J Am Acad Audiol 17:413–431 (2006)

Use of Neural Response Telemetry Measures to Objectively Set the Comfort Levels in the Nucleus 24 Cochlear Implant

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Abstract

Cochlear implant programming necessitates accurate setting of programming levels, including maximum stimulation levels, of all active electrodes. Frequently, clinical techniques are adequate for setting these levels; however, they are sometimes insufficient (e.g., very young children). In the Nucleus 24, several methods have been suggested for estimation of comfort levels (C levels) from neural response telemetry (NRT); however, many require co-application of clinical measurements. Data was obtained from 21 adult Nucleus 24 recipients to develop reliable predictions of C levels. Multiple regression analysis was performed on NRT threshold, slope of the NRT growth function, age, length of deafness, length of cochlear implant use and electrode impedance to examine predictive ability. Only the NRT threshold and slope of the growth function measures were significant predictors yielding R^2 values from 0.391 to 0.769. Results demonstrated that these measures may provide an alternative means of estimating C levels when other clinical measures are unavailable.

Key Words: Cochlear implants, neural response telemetry, programming levels

Abbreviations: AGE = subject age at time of cochlear implantation; C levels = comfort levels, maximum stimulation levels for the Nucleus device; C_{BEHAV} = C levels set using behavioral psychophysical techniques; C_{eSRT} = C levels as set using electrically evoked stapedial reflexes; C_{REG} = C levels predicted using regression equations developed in the study; CI = cochlear implant; DUR_{CI} = duration of cochlear implant use as of time of participation in study; DUR_{DEAF} = duration of deafness prior to cochlear implantation; eSR = electrically evoked stapedial reflex; IMP_{MP1+2} = cochlear implant electrode impedance, specifically monopolar 1+2 configuration; NRT = neural response telemetry; NRT_{SLOPE} = slope of the growth function of the NRT response; NRT_T = threshold of the NRT response

Sumario

La programación del implante coclear necesita de parámetros exactos en los niveles de programación. Frecuentemente, las técnicas clínicas son adecuadas para establecer dichos niveles; sin embargo, a veces son insuficientes (p.e.,

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Presented at the Association for Research in Otolaryngology 2004 Midwinter Meeting, February 24, 2004, Daytona, Florida.

This study composed a portion of the dissertation of the first author, submitted April 19, 2004, University of Miami, Coral Gables, Florida.

Cochlear Americas provided incentive to subjects for participation. League for the Hard of Hearing provided facilities for conducting the study.

en niños muy pequeños). En el Nucleus 24, se han sugerido varios métodos para la estimación de niveles de comodidad (niveles C) basados en la telemetría de respuesta neural (NRT); sin embargo, muchos exigen co-aplicación de mediciones clínicas. Se obtuvo información de 21 adultos implantados con un Nucleus 24 para desarrollar elementos confiables de predicción de los niveles C. Para analizar la capacidad de predicción se realizó un análisis de regresión múltiple sobre el umbral de la NRT, la pendiente de la función de crecimiento de la NRT, la duración de la sordera, la duración del uso del implante coclear y la impedancia del electrodo. Sólo las medidas del umbral de la NRT y la pendiente de la función de crecimiento fueron elementos significativos de predicción, rindiendo valores R^2 de 0.391 a 0.769. Los resultados demostraron que estas medidas pueden aportar un medio alternativo de estimación de los niveles C, cuando no existan otras mediciones clínicas.

Palabras Clave: Implantes cocleares, telemetría de respuesta neural, niveles de programación

Abreviaturas: AGE = edad del sujeto en el momento del implante coclear; C levels = niveles confortables, niveles máximos de estimulación para el dispositivo Nucleus; C_{BEHAV} = niveles C utilizando técnicas psicofísicas conductuales; C_{eSRT} = niveles C establecidos usando reflejos estapediales evocados; C_{REG} = predicción de niveles C usando ecuaciones de regresión desarrolladas en el estudio; CI = implante coclear; DUR_{CI} = duración del uso del implante coclear en el momento de la participación en el estudio; DUR_{DEAF} = duración de la sordera antes del implante coclear; eSR = reflejos estapedial evocado eléctricamente; IMP_{MP1+2} = impedancia del electrodo del implante coclear, especialmente en la configuración monopolar 1+ 2; NRT = telemetría de respuesta neural; NRT_{SLOPE} = pendiente de la función de crecimiento de la respuesta de la NRT; NRT_T = umbral de respuesta de la NRT

