NRT: Comparison of Artefact Cancellation and Threshold Estimation Techniques

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APRIL 2007.

Dedicated To

MAA, BABU,

DIDI,

& DIMMA

CERTIFICATE

This is to certify that this dissertation entitled **"NRT: Comparison of Artefact Cancellation and Threshold Estimation Techniques"** is a bonafide work in part fulfillment for the degree of Master of Science (Audiology) of the student with Registration No. 05AUD015. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other university for the award of any diploma or degree.

Dr. Vijayalakshmi Basavaraj,
Director,
All India Institute of Speech & Hearing,
Mansagangothri, Mysore - 570 006

Mysore
April 2007

CERTIFICATE

This is to certify that this dissertation entitled **"NRT: Comparison of Artefact Cancellation and Threshold Estimation Techniques"** has been prepared under my supervision and guidance. It is also certified that this dissertation has not been submitted earlier to any other university for the award of any diploma or degree.

Manjula.P
30.4.07

Ms. P. Manjula
Guide,
Lecturer in Audiology,
All India Institute of Speech & Hearing,
Mansagangothri, Mysore - 570 006

Mysore
April 2007

DECLARATION

This is to certify that this master's dissertation entitled **"NRT: Comparison of Artefact Cancellation and Threshold Estimation Techniques"** is the result of my own study and has not been submitted earlier to any other university for that award of any degree or diploma.

Mysore
April 2007

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CHAPTER I

Introduction

The first published report of electrical stimulation of the auditory system in an individual with hearing loss was provided by Djourno and Eyries in 1957. Since then, there have been several advancements in the field of electrical stimulation of the auditory system, which has led to the development of modern day cochlear implants. Cochlear implants are surgically implanted electronic devices coupled to external components that provide useful hearing and improved communication to adults and children with severe to profound hearing loss (Zwolan, 2002). A cochlear implant by-passes the middle ear and damaged inner ear and provides direct electrical stimulation to the spiral ganglions in the auditory nerve.

Cochlear implants are proven devices that provide high levels of open-set speech understanding. However, many subjects do not achieve similar results as the best user. The variability in performance among users can be the result of a number of factors, including electrode placement, nerve survival, changes in the central auditory nervous system secondary to hearing loss, effects of electric stimulation over time, and cognitive differences among individuals (Abbas & Brown, 2000). The amount of useful auditory information that an individual can expect to obtain from a cochlear implant is extremely variable (Tyler, 1987; Shannon, 1983; Gantz et al., 1988; Parkin & Stewart, 1988; Youngblood & Robinson, 1988). Although through imaging techniques determination of electrode position with in the cochlea is possible, it is not possible to gain knowledge about the neural survival pattern using the imaging techniques. As a result, the need for objective measures evolved that could check the functioning of the device in vivo as well as to assess the characteristics of the electrically stimulated auditory nervous system.

There are various physiological and electrophysiological tests by which the integrity of the cochlear implant system can be assessed, both intra-operatively and post-operatively. The most common among them are electrically evoked compound action potential (ECAP), electrically evoked auditory brainstem response (EABR) and the electrically evoked stapedial reflex test (ESRT). Among these, the most popular and commonly used is the ECAP measurement, because in present day cochlear implant systems, it can be performed quickly and does not require any additional evoked potential averaging system, like in EABR measurement or an immittance system to monitor stapedial reflex, as required in an ESRT measurement. These tests not only confirm the device integrity and functioning, but also findings from these tests are used for studying the neural survival rate and programming the speech processor of the cochlear implant.

The pioneering step towards recording of ECAP in humans was the recording of electrically evoked whole nerve action potential from human cochlear implant users, in 1990, by Brown, Abbas and Gantz. They described a method of recording the ECAP in humans who have been implanted with the Ineraid intra-cochlear electrode array. The procedure described was an adaptation of a paradigm described by Sauvage, Cazals, Erre, and Aran (1983).

The ECAP is a very short duration neural potential that reflects the synchronous firing of a large number of electrically stimulated auditory nerve fibers. In humans, this response consists primarily of a negative peak (often referred to as N1) with a latency of

0.2 to 0.5 ms (Brown, 2004). At high presentation levels, the initial negative peak is followed by a less robust positive peak that is referred to as P2 (Brown, 2004). The amplitude of the response should be directly proportional to the number of synchronously firing auditory nerve fibers.

The ECAP measurement in various commercially available cochlear implant systems are known by different names. The ECAP measurement is called Neural Response Telemetry (NRT) when measured using Nucleus cochlear implant systems, Neural Response Imaging (NRI) when measured through Advanced Bionics cochlear implant systems, and Auditory Nerve Response Telemetry (ART) when recorded with Med El systems. However, the present study concerns with subjects implanted with Nucleus Freedom cochlear implant system and so only NRT is being discussed in details.

The NRT process involves electrical stimulation of auditory nerve fibers through an intra-cochlear electrode and then recording of the resultant neural response by the same or an adjacent intra-cochlear electrode. The NRT delivers certain amplitude of current which is sent to the internal device utilizing a radio frequency (RF) link through the skin. The resultant neural response is recorded by an intra-cochlear electrode and sent, using the same RF link, back to the NRT software for analysis. NRT has been so named because the process involves neural response measurements from far placed electrodes using RF communication link, i.e., tele measurement of neural responses.

Theoretically, the best way to record ECAP might be stimulating a given intra-cochlear electrode and use the same or one electrode adjacent to it to record the evoked neural activity (Brown, 2004). However, the raw ECAP recording not only consists of a neural activity, but also a very large stimulus artefact. The neural response is embedded with in the stimulus artefact, because the latter is of much higher amplitude. The stimulus artefact is often large enough to saturate the recording amplifier. A saturated amplifier will take a finite amount of time to recover. Amplifier saturation is not a problem in cases where the recorded neural activity is of relatively long latency, giving the amplifier enough time to come out of saturation. Unfortunately, because of its very short latency, saturation of the recording amplifier and the distortion produced by this saturation can present major problems when electrically evoked intra-cochlear potentials are recorded (Brown, 2004). This problem has led to several proposals for reducing or minimizing the stimulus artefact recorded during ECAP measurement.

The Custom Sound EP is one of the latest softwares from Cochlear Corporation which has facilities for advanced electrophysiological measurements, including NRT. In Custom Sound EP (version 1.3), there are four different options, to minimize the stimulus artefact. These have been referred to as Artefact Cancellation Techniques. They are 1) Forward masking, 2) Artefact template, 3) Alternating polarity, and 4) Masked response extraction. The present study is concerned with only the first three Artefact Cancellation Techniques. The participants in the present study were young children and it was difficult to get their co-operation for long testing sessions. So, the fourth technique i.e., masked response extraction was not included in the present study.

The forward masking method was proposed Brown, Abbas and Gantz, in 1990. This method involves a two-pulse subtraction technique (Brown, 2004). Hence, this method is also known as the subtraction paradigm. The method involves a non-simultaneous forward masking paradigm, using a masker plus probe condition, to put the auditory nerve fibers into refractory period and thereby recording only the stimulus and masker artefact. This is subtracted from the probe alone condition which consists of both stimulus artefact and neural response. The resultant is a neural response with a masker artefact. The masker artefact is then removed by recording of a masker alone condition.

The artefact template method was proposed by Miller, Abbas, Rubinstein, Robinson and Matsuoka, in 1998. The method involves recording of a scaled down template of the stimulus artefact at a sub-threshold level that consists of only stimulus artefact and no neural response (Brown, 2004). The template of the artefact is then systematically scaled up during recording at threshold or supra-threshold level and deducted from the raw ECAP measurement, to reduce the effect of the stimulus artefact.

The alternating polarity method is based on the phenomenon that the stimulus artefact always follows the stimulus polarity (Brown, 2004). Hence, the stimulus recorded using an anodic-leading and a cathodic-leading biphasic current stimuli will be opposite in phase. However, the polarity of the neural response does not change with stimulus polarity. Hence, when a number of recordings of anodic-leading biphasic current stimuli alternatively followed by cathodic leading biphasic current stimuli are averaged, the stimulus artefact is cancelled out without affecting the neural response much.

However, it is to be remembered that although in the Custom Sound EP software they are named as Artefact Cancellation techniques, no technique can essentially be expected to cancel out the stimulus artefact fully. There are differences in the working principle used to reduce the stimulus artefact in these three different artefact cancellation techniques mentioned above. Hence, the NRT or the ECAP recorded using them might be expected to vary in terms of latency, threshold, amplitude and morphology. Therefore, the need arises to study systematically, in detail, and compare the NRT recorded using the three different artefact cancellation techniques mentioned.

Further, there is a dearth of literature comparing various techniques to reduce artefact while recording NRT/ECAP. A study by Klop, Hartlooper, Briare and Frijns (2004) compared only between the forward masking paradigm with the alternating polarity method with respect to morphology and latency only. Also, comparing the threshold and the amplitude at the threshold of the recorded NRT/ECAP using different techniques to reduce stimulus artefact is also required.

The artefact template method of artefact stimulus reduction has been incorporated for clinical use recently in the Custom Sound EP software. There is a dearth of literature describing the NRT/ECAP recorded with this technique.

Once the NRT is recorded at different current levels, there is a need to identify the threshold of NRT (T-NRT), i.e., the minimum current level at which a NRT response is obtained. Threshold estimation of NRT can be done by visual inspection of the NRT waveform or by automatically by the software that record NRT, based on some predefined rules.

The Custom Sound EP software has the option of "peak picker" which offers the facility of automated NRT response identification. Threshold can be defined as the lowest current level, at which the peak picker identifies a NRT response. Also, there is an option for extrapolated NRT threshold identification using regression analysis.

Hence, the efficacy of the peak picker and the regression analysis in order to extrapolate threshold of NRT or T-NRT, with the NRT recorded using the three different artefact cancellation techniques needs to be studied. These methods of T-NRT estimation needs to be compared to that of obtained by the visual method of NRT estimation.

The relationship between T-NRT and behavioral thresholds have been used to program the speech processors of the cochlear implant (Brown, Hughes, Luk, Abbas, Wolaver & Gervais, 2000; Hughes, Brown, Abbas, Wolaver, & Gervais, 2000; Cooper et al., 2003). If T-NRT varies with different artefact cancellation techniques, the same relation cannot be used. So, there is a need to study the variation, if any, in T-NRT for NRT recorded with different artefact cancellation techniques.

The present study was designed to meet the above research needs. The objectives of the present study are as follows:-

1. To record NRT using three different artefact cancellation techniques, namely forward masking, artefact template and alternating polarity, on a basal, medial and apical electrode sites in the cochlea.
2. To compare the NRT recorded with the three different artefact cancellation techniques.
3. To compare the T-NRT estimated using the visual, peak picker and regression analysis techniques.
4. To compare the amplitude of the visually estimated T-NRT for NRT recorded with the three different artefact cancellation techniques.

