to assess channel interactions as well as neural growth functions. Understanding channel interactions, in turn, will enable optimization of channel number and electrode pairing during simultaneous stimulation. Furthermore, comparing NRI responses to evoked potentials from higher auditory centers may reveal more about the status of the entire auditory pathway in cochlear-implant users. Studies are underway that explore further the applications of NRI (Abbas et al. 2003, Firszt et al. 2003, Perry and Somarriba 2003).

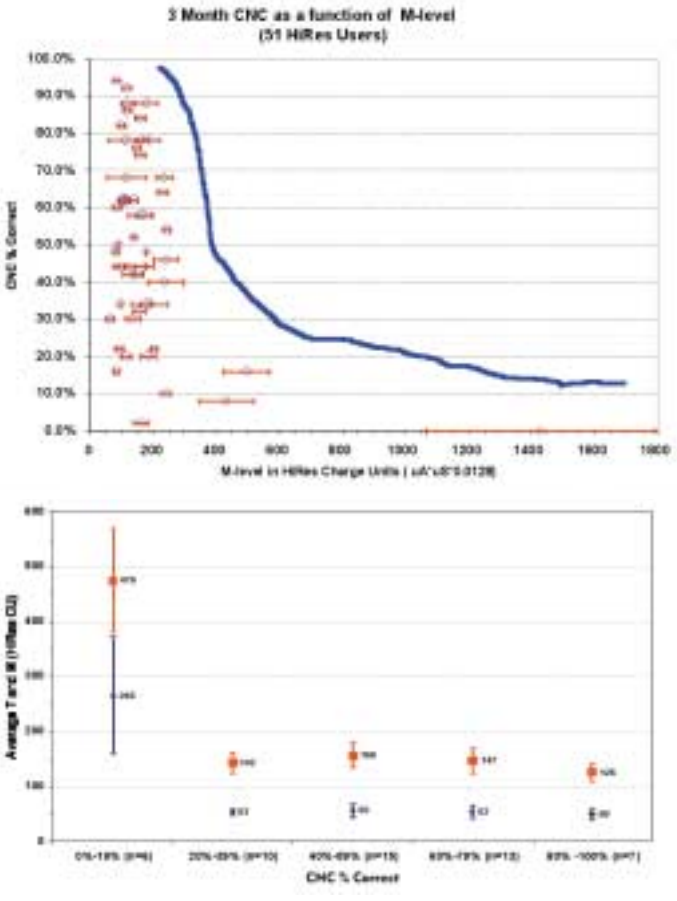

Figure 6. CNC scores vs. M levels for 51 HiRes patients who participated in the HiRes clinical trial. Upper panel: Individual CNC scores vs. M levels (average and range over 16 electrodes) for all patients. Lower panel: Average M levels (live speech adjusted HiRes M) and T levels (75 µsec pulses, 877 pulses per second) vs. grouped CNC scores.

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