BACKGROUND

As a result of the relaxation in criteria for cochlear implant candidacy in recent years, the minimum age for implantation has declined considerably. Consequently, we are faced with the dilemma of programming devices for pre-lingual children who cannot provide adequate feedback during the programming session. At present, comfort levels (C levels) can be objectively set utilizing electrically evoked stapedial reflexes (eSR) (Hodges et al, 2003). The use of eSR has been validated by several investigators who found no significant difference in the listening performance of subjects when comparing measured versus eSR-set C levels (Spivak et al, 1994; Hodges et al, 1997; Bresnihan et al, 2001). In the Nucleus 24 patient population, these reflexes are present in approximately 80% of pediatric users (Bresnihan et al, 2001; Hodges et al, 2003); however, compromised middle ear status as well as history of meningitis can further reduce the chance of obtaining the eSR. For the patients who do not have eSR, alternative means of setting C levels are needed if they are incapable of providing subjective feedback.

The electrically evoked auditory brainstem response (eABR) was first reported by Starr and Brackmann (1979) and was subsequently reported in cochlear implant recipients (Miyamoto, 1986; Brown et al, 1993; Mason et al, 1993). The relationship between the eABR and both threshold (T Level) and C Level has been reported to be poor (Mason et al, 1993; Brown et al, 1994; Firszt et al, 1999). Difficulties that diminish the attractiveness of eABR as an alternative objective programming tool in obtaining the eABR include preparation time, the large number of averages required, and that subjects must be relaxed and remain still during the acquisition process (Gantz et al, 1994).

The neural response telemetry (NRT) software (version 2.04) was developed in 1995 at the University of Zurich, Zurich, Switzerland, in collaboration with Cochlear Limited (Cochlear, 2001). This software was designed to utilize the bidirectional capabilities of the Nucleus 24 cochlear implant system to obtain the electrically evoked compound action potential (eCAP) of the auditory nerve without the use of surface electrodes. That is, the eCAP response is obtained directly from the internal device by recording the response on an electrode after another electrode has been used to stimulate the spiral ganglion fibers. Since the implementation of NRT, many investigators have reported success obtaining the eCAP in Nucleus 24 users (Brown et al, 1996; Brown et al, 1998; Abbas et al, 1999; Abbas et al, 2000; Cullington, 2000; Hughes, Abbas, et al, 2000; Franck and Norton, 2001; Dillier et al, 2002). The NRT response, like the eABR, has been reported to fall within the dynamic range of cochlear implant users (Shallop et al, 1999; Cullington, 2000; Hughes, Abbas, et al, 2000; Cochlear, 2001; Gordon et al, 2002). However, the NRT is dissimilar in that it is far less affected by the difficulties typically experienced with eABR.

The NRT response is characterized by a negative peak (N1) occurring between 0.2 and 0.4 msec followed by a positive peak (Abbas et al, 1999; Cullington, 2000; Franck and Norton, 2001; Dillier et al, 2002). The amplitude of the eCAP obtained using NRT has been reported to range between 100 to as high as 1300 microvolts (Shallop et al, 1999; Cullington, 2000). It should be noted that the amplitude differs greatly when obtained intra-operatively versus postoperatively. When the amplitude of the eCAP is measured by using various stimulus levels, an input/output function of the resulting eCAP is obtained. In NRT, a plot of this function is called the "slope of the growth function" and will be referred to as "NRT_{SLOPE}" in this paper. Hall (1990) reported data from animals that suggested that the presence of a positive relationship between the eCAP slope of the growth function and the number of surviving spiral ganglion cells.