CHAPTER II

Review of literature

The present study compared different artefact cancellation techniques to record neural response telemetry (NRT) and, different threshold estimation techniques used in NRT. The review of the literature is discussed under the following heads:

- Recording of ECAP using telemetry
- Features in Custom Sound EP (Version 1 .3)
- Artefact Cancellation Techniques
- Estimation of NRT thresholds and amplitude

Factors affecting NRT

Recording of ECAP using Telemetry

The most direct measure of auditory nerve activity in cochlear implant users is the ECAP (Abbas et al., 1999). Initially, it was only possible to record ECAP potentials intra-operatively (Gantz, Brown & Abbas, 1994), or from cochlear implant devices which used percutaneous plug to connect the speech processor with the internal electrode array (Brown, Abbas & Gantz, 1990; Wilson, 1997). The telemetry system to measure ECAP was introduced by Cochlear Corporation in Nucleus CI24 cochlear implant. The term "Telemetry" describes the measurement of data and transmission of data from a remote source to a receiving station for recording and analysis (Mens, 2004). The telemetry system used to measure the ECAP in Nucleus CI24M users is referred to as NRT (Abbas et al., 1999). However, recording of ECAP through telemetry system of any Nucleus cochlear implant systems is known as NRT. NRT was implemented in the Nucleus C124M cochlear implant system for the first time in 1992.

All currently produced cochlear implant systems rely on radio frequency transmission link through the skin to send data or stimulate the implanted parts and electrodes of the implant (Mens, 2004)

The name neural response telemetry signifies wireless communication between the external and internal devices of the implant for measurement of neural responses. The NRT process utilizes a radio frequency (RF) link to stimulate the auditory nerves through an intra-cochlear electrode and as well as obtaining neural responses picked by another intra-cochlear electrode. Obtaining data from the intra-cochlear electrodes of the implant is sometimes referred to as 'reverse telemetry' or 'back telemetry', because speech processor perform 'forward telemetry' by measuring sound and sending the encoded signal to the internal device (Mens, 2004). NRT is a simple method of recording the electrically evoked compound action potential (ECAP) or the auditory nerve response using the intra-cochlear electrodes of Nucleus CI24 cochlear implant and later generation Nucleus cochlear implant systems.

The NRT system works by sending an electrical signal to any selected intra-cochlear electrode. When this signal is large enough to elicit a synchronous neural response from the local spiral ganglion cells, the compound action potential is recorded from an adjacent electrode, amplified, encoded, and transmitted via radio frequency to the external processor and displayed on a screen via the standard Nucleus Clinical Programming System. The recording of ECAP via NRT does not require extra electrodes and evoked response averaging equipments. In humans, this response consists primarily of a negative peak often referred to as NI with a latency of 0.2 to 0.5

ms, and at high presentation levels, the initial negative peak is often followed by a less robust positive peak that is referred to as P2 (Brown, 2004).

Features in Custom Sound EP (Versionl .3)

The Custom Sound software offers additional features for advanced electrophysiological testing in Nucleus Freedom cochlear implant systems, known as the Custom Sound EP which has advanced NRT options apart from other electrophysiological measurement facilities.

The Custom Sound EP (version 1.3) has four different options, to minimize the stimulus artefact. These have been referred to as Artefact Cancellation Techniques. These four different artefact cancellation techniques available for recording NRT in Custom Sound EP (version 1.3) are 1) Forward masking, 2) Artefact template, 3) Alternating polarity, and 4) Masked response extraction. As compared to this, NRT software (version 3.1) has only two options and these are 1) Subtraction paradigm and 2) Alternating polarity. It is to be noted that forward masking and subtraction paradigm are essentially same procedures.

Artefact Cancellation Techniques

While recording ECAP, the problem faced is that in addition to the neural response evoked by the electrical stimulus pulse, a very large stimulus artefact will also be recorded which is often large to saturate the recording amplifier (Brown, 2004). Several different techniques are now available to minimize the stimulus artefact.

In the present study we are concerned only with three different artefact cancellation techniques namely forward masking, artefact template, alternating polarity.

Following is a review of the technical details and literature behind these artefact cancellation techniques.

Forward Masking

The first recording of electrically evoked whole nerve compound action potential (ECAP) from human cochlear implant users was reported by Brown, Abbas and Gantz in 1990. The method used was an adaptation of the paradigm described by Sauvage, Cazals, Erre, and Aran 1983. The difficulty that is faced during recording of ECAP is that of the stimulus artefact which is always of several orders of magnitude higher than the simultaneously recorded neural potential. As a result, the ECAP could not be visualized in the presence of the artefact. Hence, artefact subtraction was used to extract the neural response from the stimulus artefact. The paradigm used in the above study was the forward masking paradigm. This was the first time when forward masking paradigm was used to control stimulus artefact while recording ECAP from humans implanted with cochlear implants. The forward masking paradigm used is explained below.

In the forward masking artefact cancellation technique, two biphasic current pulses are presented in a forward masking paradigm. They first pulse is referred to as "masker" and the second pulse as "probe". Recordings were made in each of three different stimulating conditions that were interleaved in the average. The first stimulus condition, the probe-alone condition, consisted of the presentation of a single biphasic current pulse. The recording made in this condition consisted of both stimulus artefact and the buried neural response. In the second stimulation condition, the masker-plus-probe condition, two biphasic current pulses were presented separated by a short inter-stimulus interval (ISI). A sufficiently short ISI are used, so that the neural response to the probe is adapted by the presence of the preceding masker, as seen in non-simultaneous masking. The recording made in this stimulus condition consists of a combination of the two stimulus artefact and the neural response to the masker alone. In the masker-plus-probe stimulation condition, the neural response to the probe is absent or reduced. This is because; the relatively high level of masker which precedes the probe by a short ISI puts the auditory nerve fibers in the adjacent areas of the masker electrode into refractory period. The probe which is presented in the same or an adjacent electrode after a short ISI interval either cannot elicit any neural response or elicits a reduced neural response. This is because the auditory nerve fibers in that area are still in the refractory period and do not fire with full strength. In the third condition, the masker-alone condition, a single pulse coincident in time with the masker of the two-pulse sequence is presented. This third condition allows the stimulus artefact obtained by the presentation of the masker and associated neural activity to be recorded without contamination by the probe stimulus.

Once the recordings have been made in each of these three stimulation conditions, extraction of the ECAP from the stimulus artefact is accomplished in two steps. First, the average response recorded in the second condition (masker plus probe) is subtracted from the averaged response recorded in the first condition (probe alone). This subtraction yields a response in which the masker artefact has been inverted 180 degrees and the probe artefact has been minimized. The second step is to add the response recorded in the third condition (masker alone) to the product of the subtraction. This step allows elimination, or at least reduction, of the artefact associated with the masker. This is illustrated in Figure 2.1 In addition, in the present day Forward Masking paradigm a 4th recording is done without any stimulus presentation. This helps to eliminate the switch-on artefact or the system artefact.

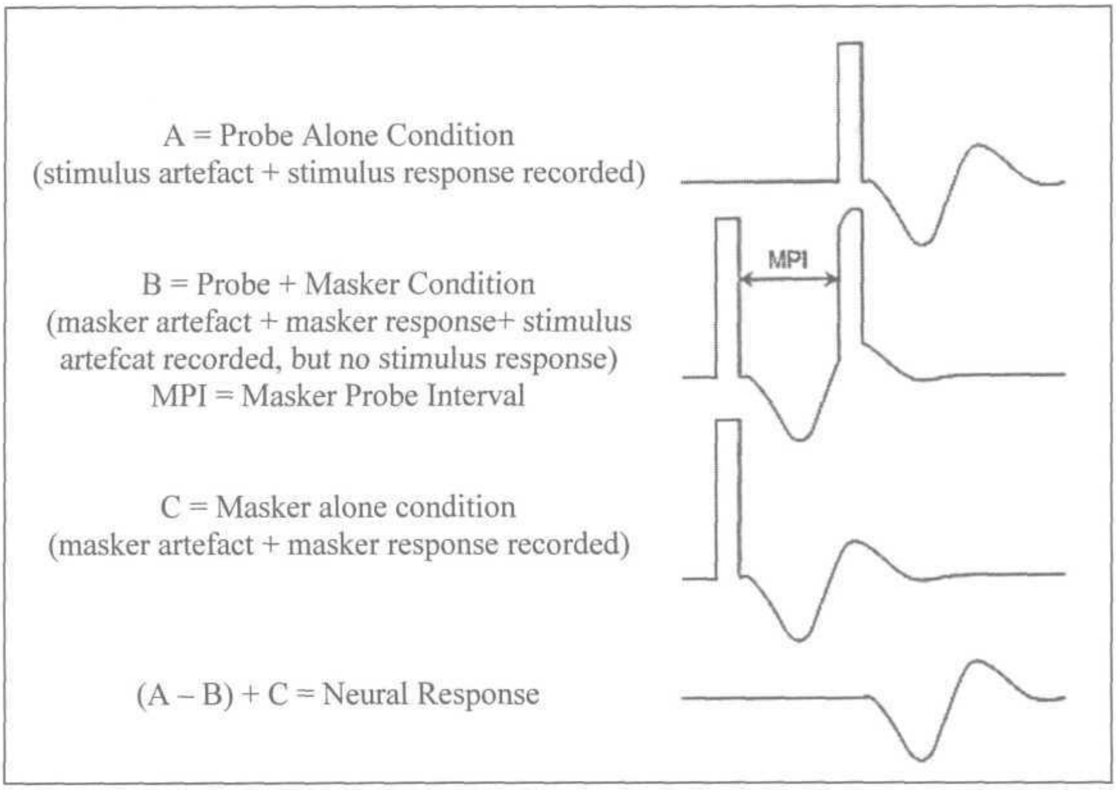


Fig. 2.1: Illustration of forward masking paradigm.

One of the main assumptions in this paradigm is that the masker-probe interval is short enough (<0.5 ms) for all the nerves to be in their absolute refractory state (Brown & Abbas, 1990). If the masker-probe interval is > 0.5 ms, there is a relative refractory component at the moment of the probe stimulus in the masker-probe frame. This is caused by some of the nerves that have recovered from their refractory state (Klop, Hartlooper, Briare & Frijns, 2004). This will result in unwanted neural response to this probe, which influences the final response calculated. Another potential problem is the fact that the masker in the masker-probe frame not only excites a certain area around the electrode, but also charges the membranes of the nerve fibers in surrounding areas. These nerve fibers, although not depolarized by the masker, approach their threshold due to their proximity to the stimulating electrode. Then, the probe stimulus in the masker-probe frame can excite these fibers, adding a neural response to the frame intended to record just the probe stimulus artefact (Klop, Hartlooper, Briare & Frijns, 2004).

Artefact Template

A second technique for reducing the effects of stimulus artefact is template subtraction (Miller, Abbas, Rubinstein, Robinson, Matsuoka & Woodworgh, 1998). This procedure of dealing with the stimulus artefact requires collection of a response with a stimulus that is known to be below the threshold. If the tissue impedance and the amplifier are linear, a current that is twice as high will produce an artefact that is twice as large. This principle can be used to record a scaled version of the artefact, by measuring the artefact at a low, sub-threshold current level. Since at a sub-threshold current level there is no response, the measured trace will only contain artefact. If now, a measurement is performed at threshold or supra threshold level which is n times more current level, it will contain both an artefact and a response. The artefact template can be scaled up by multiplying it by n. The measured trace minus the scaled up artefact template should result in a pure neural response. The paradigm is illustrated in Figure 2.2 The principal limitation to this method is that the amplifier and tissue conductance should be perfectly linear to produce exactly the same shaped artefact at a lower current level. In general, this is not the case. It also requires a system with very low levels of ambient noise. Template subtraction will not work if the stimulus artefact saturates the recording amplifier (Brown, 2004). In the Custom Sound EP 1.3 software, there is a facility for recording NRT using template subtraction method. However, in the Custom Sound EP 1.3 software, this method is known as Artefact Template.

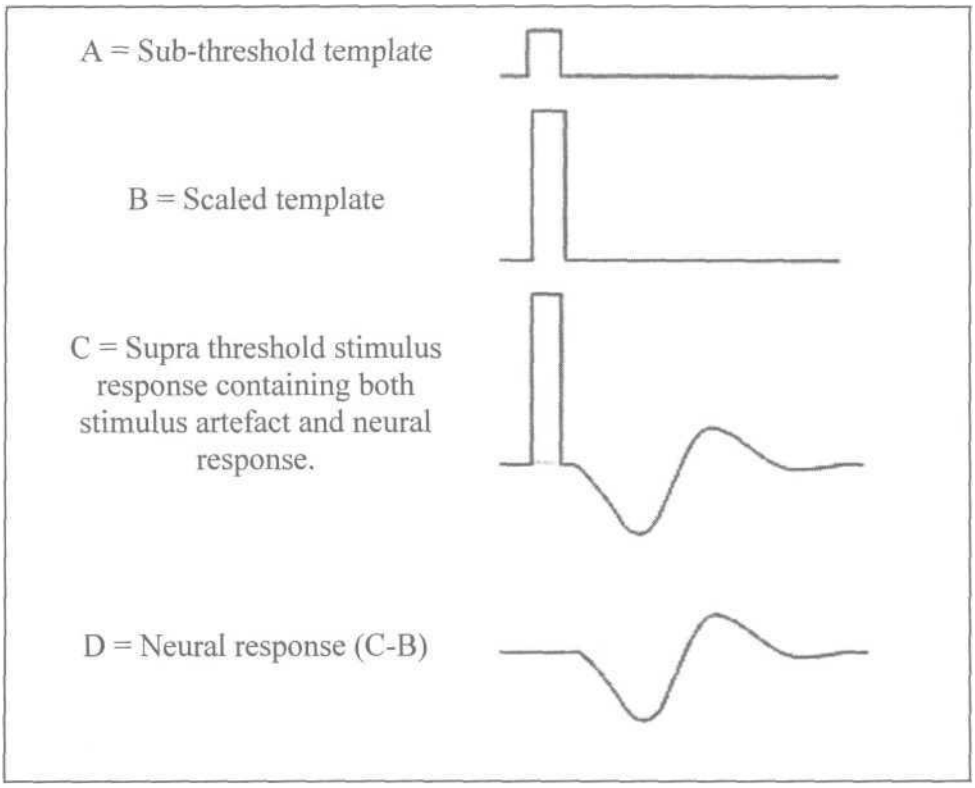


Fig. 2.2: Illustration of artefact template paradigm.

Alternating Polarity

Another common technique by which the stimulus artefact contamination can be minimized is by alternating the polarity of the stimulus in successive presentations and then averaging the response that is recorded. The stimulus artefact always follows the stimulus polarity. So, when anodic-leading and cathodic-leading biphasic current stimuli are alternated in successive stimulations, the stimulus artefacts recorded are out of phase for the anodic-leading and cathodic-leading biphasic current stimuli. When averaging is done, the out of phase stimuli artefacts are averaged out. Use of alternating polarity when recording averaged evoked potentials, will minimize both the stimulus artefact and any cochlear potential that follow the stimulus polarity. The neural response evoked by the stimulus should not reverse the polarity as the stimulus polarity is changed and therefore will be preserved in the average (Brown, 2004). An illustration is done in Figure 2.3

In specific cases, the use of alternating polarity has been shown to reduce stimulus artefact enough to record an ECAP from intra-cochlear electrodes of human cochlear implant users (Brown, Abbas & Gantz, 1990). However, the assumption underlying the success of this procedure is that the neural response is identical in response to either anodic or cathodic leading biphasic current pulses. This assumption is not always true (Van Den Honert & Stypulkowski, 1987; Miller, Abbas, Rubinstein, Robinson, Matsuoka & Woodworgh, 1998; Miller, Robinson, Rubinstein & Matsuoka, 1999). The EAP response measured for cathodic leading biphasic current pulses can have different latency, amplitude and threshold from similar responses measured using anodic leading biphasic current pulses (Miller, Robinson, Rubinstein & Matsuoka, 1999). Klop, Hartlooper, Briare, and Frijns (2004) analyzed the ECAP latency differences between cathodic- and anodic-first stimuli in more detail. They recorded ECAP with the forward masking paradigm with artefact compensation using both anodic-first and cathodic-first pulses. It turned out that the N1 and P2 latencies are shorter for cathodic-first (0.13 and 0.32 ms, respectively) than for anodic-first stimuli (0.16 and 0.38 ms, respectively). The current level used does not influence this effect. The alternating polarity method tends to be significantly smaller than that obtained with the subtraction method (r = 0.97, p<0.0001), yielding higher thresholds with alternating polarity (r = 0.86, p = 0.01) (Hughes, Abbas, Brown, Behrens. & Dunn. 2003). The above result was however reported from patients implanted with Clarion CII cochlear implant device.

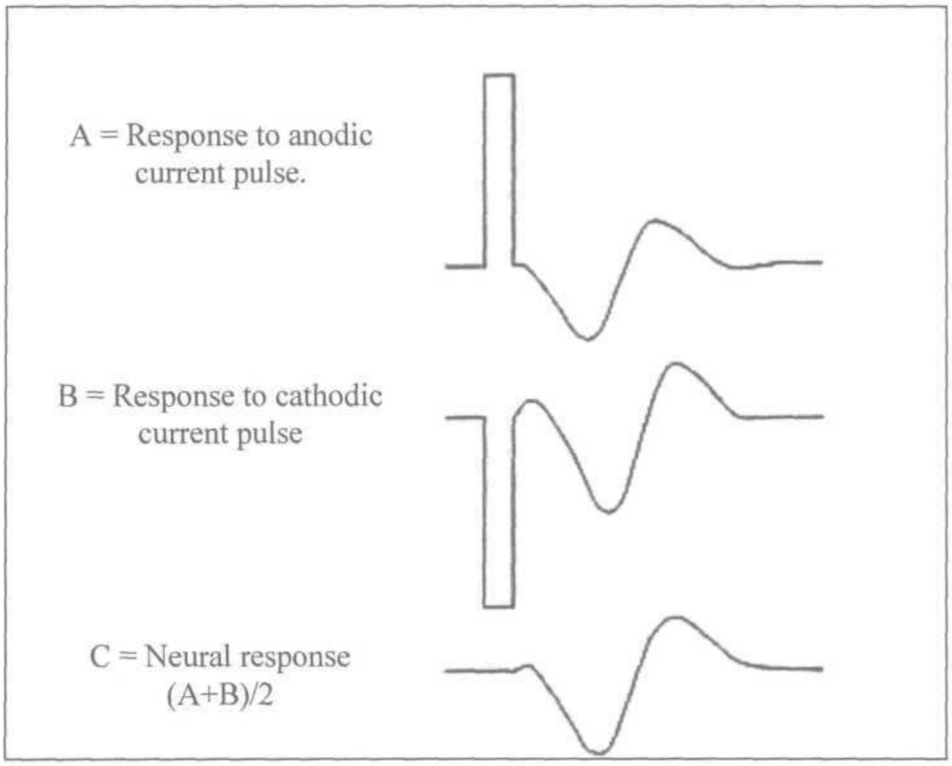


Fig. 2.3: Illustration of alternating polarity paradigm.

NRT thresholds and amplitudes

Once the NRTs are recorded at different electrode sites by varying the current levels, the threshold of the NRTs are estimated, i.e., the T-NRT which is the lowest current level required to elicit a measurable NRT needs to be estimated. There are three popular methods for estimation of T-NRT.

ECAP thresholds can be determined either by the visual method, or by the peak picker, or by regression analysis. The first method uses a visual observation of the NRT recordings and determination of the lowest current level of the stimulus that elicits a measurable response. This can be used either through ascending or descending approach. Ideally, initial responses should be obtained at a high enough supra threshold level so that the user can be sure that the neural response decreases with amplitude. One drawback to the visual detection method is that for systems with a relatively high noise floor, the true threshold can be obscured by the noise, yielding a threshold estimate that is likely to be too high (Hughes, 2006b).

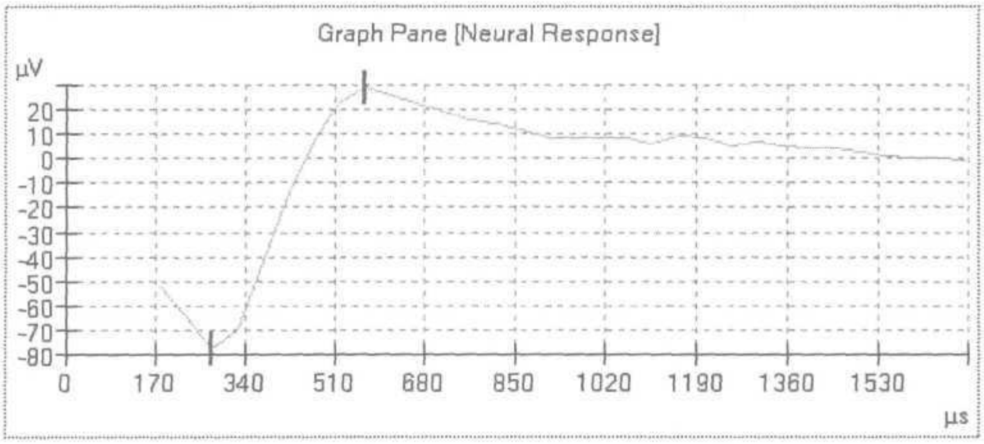


Fig 2.4: Peaks identified by the peak picker in an NRT waveform.

The second option to determine T-NRT is the peak picker. The peak picker identifies the Nl and P2 of the NRT waveforms based on a set of rules that dependent on a set of parameters such as, signal to noise ratio, current level, correlation of the recording with the previous current level and correlation of the recording with a known response. These set of rules constitute the peak picker algorithm. The T-NRT can be defined as the lowest current level at which the peak picker identifies a NRT response.

The third method of threshold estimation in NRT involves applying a regression analysis to points on an input-output (or amplitude growth) function. Threshold is determined as the level at which the regression line crosses zero amplitude (i.e., intercept of the x-axis where y = 0). This is illustrated in Figure 2.5. The advantage to this method is that lower thresholds can be extrapolated for high-noise systems (Hughes, 2006b). It is crucial to not include data points for regression analysis where (1) the function rolls over or saturates at higher stimulus levels or (2) there are multiple zero-amplitude points or points within the noise floor (Hughes, 2006b). One drawback to this method is that at least three supra threshold data points are needed to reasonably calculate a regression intercept or threshold, which can be difficult to do for patients whose ECAP thresholds are near their maximum loudness comfort levels (Hughes, 2006b).