The use of NRT measures to predict programming levels was first published by Brown et al (2000), who measured NRT thresholds, T levels, and C levels in 44 adult participants. The difference between NRT threshold and the T level was calculated for electrode number 10, and this difference was subtracted from all NRT thresholds obtained to estimate the T level for measured electrodes. The C level was estimated using the same principle by adding the difference between the NRT threshold and measured C level for electrode number 10 to all NRT thresholds obtained. The predicted T and C levels for electrodes that were not measured as part of the study were set via interpolation. The correlation between predicted and measured T levels (0.83) was larger than that between NRT thresholds and measured T levels (0.55). Similarly, the correlation between predicted and measured C levels (0.77) was larger than that between NRT thresholds and measured C levels (0.57). These results indicated that NRT measures, when combined with subjective feedback, could be used as an alternative technique to determine appropriate stimulation levels.

Hughes, Brown, et al (2000b), used the same prediction technique proposed by Brown et al (2000) for 15 children and obtained similar patterns of results. That is, the data presented by Hughes, Brown, et al, showed higher correlations than that obtained by Brown et al; however, the pattern of improved correlation with predicted programming levels was reproduced, thus showing agreement with the results of Brown et al. Gordon et al (2002) also used the same method for prediction of T levels in 37 children between the ages of 12 and 24 months. Data from this study indicated that the differences between the mean predicted T levels and mean measured T levels were not significantly different at the .05 level when apical and basal electrodes were examined.

Franck and Norton (2001) presented a novel means of estimating programming levels based on data from 12 adults. In this method, the contour of the NRT thresholds was used to set the contour of the predicted T and C levels. The NRT threshold contour was globally decreased to below audible levels in live mode. The NRT thresholds were then globally increased in live mode until a threshold level could be established. This was set as the T level, and then the NRT threshold contour was globally raised until the subject reported that the maximum comfortable level was reached, and the current levels were defined as the predicted C levels. This technique differs from that proposed by Brown et al (2000) in that the electrical dynamic range is not considered uniform across the electrode array. That is, the method proposed by Franck and Norton does not set the dynamic range based on measurements from a single (e.g., number 10) electrode. Another difference is that Franck and Norton obtained NRT measurements from all active electrodes, and thus did not use interpolation to set the nonmeasured electrodes. Further detailed explanation and discussion of the method proposed by Franck and Norton may be found in Franck (2002).

Smoorenburg et al (2002) set T and C levels using the same technique described by Franck and Norton (2001) in 13 adults and compared speech discrimination performance between MAPs based on this method of setting T and C levels versus the traditional clinical method of setting them. Subjects were given two weeks to listen to the experimental MAP; however, they were also given the MAP with clinically measured levels in case they did not want to listen to the experimental MAP. Despite the lack of control over listening experience, the scores of the MAP with estimated levels versus the MAP with measured levels were "remarkably close." Smoorenburg et al noted that while the profile of the NRT threshold was highly correlated with the T level profile (r = 0.82), the relationship between the NRT threshold profile with the slope of the C level was not significant.

While the results obtained from these studies suggest that NRT can be used to help determine stimulation levels in Nucleus 24 users, the proposed methods as described require some degree of subjective feedback. Unless completely objective methods of determining stimulation levels are developed, the use of NRT will be ineffective for children and other patients who are unable to provide feedback during the programming session. In addition, it has been demonstrated that the amplitude and slope of the growth function of NRT responses are systematically ordered in that they increase as the recording electrode is moved apically (Polak et al, 2004). This trend indicates a need for consideration of electrode-specific data when estimating programming levels.

Electrode impedance measures provide indication of both electrode and electrode-tissue interface status and varies systematically such that on average it is lowest for basal electrodes and highest for apical electrodes (Hughes et al, 2001). Since changes in the electrode impedance may indicate changes in the electrode environment, it is possible that electrode impedance may interact with the relationship between the NRT measures and C levels because the electrode impedance directly affects the ability of the electrodes to stimulate and record during the NRT measurements.

Age-related changes in the auditory system, specifically the spiral ganglion cells, have been reported (Nadol, 1997; Syka, 2002). That is, there is a progressive loss of spiral ganglion cells that occurs due to aging, which could directly impact both the NRT measures and the stimulation level needs. Also, when deafness is significant, effects on survival of the spiral ganglion cells have been reported (Hardie, 1998; Geier et al, 1999; Shepherd and Hardie, 2001; Syka, 2002). Benefits of chronic electrical stimulation in deafened animals and humans have been demonstrated, suggesting that duration of cochlear implant use may influence the NRT response and/or stimulation level requirements (Truy et al, 1995; Hartmann et al, 1997, Hardie, 1998; Klinke et al, 1999; Ponton et al, 2000; Kral et al, 2001; Sharma, Spahr, et al, 2002, Sharma, Dorman, et al, 2002). Changes in stimulation level requirements over time have been documented for cochlear implant patients (Hughes et al, 2001).

The aforementioned factors, because they potentially can influence the NRT measurements, also have the potential to alter the interaction between the NRT measures and the stimulation levels. Hence, the decision was made to investigate electrode impedance (IMP_{MP1+2}), age (AGE), length of deafness (DUR_{DEAF}), and duration of cochlear implant use (DUR_{CI}) to determine whether these factors are significant copredictors of C levels when paired with NRT measures.

Statement of Problem

The use of electrically evoked stapedial reflexes (eSR) is an example of a method for overcoming difficulties in setting maximum stimulation levels; however, this measure is absent in approximately 20% of children and 30% of adults (Hodges et al, 2003). Although the use of neural response telemetry (NRT) has been proposed as another solution for estimation of appropriate stimulation levels, no other studies have yet been published that utilize NRT measurements in totally objective ways to predict C levels. In addition, there is concern that even with the strong correlations reported between NRT measures and behaviorally set electrical stimulation levels, all predictions have some degree of error. That is, predicted stimulation levels may be higher or lower than the optimal level for each electrode, potentially resulting in less than optimal MAPs.

The purpose of this study was to investigate whether NRT and/or other factors could be utilized in a totally objective manner to estimate C levels. The hypotheses tested in this study were (1) NRT threshold (NRT_T), NRT slope of the growth function (NRT_{SLOPE}), electrode impedance with both MP1 and MP2 extracochlear electrodes acting as reference electrodes (IMP_{MP1+2}), age of subject at time of cochlear implantation (AGE), duration of cochlear implant use at time of participation in the study (DUR_{CI}), and duration of profound deafness at time of cochlear implant surgery (DUR_{DEAF}) are all significant predictors of C levels; (2) the relationships between these predictors and C levels set using eSRT (C_{eSRT}) will be high for all electrodes; that is, there will be no significant difference between the strengths of correlation between the predictors and C_{eSRT} for all of the electrodes measured; and (3) the predicted C levels will not be significantly different from C levels obtained via eSR (C_{eSRT}).

METHODS

Subjects

For this study, subjects were drawn from the patient population of the University of Miami Cochlear Implant Program as it provided access to over 500 patients implanted with all three cochlear implant devices currently approved by the Food and Drug Administration (FDA). The system of interest, neural response telemetry, is a proprietary feature of the Nucleus 24 Cochlear Implant System. Consequently, potential subjects by default had to be users of the Nucleus 24 device with which most cochlear implant patients at the University of Miami Program have been implanted. Patients from other centers were not considered due to factors including travel distance and lack of control with respect to subject tracking during the study.

Minimum Experience

To reduce the presence of learning effects, participation was limited to patients who had a minimum device usage of three months. The rationale for the three-month limit came from clinical observations that the performance plateau of most patients at the University of Miami tends to occur within the three-month period following device activation. In addition, it has been our experience that the MAP parameters tend to stabilize within this period. If a potential subject's MAP parameters were not yet stabilized, they were not included into the study.

Reliable Responders

The use of discrimination tasks and subjective programming measures in this study required that subjects be reliable reporters. Typically, adults tend to be better respondents than children, especially younger children. In addition to contaminating the data, inaccurate reporting can result in loudness percepts exceeding a person's level of comfort. Further, children experience stages during their development when their MAP parameters tend to become temporarily unstable. To eliminate the chance of these irregularities potentially flawing the data and to prevent the possibility of causing undue discomfort that would likely result from the inclusion of children, the decision was made to include only adult subjects.