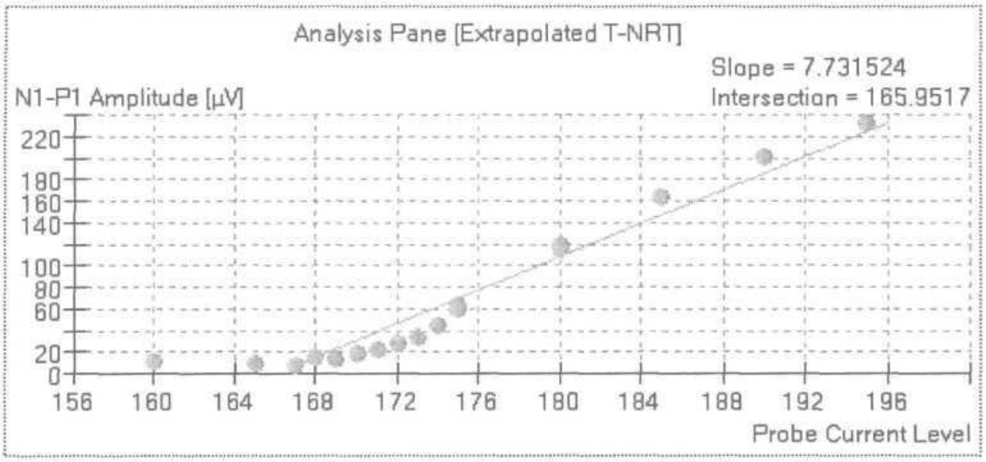


Fig 2.5: NRT amplitude growth curve used in regression analysis.

The amplitude of the NRT is typically measured from the leading trough, i.e., negative peak or Nl to the following positive peak or plateau, i.e., P2. As discussed previously, NRT has built-in algorithms known as the "peak picker'" that identifies peaks automatically so that the user does not have to measure ECAP amplitudes manually. However, sometimes the automatic "peak-picker" will mark artefact or noise in the absence of a neural response, or it will inaccurately mark a neural response contaminated with artefact (Hughes, 2006b). The NRT software uses a series of decision-making rules to determine whether a response exists or not. If it determines that there is no response in an NRT tracing at a particular current level, then no peaks will be picked and the software will indicate no response for the NRT tracing at the current level.

Nl and P2 peaks are not always prominent, and traces that are dominated by stimulus artefact can display peak-like characteristics. Furthermore, a P2 peak may not always be present - the peak picker must select a suitable maximum in its place (Botros, Dijk & Killian. 2006). In Custom Sound EP 1.3 software, eight features were considered to be potentially useful in distinguishing artefact traces. They were the latency between Nl and P2; the latency between Nl and the global maximum after N1; the latency between P2 and the global maximum after N1; the ratio of N1-P2 amplitude to the global range from Nl onwards (intuitively, N1-P2 amplitude should be a significant proportion of the global range) (Botros, Dijk & Killian, 2006). From these features there were some machine learnt rules such as if N1-P2 latency >12 samples, reject peaks if the latency between Nl and the global maximum after Nl >23 samples and the ratio of N1-P2 amplitude to the global range from Nl onwards <0.69, reject peaks; otherwise, accept peaks (Botros, Dijk & Killian, 2006).

Based on these rules, out of 2187 ECAP positive measurements. 7 measurements were rejected and out of 24 artefact traces, 2 measurements were falsely accepted, giving an overall 0.4% error rate. Also, no peaks occur at consecutive samples, so a simple added rule is that if N1-P2 latency <2 samples, reject peaks (Botros, Dijk, & Killian, 2006).

Factors affecting NRT

The most common user controlled parameters that affect ECAP measures are: recording delay (NRT only), recording electrode, current level, amplifier gain, number of averages and stimulation rate (Hughes, 2006a). Other than these, the total number of functioning auditory nerve fibers also affects the ECAP measure.

Recording delay

The recording (or sampling) delay is the amount of time between offset of the probe pulse and onset of recording. The purpose of introducing a delay between offset of the stimuli and onset of recording is to avoid saturation of the recording amplifier (Abbas et al., 1999; Diller et al., 2002). Shorter delays are more likely to yield amplifier saturation, which can obscure or distort the ECAP response. However, if the delay is too long, the recording may not capture the leading negative peak of the ECAP, which makes it impossible to correctly measure the amplitude (Hughes, 2006a). Thus, the delay should be decreased (shortened) if a negative peak cannot be resolved, and the delay should be increased if morphology is poor (Hughes, 2006a). Generally, delays between about 50 and 120 microseconds yield the best NRT results (Hughes, 2006a). Recording delay is typically the first parameter that should be manipulated to optimize ECAP recordings obtained with NRT (Hughes, 2006a).

Recording electrode

With Nucleus NRT system, often the stimulus artefact is too large to allow successful recording of the ECAP when the recording electrode is located immediately adjacent to the stimulating electrode (Brown, 2004). The default recording electrode setting in NRT is two electrode positions apical to the stimulating electrode. In most cases, this setting works well and does not often need to be adjusted (Hughes, 2006a). In some cases, however, the default position yields a recording that is contaminated by effects of amplifier saturation from stimulus artefact. The easy solution is to either change the recording electrode to one or two additional positions apically or try recording from two to three electrode positions on the basal side of the stimulating electrode (Hughes, 2006a). It should be noted, however, that the overall ECAP amplitude will generally get smaller as the recording electrode is moved farther away from the stimulating electrode (Abbas et al., 1999; Cohen, Saunders & Richardson, 2004; Frijns, Briaire, Laat & Grote, 2002). This is something to be considered if ECAP amplitudes or thresholds are to be compared across electrodes; it is generally best to use fairly consistent recording electrode spacing across the array in those cases.

Current level

As with any evoked potential, ECAP amplitude increases with stimulus level. If there is no neural response, generally the first step is to increase stimulus level, while keeping in mind the subjective tolerance levels of the subject. It is important to be mindful of voltage compliance limits within the device when requesting high cunent levels. If the requested current level is high and the electrode impedance is relatively high, the device will consequently produce insufficient voltage for the amount of current that the user is requesting (Hughes, 2006a). In NRT with Custom sound EP 1.3, a red "X" mark will appear next to any recording that is "invalid": this would include recordings made when voltage compliance was exceeded (Hughes, 2006a). It can be understood whether the recording is invalid because of voltage compliance limits, an explanation box will appear stating that the electrode is out of compliance, when the cursor is moved over the "X" mark (Hughes. 2006a). Additionally, very high stimulus levels may result in amplifier saturation. If changing the recording delay or recording electrode does not alleviate artefact contamination, then a reduction in stimulus level may help, as long as a measurable ECAP response can still be obtained (Hughes, 2006a).

Amplifier gain

If amplifier saturation presents a significant problem that cannot be resolved by extending the recording delay (if that option is available), recording from an electrode that is farther away or reducing the stimulus level, then reducing the amplifier gain may help (Abbas et al., 1999; Dillier et al., 2002). NRT in Custom Sound EP has four gains to choose from: 40, 50, 60, and 70. The default gain is 50. In all previous versions of NRT the default gain was 60 (the only other useable option was 40) (Hughes, 2006a). The new default of 50 seems to produce less amplifier saturation than the old default of 60, with less noise problems than a gain of 40 (Hughes, 2006a). The noise level typically increases when the gain is reduced, so the number of averages should be at least doubled when reducing gain (Hughes, 2006a).

Number of averages

The current default setting for the number of sweeps in Custom Sound EP is 35 for AutoNRT and 50 for Advanced NRT, regardless of whether intra-operative or post-operative testing mode is chosen. Typically 50 to 100 averages work best in most cases (Hughes, 2006a). Fewer averages are typically used in the operating room due to limitations in testing time. Generally, the number of averages should be increased for lower amplifier gains and for lower stimulus levels to compensate for the increased noise level in the recording (Hughes, 2006a).

Rate of stimulation

The default stimulation rate differs for the automatic/AutoNRT and the manual NRT/Advanced NRT modes in Custom sound EP 1.3. The default stimulation rate for the manual mode (Advanced NRT) is 80 Hz, whereas, in AutoNRT it is 250 Hz, when the intra-operative mode is chosen. In post-operative mode, both AutoNRT and Advanced NRT defaults are 80 Hz. This is important to note if some one is switching back and forth between Auto and Advanced modes to make intra-operative ECAP measures across the electrode array within a subject or if some one is comparing intra-operative to post-operative AutoNRT measures (Hughes, 2006a). Thresholds can be slightly higher (and amplitudes slightly smaller) for the faster stimulation rates (Hughes, 2006a).

Changes that are required to overcome the shortcomings of the present day technology can only be decided based on thorough investigations. This research outcome will then guide the development of future technology.

Chapter III

Method

Following method was used to study and compare the artefact cancellation and threshold estimation techniques used in NRT. The method is explained under the following headings.

Subjects

A total number of eight children (4 male and 4 female) with pre-lingual hearing loss, of severe to profound degree, participated in the study. All of the participants had CT and MRI findings of the temporal bone region that showed no contradictions for cochlear implantation. Participants who were implanted in deformed cochlea, such as, Mondini's dysplasia were not included in the study. All the participants were implanted with the Nucleus Freedom Contour Advanced cochlear implant systems from Cochlear Corporation, Australia. The mean age of the participants was 6.2 years. Out of the eight participants, 7 were implanted in the right ear and one received the implant in the left ear. All the participants had a post switch-on experience of electrical hearing with the cochlear implant system for at least 3 months.

Instrumentation

Custom Sound EP (version 1.3), from Cochlear Corporation, was the software that was used to record the NRT from the participants implanted with Nucleus Freedom cochlear implant systems. A laptop computer was used to run the Custom Sound EP (version 1.3) program. The programming POD, a hardware interface, established the link between the speech processor of the Nucleus Freedom cochlear implant system and the Custom Sound EP software installed in a computer. The POD was connected to the speech processor of the Freedom Cochlear implant, and the other end of the programming POD was connected by a USB cable to the USB 2.0 port of the laptop.

Procedure

All measurements were done post-operatively with 4, 12 and 20 as the recording electrode, which represented the basal, medial and apical part of the cochlea. During the recording process the participants were comfortably seated and were allowed to watch an animation film which held their attention.

After the connection between the computer and the speech processor was established, the advanced NRT option was selected in the Custom Sound EP (version 1.3) First an electrode impedance check was carried out in all participants to rule out any open circuit or abnormally high electrode impedances in the selected electrode pairs. NRT was then recorded, at each of the three electrodes, using three different artefact cancellation techniques. The artefact cancellation techniques were forward masking, alternating polarity and artefact template.

A test for optimized recording parameters (ORP) was carried out with each of the artefact cancellation techniques to establish the optimum gain and delay measures for recording NRT. An internal amplifier gain of 50 dB and a recording delay of 122us were found to be optimal at all the three electrodes, for all the participants, and with each of the three different artefact cancellation techniques.

The NRT was recorded with the three different artefact cancellation techniques at various simulation levels so as to establish the threshold NRT. To be able to find the exact threshold of NRT, recording was a done at 1 current level steps near the NRT threshold (T-NRT). During NRT recordings, the sequence of the use of the three different artefact cancellation techniques was varied to rule out any sort of order effect.

In three of the eight participants, NRT could be recorded only with forward masking and alternating polarity methods of artefact cancellation, as they did not co-operate for long testing sessions. In the rest of the five participants, NRT was recorded with all the three different artefact cancellation techniques. This resulted in a total data pool of 63 T-NRT values from 24 different electrode sites.

The NRT waveforms were recorded using the protocol described in Table 3.1 for the three artefact cancellation techniques. Once the NRT recordings were made, T-NRT values, given by the peak picker and regression analysis of the software, were recorded. In the present study the AutoNRT peak picker option was used. Peak-to-peak amplitude of visually determined Nl and P2 was recorded for the visually estimated T-NRTs. The peak picker identifies the Nl and P2 of the NRT waveforms based on a set of rules that dependent on a set of parameters such as, signal to noise ratio, current level, correlation of the recording with the previous current level and correlation of the recording with a known response. The regression analysis identifies the T-NRT based on amplitude growth of the NRT waveforms at supra threshold current levels. The regression line extrapolates the T-NRT at zero crossing level. The subjective T-NRT taken was that which was agreed upon by a panel of three experienced audiologists so as to avoid any individual bias. This was the T-NRT estimated based on the visual observation, for the purpose of the study. T-NRT was recorded based on the identification of N1:

for each of the three recording electrodes i.e., electrode number 4, 12, and 20.

with each of the threshold estimation techniques, for NRT recorded with the different artefact cancellation techniques.

- for each of the participant.

Table 3.1 shows the stimulating and recording parameters used in the study for each of the artefact cancellation techniques.

Table 3.1: Stimulating and recording parameters for NRT

Stimulation and recording parameters	**Artefact cancellation techniques**		
	Forward Masking	***Alternating Polarity***	***Artefact Template***
Probe indifferent electrode	MPl	MP 1	MP 1
Probe pulse width	25 us/phase	25 us/phase	25 us/phase
Probe rate	80 Hz	80 Hz	80 Hz
Probe inter phase gap	7 us	7 us	7 us
Masker active electrode	Probe active electrode	NA	NA
Masker indifferent electrode	MPl	NA	NA
Masker current level	Probe current level+ 10	NA	NA
Number of maskers	1	NA	NA
Masker rate	100 Hz	NA	NA
Masker inter phase gap	7 us	NA	NA
Masker probe interval	400 us	NA	NA
Recording active electrode	Probe active electrode + 2	Probe active electrode + 2	Probe active electrode + 2
Recording indifferent electrode	MP2	MP2	MP2
Recording Gain and Delay	Based on ORP	Based on ORP	Based on ORP
Number of sweeps	50	50	50
Measurement window	1600 us	1600 us	1600 us
Effective sample rate	20 kHz	20 kHz	20 kHz
Artefact template current level	NA	NA	Probe current level-15
Scaling factor	NA	NA	Auto
No. of sweeps for template	NA	NA	500

Note.

NA: Not applicable

MPl, MP2: Monopolar stimulation modes.

The artefact cancellation techniques were statistically compared under the following stages:

Stage I: Comparison across different artefact cancellation techniques based on visually estimated T-NRT at each of the three electrodes.

Stage II: Comparison across different artefact cancellation techniques based on peak picker estimated T-NRT at each of the three electrodes.

Stage III: Comparison across different artefact cancellation techniques based on regression analysis estimated T-NRT at each of the three electrodes.

Stage IV: Comparison across different artefact cancellation techniques based on the amplitude of the visually estimated T-NRT at each of the three electrodes.

The methods of threshold estimation were statistically compared under the following stages:

Stage V: Comparison across different methods of threshold estimation for NRT recorded with forward masking at each electrode.

Stage VI: Comparison across different methods of threshold estimation for NRT recorded with artefact template at each electrode.

Stage VII: Comparison across different methods of threshold estimation for NRT recorded with alternating polarity at each electrode.

CHAPTER IV

Results and Discussion

The study aimed at comparing the three different artefact cancellation techniques and the three different threshold estimation methods used in NRT. The three different artefact cancellation techniques were forward making, alternating polarity and artefact template. The threshold NRT (T-NRT) was estimated based on three different procedures i.e., visual detection, peak picker and regression analysis. NRT was recorded on electrode numbers 4, 12 and 20, in participants implanted with Nucleus Freedom cochlear implant.

The T-NRT data collected with different artefact cancellation techniques were statistically analyzed in four stages as mentioned in the method chapter. The T-NRT estimated using different techniques of threshold estimation were also statistically analyzed, in three stages, as mentioned in the previous chapter. For statistical comparison, Friedman's test of significance was carried out across the artefact cancellation techniques and threshold estimation methods in the all the seven stages described earlier. Upon the presence of any significant statistical difference, Wilcoxon signed ranks test was carried out to find out which of the artefact cancellation techniques or threshold estimation methods had significant difference. The results for seven different stages of comparison are discussed below.

Stage I

In this stage, comparison across the artefact cancellation techniques based on the visually estimated T-NRT was made, in each of the electrodes. Table 4.1 shows mean and standard deviation values for visually estimated T-NRT values with forward masking, alternating polarity and artefact template on the 4th, 12th and 20th electrodes.

Table 4.1: Mean and standard deviation (SD) values of visually estimated T-NRT for different electrodes, using different artefact cancellation techniques.

Recording Electrode	Artefact Cancellation Techniques	Mean	Standard Deviation
Electrode 4	Forward Masking	178.88	4.73
	Alternating Polarity	181.63	4.21
	Artefact Template	180.60	7.70
Electrode 12	Forward Masking	179.75	14.37
	Alternating Polarity	182.38	14.79
	Artefact Template	184.00	13.00
Electrode 20	Forward Masking	164.00	14.37
	Alternating Polarity	172.13	14.79
	Artefact Template	171.80	13.00

The comparison across the artefact cancellation techniques based on the visually estimated T-NRT in each of the electrodes revealed that there was no significant difference, even at 0.05 level of significance, in any of the electrodes.

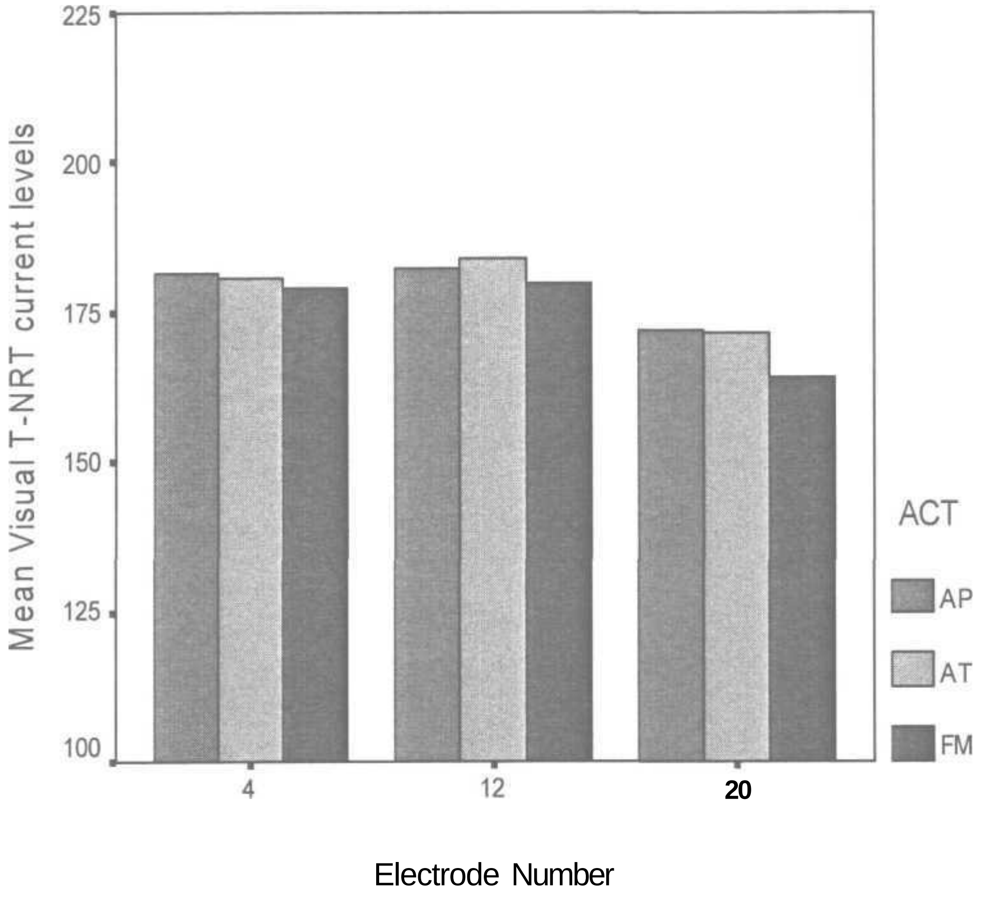
Although there was no significant difference seen, comparison of the mean threshold revealed that the mean threshold of the visually detected T-NRT was lowest for NRT recorded with forward masking paradigm (Table 4.1 and Figure 4.1). In the forward masking paradigm, the stimulus artefact is recorded separately in the absence of any stimulus response as the nerve fibers are put to refractory period. The stimulus artefact present in the probe alone condition and probe-plus-masker condition is expected to be similar as in both cases the probe level is same. Since, the stimulus artefact is measured with precision, it can be expected to be cancelled out and the true neural response be recorded.

In the alternating polarity method of artefact cancellation, it is not always true that the neural response is identical in response to either anodic-leading or cathodic-leading biphasic current pulses (Van Den Honert & Stypulkowski, 1987; Miller, Abbas, Rubinstein, Robinson, Matsuoka & Woodworgh, 1998; Miller, Robinson, Rubinstein & Matsuoka, 1999). Klop, Hartlooper, Briare, and Frijns in 2004 reported that the Nl and P2 latencies are shorter for cathodic-first (0.13 and 0.32 ms, respectively) than for anodic-first stimuli (0.16 and 0.38 ms, respectively). As the N1-P2 peaks vary for anodic-leading and cathodic-leading biphasic current pulses, it may affect the averaged response and thereby the threshold.

As with the artefact template technique, the scaled down template of the artefact is always measured at a lower probe level than the probe level used for measuring the NRT. The artefact template is then scaled up accordingly when a recording is done at supra threshold level. The principal limitation to this method, as reported by Brown in 2004, is that the amplifier and tissue conductance should be perfectly linear to produce exactly the same shaped artefact at a lower current level, which is generally not the case. As a result, the scaled up template of the artefact can be either overestimating or underestimating the actual artefact at certain probe level. In either case, it will distort the ECAP to a certain extent, and hence might be expected to overestimate the NRT threshold. It also requires a system with very low levels of ambient noise.

The T-NRT recorded with visual estimation was lowest in the forward masking technique in all the three electrodes. However, as there were no statistical differences between the different artefact cancellation techniques based on the visually detected

T-NRT, it is suggested that all the three artefact cancellation techniques can be put to use for recording T-NRT.



ACT: Artefact cancellation techniques, AP: alternating polarity, AT: artefact template, FM: forward masking.

Fig. 4.1: Bar diagram of the mean T-NRT estimated visually with the different artefact cancellation techniques.

Stage II

In this stage comparison across the artefact cancellation techniques based on the peak picker estimated T-NRT was made, in each of the electrodes. Table 4.2 shows mean and standard deviation (SD) values of T-NRT estimated by peak picker, using the three different artefact cancellation techniques, for the 4th, 12th, and 20th electrode. The mean T-NRT was lowest with the forward masking technique in all the three electrodes.

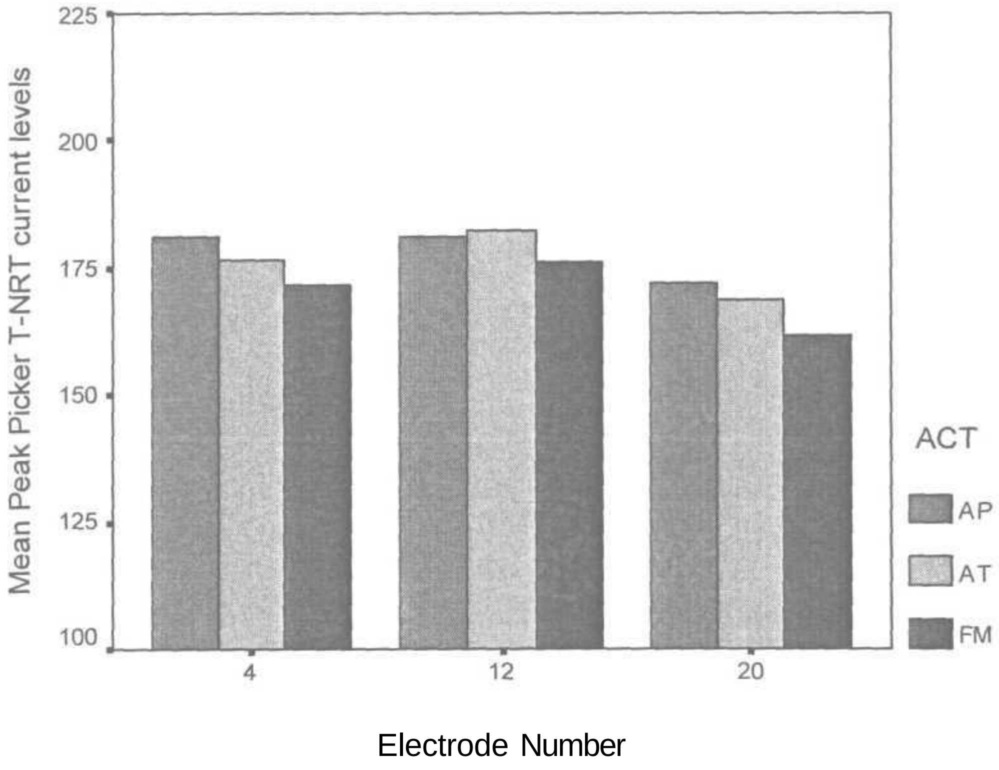
Table 4.2: Mean and standard deviation (SD) values of peak picker estimated T-NRT for different electrodes using different artefact cancellation techniques.

Recording Electrode	Artefact Cancellation Techniques	Mean	Standard Deviation
Electrode 4	Forward Masking	171.75	6.02
	Alternating Polarity	181.00	4.04
	Artefact Template	176.60	9.32
Electrode 12	Forward Masking	176.25	15.66
	Alternating Polarity	181.00	14.52
	Artefact Template	182.20	13.66
Electrode 20	Forward Masking	161.50	18.37
	Alternating Polarity	172.00	23.60
	Artefact Template	168.60	12.66

The comparison across the different artefact cancellation techniques based on the peak picker estimated T-NRT in each of the electrodes revealed that there was a significant difference between forward masking and alternating polarity techniques for the 4th electrode ($p<0.05$) and 20th electrode ($p<0.05$).

It is to be remembered that there are two peak picker options. One is the AutoNRT peak picker and the other one is the standard peak picker. The standard peak picker can be user defined with respect to noise ratio, threshold and the minimum and maximum latency of the first and the second peak. In the present study, the AutoNRT peak picker was used, because it was expected that the standard peak picker which can be user defined will have good correlation with the visually estimated T-NRT.

The significant difference seen between forward masking and alternating polarity based on peak picker estimated T-NRT is because of the fact that with the alternating polarity, the peak picker was identifying NRT tracings as response at a higher stimulation level that were very near to actual T-NRT. Where as, with forward masking, peak picker was identifying many NRT tracings as response at very lower stimulation levels, which were not NRT response as there were no visible ECAP. The peak picker estimated T-NRT responses with artefact template were generally near to that picked with the alternating polarity or in between that of the T-NRT recorded with forward masking and alternating polarity. The mean T-NRT based on peak picker was always lowest for NRT recorded with the forward masking paradigm, in all the electrodes, as it detected many tracings as NRT responses, at sub-threshold levels where no visible ECAP were present.



ACT = artefact cancellation techniques, AP = alternating polarity, AT = artefact template FM= forward masking.

Fig. 4.2: Bar diagram of the mean T-NRT estimated with peak picker for different artefact cancellation techniques.

Stage III

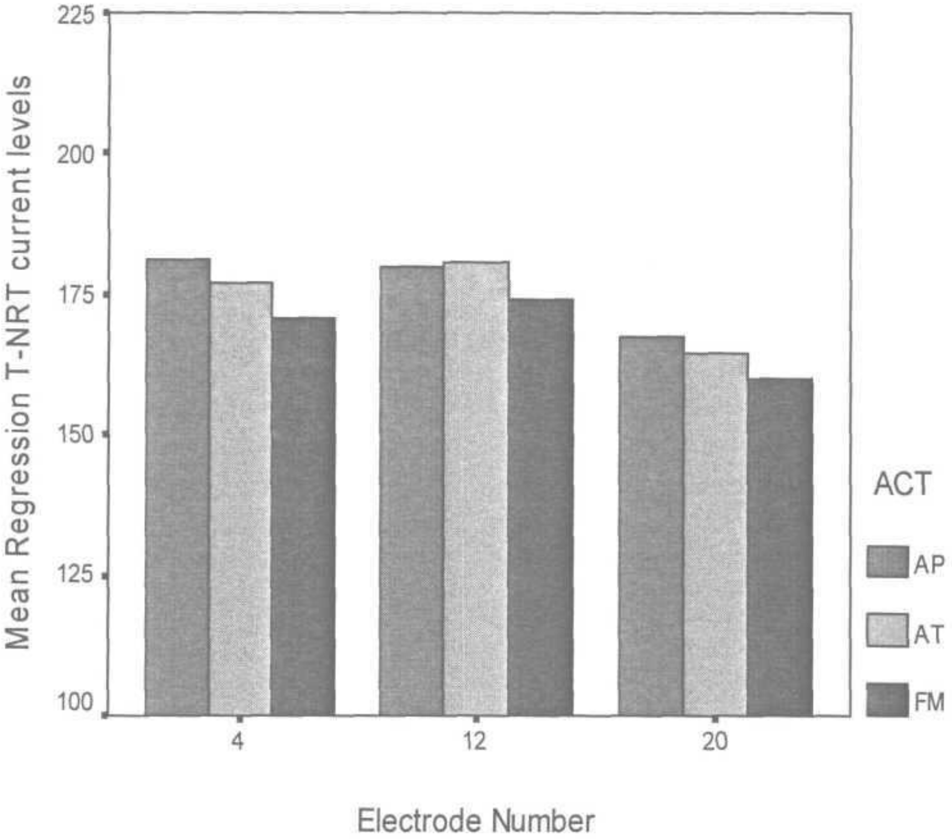
In this stage comparison across the artefact cancellation techniques based on the regression analysis estimated T-NRT was made in each of the electrodes. Table 4.3 shows mean and standard deviation (SD) value for T-NRT estimated by regression analysis, using three different artefact cancellation techniques on different electrodes.

Table 4.3: Mean and standard deviation (SD) values T-NRT estimated from regression analysis for different electrodes using different artefact cancellation techniques.

Recording Electrode	Artefact Cancellation Techniques	Mean	Standard Deviation
Electrode 4	Forward Masking	170.82	6.29
	Alternating Polarity	180.98	4.00
	Artefact Template	177.06	9.13
Electrode 12	Forward Masking	174.15	14.30
	Alternating Polarity	180.07	12.97
	Artefact Template	180.65	13.40
Electrode 20	Forward Masking	160.13	19.41
	Alternating Polarity	167.58	21.83
	Artefact Template	164.57	13.07

The comparison across the artefact cancellation techniques based on the T-NRT estimated by regression analysis in each of the electrodes, revealed that there was significant difference ($p<0.05$), between forward masking and alternating polarity, based on the T-NRT established by regression analysis, on the 4th electrode.

Though the mean differences of were not significant at the other electrodes with different artefact cancellation techniques, the T-NRT estimated with regression analysis were again the lowest with the forward masking technique for all the electrodes



ACT = artefact cancellation techniques, AP = alternating polarity, AT = artefact template, FM= forward masking.

Fig. 4.3: Bar diagram of mean T-NRT estimated by regression analysis for different artefact cancellation techniques

The extrapolated T-NRT given by linear regression analysis is based on the correct responses identified by the NRT software at different stimulation levels and involves applying a regression analysis to points on an input-output (or amplitude growth) function. Threshold is determined as the level at which the regression line crosses zero amplitude (i.e.. intercept of the x-axis where y = 0). The T-NRT based on regression analysis can be affected if the peak picker marks the amplitude measures in NRT tracings where there are actually no responses. Similar finding was reported by Hughes (2006b). where in, when the amplitude measures were unmarked on the no-response waveforms, the linear regression based T-NRT became virtually the same as the visual detection threshold. Since, peak piker identification of correct NRT responses with alternating polarity and forward masking is significantly different, a significant difference, at times, can be expected in the regression analysis based estimations for T-NRT recorded with these two methods.

The regression analysis estimated T-NRT is also based on the amplitude growth function linearity assumption. Typically, the amplitude growth function is linear at higher current levels and tails of near threshold, but also flattens out at very high current levels, giving a over all sigmoidal function (Botros, Dijk & Killian, 2006). These authors also reported that non-linearity near threshold poses a difficulty for automated systems that are based on extrapolated threshold method.

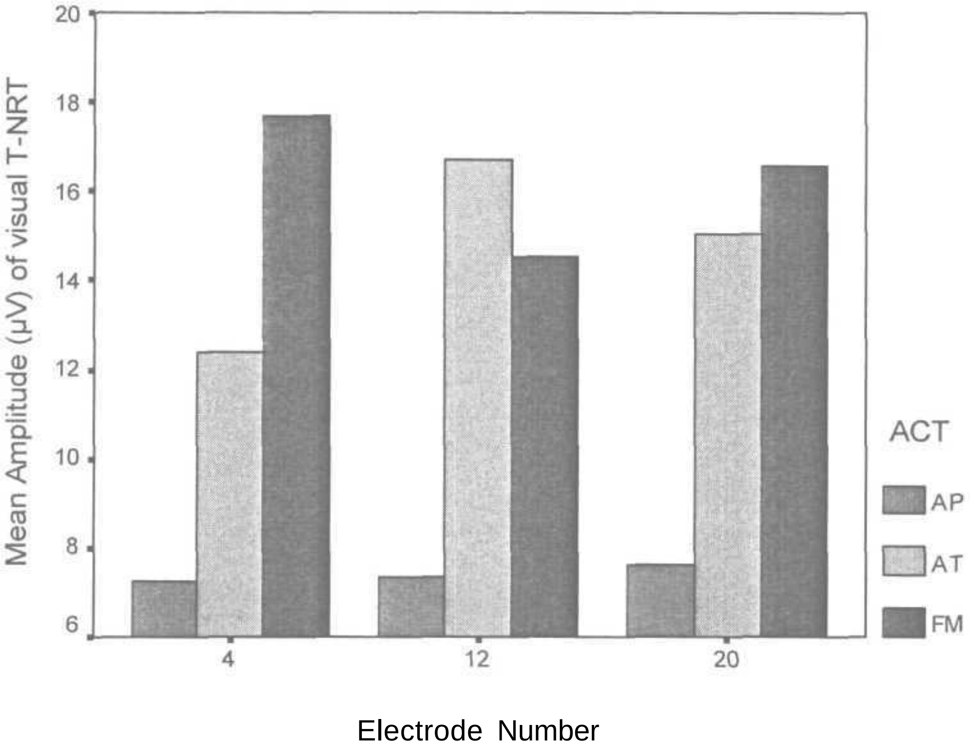
Stage IV

In this stage the three artefact cancellation techniques were compared based on the amplitude of the visually estimated T-NRT waveform, recorded with different artefact cancellation techniques. The amplitude of the N1 and P2 peaks in the T-NRT tracings were recorded and the peak to peak amplitude between the N1-P2 complex was taken as the amplitude of the T-NRT. Table 4.4 shows mean and standard deviation (SD) values of the amplitude (uV) of the visually estimated T-NRT recorded with the three different artefact cancellation techniques on electrode number 4, 12 and 20.

Table 4.4: Mean amplitude of the visually estimated T-NRT for different artefact cancellation techniques on different electrodes.

Recording Electrode	Artefact Cancellation Techniques	Mean	Standard Deviation
Electrode 4	Forward Masking	17.67	6.88
	Alternating Polarity	7.24	2.40
	Artefact Template	12.39	1.23
Electrode 12	Forward Masking	14.51	1.05
	Alternating Polarity	7.33	2.38
	Artefact Template	16.70	16.70
Electrode 20	Forward Masking	16.57	1.66
	Alternating Polarity	7.30	1.94
	Artefact Template	15.03	4.86

Comparison of the amplitude of the visually estimated T-NRT waveform recorded using the three different artefact cancellation techniques revealed that there was a significant difference between the amplitude of the T-NRT recorded with the three different artefact cancellation techniques($p<0.05$). Further analysis revealed significant differences between visually established T-NRT amplitude recorded with alternating polarity and forward masking, and between visually estimated T-NRT amplitude recorded with artefact template and alternating polarity for each the 4th, 12th and 20th electrode($p<0.05$). The lower mean amplitude of visually estimated T-NRT recorded with alternating polarity, as compared the mean amplitude of the visually estimated T-NRT recorded with other two artefact cancellation techniques can be observed in Figure 4.4



ACT = artefact cancellation techniques, AP = alternating polarity, AT = artefact template, FM= forward masking.

Fig. 4.4: Bar diagram of the mean amplitude of visually estimated T-NRT with different artefact cancellation techniques.

From Figure 4.4, it is noted that the NRT amplitude did not vary much across the electrodes with alternating polarity technique. The amplitude of NRT was always least with alternating polarity compared to artefact template and forward masking, in all the electrodes. This is evident from the mean amplitude of the T-NRT recorded with alternating polarity, which was always least for alternating polarity in all the electrodes. The amplitude was highest for forward masking in the 4th and 20th electrode and, for artefact template in 12th electrode.

The lower amplitude for NRT recorded with alternating polarity can be attributed to the fact that it is not always true that the neural response is identical in response to either anodic-leading or cathodic-leading biphasic current pulses as reported by Van Den Honert and Stypulkowski, in 1987; Miller, Abbas, Rubinstein, Robinson, Matsuoka and Woodworgh, in 1998; Miller, Robinson, Rubinstein and Matsuoka, in 1999. Klop, Hartlooper, Briare, and Frijns, in 2004, reported that the N1 and P2 latencies are shorter for cathodic-leading (0.13 and 0.32 ms respectively) than for anodic-leading stimuli (0.16 and 0.38 ms respectively). Since the Nl and P2 is recorded at different latencies with anodic-leading and cathodic-leading biphasic current pulses, they will lie at different sampling points, during recording for half of the anodic-leading biphasic current pulse stimuli and half of the cathodic-leading biphasic current pulse stimuli. This will lead to lesser N1-P2 peak-to-peak amplitude recorded after averaging, when compared to the averaged N1-P2 peak-to-peak amplitude of any other method where the Nl and P2 latencies fall at similar latencies, and hence at similar sampling points, for each stimulation. The findings of this study is consistent with that of the Hughes, Abbas, Brown, Behrens, and Dunn (2003), who reported that the amplitude of the NRT recorded with alternating polarity method tends to be significantly smaller than that obtained with the subtraction method ($r = 0.97$, $p < 0.0001$) yielding higher thresholds with alternating polarity ($r = 0.86$, $p = 0.01$).

Stage V

The visual, peak picker, and regression analysis estimated T-NRT for NRT recorded with forward masking were compared at each of the 4th, 12th, and 20th electrode. Statistical comparison revealed that when forward masking was used as an artefact cancellation technique, there were significant differences between the different methods of estimating T-NRT ($p<0.05$). Further analysis revealed that when forward masking was used, significant difference was seen between T-NRTs that were visually estimated and T-NRTs that were estimated using the regression analysis and the peak picker methods ($p<0.05$). No statistical difference was observed, even at 0.05 level of significance, between the peak picker estimated and regression analysis estimated T-NRTs. Similar findings were observed in all the electrodes.

There was no significant difference between peak picker estimated and regression analysis estimated T-NRT, when forward masking was used, because of the fact that the regression based extrapolated threshold considers the responses picked up by the peak picker and involves applying a regression analysis to points on an input-output (or amplitude growth) function. The same trend was observed in every case and no significant difference between peak picker and regression analysis estimated T-NRT was seen in any electrode with any artefact cancellation technique.

A significant difference between visual and peak picker based T-NRT for NRT/ECAP recorded with forward masking as artefact cancellation technique was seen because of the fact that the peak picker identified NRT tracings as responses even where no visible ECAP existed. The present finding which show that peak picker identified NRT tracings with no visible ECAP as responses is consistent with the findings of Hughes (2006b).

Figure 4.5 depicts that when NRT waveforms recorded with forward masking as the artefact cancellation technique, the peak picker identified an NRT response at current levels where no visible ECAP can be observed. The actual visually detected threshold was at 183 current levels.

Also, in Figure 4.5 we can see the improper marking of the P2 latency even when the NRT tracing is correctly identified as a response. For example, the P2 latency was picked too late by the peak picker for NRT tracing with 186 current levels. Also, P2 is expected to reduce in latency with increase in stimulus level. However, the P2 latency picked for NRT tracing with 183 current levels is less than the P2 latency picked for NRT tracing with 190 current levels.

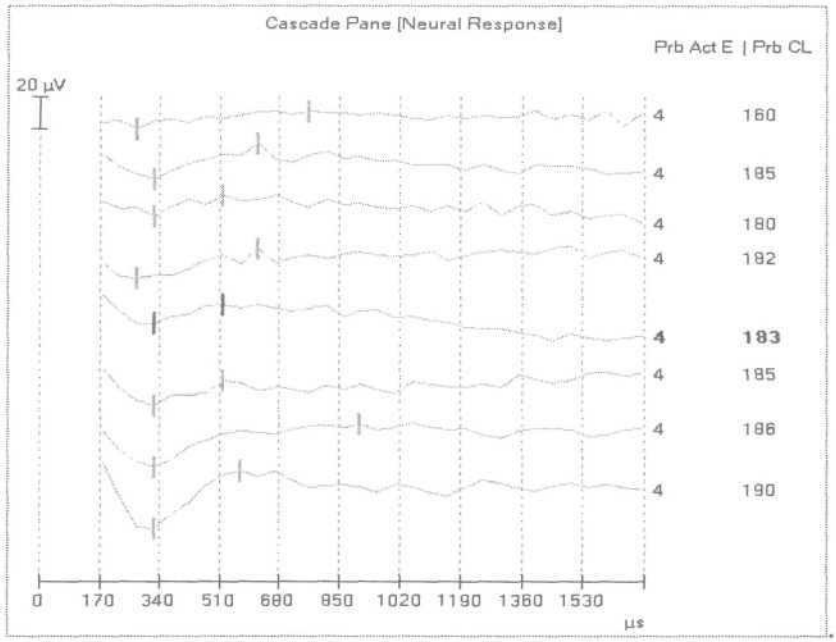


Fig. 4.5: Peak picker marked NRT waveforms recorded with forward masking at different current levels.

As discussed earlier the regression analysis based estimation of T-NRT involves applying a regression analysis to points on an input-output (or amplitude growth) to the responses picked by the peak picker, so, an incorrect marking of responses by the peak picker will also affect the regression based T-NRT. This is why a significant difference was seen between visual and regression based T-NRT with forward masking as artefact cancellation technique for recording NRT. Similar results of incorrect NRT response identification by peak picker affecting the regression T-NRT was yreported by Hughes, (2006b).

Stage VI

Similar to NRT recorded with forward masking, NRT recorded with artefact template also had significant differences between the estimated T-NRT based on visual detection and peak picker and between the estimated T-NRT based on visual detection and regression analysis..

The findings can de discussed on similar lines as discussed above. The peak picker picked up incorrect NRT tracings as responses, for NRT recorded with artefact template as artefact cancellation technique, even when there was no visible ECAP.

This is understood in Figure 4.6 where NRT tracings at 161 and 164 current levels have been picked as NRT responses. The incorrect placing of cursors of Nl and P2 peaks can also be observed.

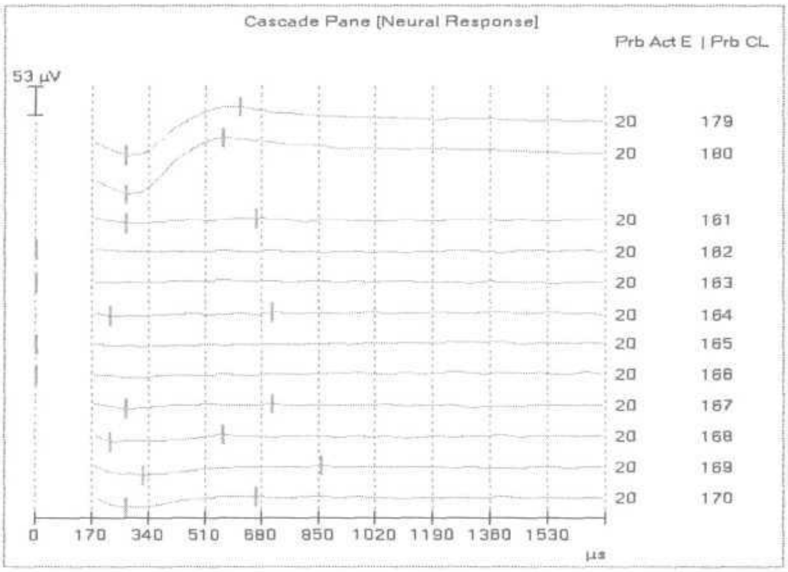


Fig. 4.6: Peak picker marked NRT waveforms recorded with artifact template at different current levels.

Stage VII

Comparison of the visual, peak picker and regression estimated T-NRT for NRT recorded with alternating polarity as artefact cancellation technique, did not show any significant difference in any of the electrodes. The reason can be attributed to the ability of the peak picker to identify NRT responses correctly when NRT was recorded with alternating polarity as artefact cancellation technique. This is understood from Figure 4.3. It is to be noted that visually, NRT with 175 current levels was taken as the T-NRT, and the peak picker picked up 174 current levels as the T-NRT.

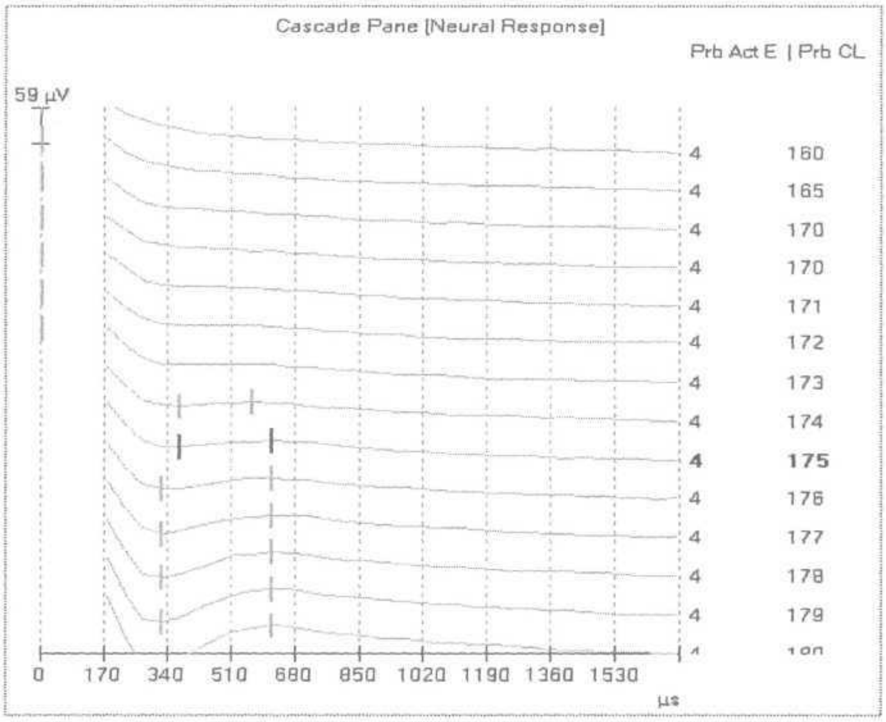


Fig. 4.7: Peak picker marked NRT waveforms recorded with alternating polarity at different current levels.

NRT could be consistently recorded using the three different artefact cancellation techniques. On visual determination, the T-NRT with each of the artefact cancellation techniques did not differ significantly.

Generally, it was observed that the NRT recorded with forward masking technique yielded higher amplitudes and hence lower NRT thresholds. On the contrary, NRT recorded with alternating polarity technique yielded lower amplitudes and higher thresholds for NRT.

The peak picker ability to identify correct NRT responses was best for NRT tracings recorded with the alternating polarity technique. Peak picker identified a number tracing as responses where no visible ECAP existed, for NRT recorded with artefact template and forward masking techniques. With in the artefact template and forward masking artefact cancellation techniques, when the threshold estimation techniques were compared, it was observed that T-NRT estimated by regression analysis and T-NRT estimated by the pick picker were in good agreement with each other, but significantly different from the visually estimated T-NRT. However, for NRT recorded with alternating polarity, all the three threshold estimation techniques had good agreement with each other.

CHAPTER V

Summary and Conclusion

The present study aimed at comparing different artefact cancellation and threshold estimation techniques used in NRT. A series of NRT recordings were made in eight participants implanted with Nucleus Freedom cochlear implant system using three different artefact cancellation techniques, namely forward masking, alternating polarity, and artefact template. In each of the participant, NRT recording was done with the different artefact cancellation techniques on the 4th, 12th and 20th electrodes to represent the basal, medial, and apical portion of the cochlea respectively. The different threshold estimation techniques used were visual, peak picker and regression analysis. The threshold of NRT (T-NRT) data consisted of 63 T-NRT values from 24 different electrode sites. Statistical analysis was carried out to compare the artefact cancellation and threshold estimation techniques. The results are summarized under the following headings.

Comparison across Artefact Cancellation Techniques

NRT recordings could be successfully carried out with all the three different artefact cancellation techniques. These results were based on the advanced NRT protocol of the Custom EP software for recording NRT. Comparison across the different artefact cancellation techniques, were made based on the visually estimated T-NRT, in each of the three electrodes. The results revealed that there was no significant difference present. Although there was no significant difference seen, NRT recorded with forward masking paradigm consistently yielded a lower visually estimated T-NRT.

All the three artefact cancellation techniques used to record NRT in the present study can be used to record NRT clinically. There is no much difference in the thresholds estimated visually. So, if the objective is to see the functioning of the device, any artefact cancellation technique can be used. It must be noted however that the time required to record NRT with artefact template was quite longer, which is approximately 17 seconds as compared to the other two artefact cancellation techniques. This is when number of sweeps for artefact template was 500 sweeps, stimulation rate 80 Hz and number of sweeps recorded for averaging was 50. The forward masking and the artefact template require approximately 3 seconds for recording each NRT waveform from each electrode, when a stimulation rate is 80 Hz and number of sweeps averaged are 50. Since, artefact template requires more time, it might not be a good choice especially while doing intra-operative NRT recordings.

However, since a difference existed between the T-NRT estimated visually for different artifact cancellation techniques, though not significant, it should be given attention to, particularly if the objective is to program the speech processor based on T-NRT levels. If NRT is recorded using different artefact cancellation techniques, it requires additional research to see the relationship between behavioral thresholds (T levels) and comfort levels (C levels), with T-NRT recorded with each of the artefact cancellation techniques.

Comparison across the artefact cancellation techniques based on the peak picker estimated T-NRT in each of the electrodes revealed that there was a significant difference in electrode number 4 and 20. In both the electrodes, a significant difference was seen between forward masking and alternating polarity based on the peak picker estimated T-NRT. These results are based on the AutoNRT peak picker.

The comparison of the artefact cancellation techniques based on the T-NRT estimated by regression analysis, in each of the electrodes, revealed that there was a significant difference seen only on the 4th electrode between forward masking and alternating polarity.

The artefact cancellation techniques seem to vary based on T-NRT estimated by peak picker and regression analysis. This warrants for revising the algorithm used in peak detection for AutoNRT peak picker, separately for each artefact cancellation techniques.

The three artefact cancellation techniques were also compared based on the amplitude of the visually estimated T-NRT, for each electrode. There was a significant difference between the amplitudes of the T-NRT recorded with the three different artefact cancellation techniques. Further analysis revealed significant differences between visually established T-NRT amplitude recorded with alternating polarity and forward masking, and, also between visually estimated T-NRT amplitude recorded with artefact template and alternating polarity. This was observed for all the three electrodes.

Comparison across Threshold Estimation Techniques

For all the NRT recordings, T-NRT was recorded based on visual, peak picker and regression analysis estimation. Comparison across the threshold estimation techniques was then carried out, at each of the 3 electrodes, based on the T-NRT estimated by each threshold estimation technique, for NRT recorded with different artefact cancellation techniques separately.

The visual, peak picker and regression analysis estimated T-NRT were compared across, for NRT recorded with forward masking, at each of the 4th, 12th and 20th electrodes. Result revealed that when forward masking was used as an artefact cancellation technique, there were significant differences between the different methods of estimating T-NRT. A significant difference was seen between visually estimated and regression analysis estimated T-NRT, and also between visually estimated and peak picker estimated T-NRT. However, no statistical difference was observed between peak picker estimated and regression analysis estimated T-NRT. Similar findings were observed in all the three electrodes.

It was observed that when forward masking was used, the peak picker identified many NRT traces as responses where actually no ECAP were visible. Also, even when the NRT responses were correctly identified, there was improper marking of the N1-P2 peaks.

The visual, peak picker and regression analysis estimated T-NRT were also compared across, for NRT recorded with artefact template, at each of the 4th, 12th and 20th electrodes. Results revealed significant differences between the estimated T-NRT based on visual detection and peak picker and between visual detection and regression analysis. The same trend was observed in all the three electrodes.

As in the peak picker identified peaks in NRT responses with forward masking, the peak picker identified peaks in the NRT recorded with artefact template technique also picked up incorrect NRT peaks as responses, even when there was no visible ECAP.

Thus with forward masking and artefact template, it is required that the tester should subjectively verify the N1-P2 peaks picked by the peak picker. NRT tracings where no ECAP exist, but the peak picker has identified as responses, should be excluded from the regression analysis. This in turn will improve the correlation between visually estimated and regression estimated T-NRT.

Comparing of the visual, peak picker and regression estimated T-NRT for NRT recorded with alternating polarity as alternating polarity technique, did not result in any significant difference in any of the electrodes. The peak picker was identifying correct NRT responses with greater precision, for NRT recorded with alternating polarity. Peak picker can be relied upon when alternating polarity is used as artefact cancellation technique for recording NRT.

Thus, if NRT is to be recorded by naive clinicians who don't have much expertise on electrophysiological testing, it is better that the alternating polarity is used, because with the alternating polarity the peak picker is able to discard false NRT responses and accept true responses with greater precision. In addition, since there are lesser number of parameters that requires to be set in the protocol for recording NRT using this technique, it will be less confusing, This calls for very less expertise from the clinician.

Generally, it was observed that the NRT recorded with forward masking technique yielded higher amplitudes and hence lower NRT thresholds. On the contrary, NRT recorded with alternating polarity technique yielded lower amplitudes and higher thresholds for NRT.

The peak picker ability to identify correct NRT responses was best for NRT tracings recorded with the alternating polarity technique. Peak picker identified a number tracing as responses where no visible ECAP existed, for NRT recorded with artefact template and forward masking techniques. With in the artefact template and forward masking artefact cancellation techniques, when the threshold estimation techniques were compared, it was observed that T-NRT estimated by regression analysis and T-NRT estimated by the pick picker were in good agreement with each other, but significantly different from the visually estimated T-NRT. However, for NRT recorded with alternating polarity, all the three threshold estimation techniques had good agreement with each other.

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