Nucleus 24 Users

Users of the Nucleus 24 cochlear implant have a choice of three programming strategies: advanced combination encoder (ACE), spectral peak (SPEAK), or continuous interleaved sampler (CIS). Currently, most recipients of the Nucleus 24 device are activated with the ACE strategy. Although upgrading to ACE from SPEAK potentially offers improvement in speech understanding, some patients have not upgraded as the process requires perceptual readjustment over a period of time. The use of the CIS strategy in Nucleus 24 recipients is rare. As indicated earlier, subject inclusion was limited to users of the ACE strategy because the programming levels are affected by strategy, and it was desired to maximize the percentage of patients that could benefit from this study.

NRT and eSR Responses

Due to the focus of the study on the NRT and C_{eSRT}, all participants were required to have both responses. Approximately 60 adult Nucleus 24 cochlear implant patients met all of the inclusion criteria as discussed. Subjects were recruited using flyers, mailings, and direct invitations (if seen in the clinic during the recruitment period). All aspects of the study were explained to potential subjects, and they were informed of their rights as required by the University of Miami's Institutional Review Board (IRB). All participants were required to indicate their consent to participate in the study by signing the informed consent for the study prior to their participation.

Procedure

Data collection involved programming of the participants' cochlear implants as well as obtaining neural response telemetry measurements including threshold (NRT_T) and slope of the growth function (NRT_{SLOPE}). During the cochlear implant programming session, two measures were obtained for all active electrodes: counted thresholds (T_{COUNT}) and C levels obtained with electrically evoked stapedial reflex thresholds (C_{eSRT}).

The T_{COUNT} measure was obtained first since it has been previously demonstrated that the accuracy of behavioral thresholds can be affected by previous experience with louder stimuli. A modified up-down procedure was used to obtain T_{COUNT} for each active electrode. In this procedure, stimuli were initially presented at a subthreshold level of 15 programming levels (PL) below the currently set threshold level. Stimulus intensity was raised in steps of 4 PL until the subject could correctly count the number of stimulus pulse trains presented, which was randomly varied between 2 and 6 trains. Once the subject correctly counted the number of pulse trains, another train was presented. If the subject was unable to correctly count both series, the stimulation level was further increased by 4 PL. This procedure was repeated until two consecutive series of pulse trains of the same intensity could be correctly counted. At this point, the stimulus level was dropped in steps of 3 PL until the subject was no longer able to correctly count the pulse trains. The stimulation level was then increased in steps of 2 PL until the subject was able to correctly count two consecutive pulse trains—this stimulus level was set as T_{COUNT} for the electrode being tested. This procedure was repeated for all remaining electrodes with normal function.

Following measurement of T_{COUNT}, C_{eSRT} was then measured on all active electrodes. The subject was instructed to sit quietly and was given the option to watch a videotape or read during this procedure. The probe from the impedance bridge was then inserted into the nonimplanted (i.e., the ear contralateral to the cochlear implant) ear. Tympanometry was performed to confirm the presence of normal middle ear status prior to measurement of the eSRT. Fixed-trains of three pulses were used for each stimulus presentation during eSRT measurement. The initial stimulation level was set 15 PL below the clinical C level for each respective electrode. The stimulus level was increased in steps of 3 PL until the reflex was clearly visualized and then decreased in steps of 2 PL until the reflex was absent. Figure 1 demonstrates the visualization of eSR in response to the pulse trains and the method of decreasing stimulation level to determine the threshold of the eSR response, which was defined as C_{eSRT}. Following the measurement of T_{COUNT} and C_{eSRT}, subjects were given a short break prior to starting the NRT measurements.

As the acquisition of neural response telemetry responses does not require subjects to remain motionless as for the eSRT procedure or to provide feedback, they were invited to read a book or rest during measurements. Although it was not essential for them to remain still, the option of watching a video was offered to maximize their comfort during their participation. They were also advised that they would be hearing moderately loud stimuli commonly described as "buzzing sounds" by other patients. NRT_T and NRT_{SLOPE} were obtained for all active

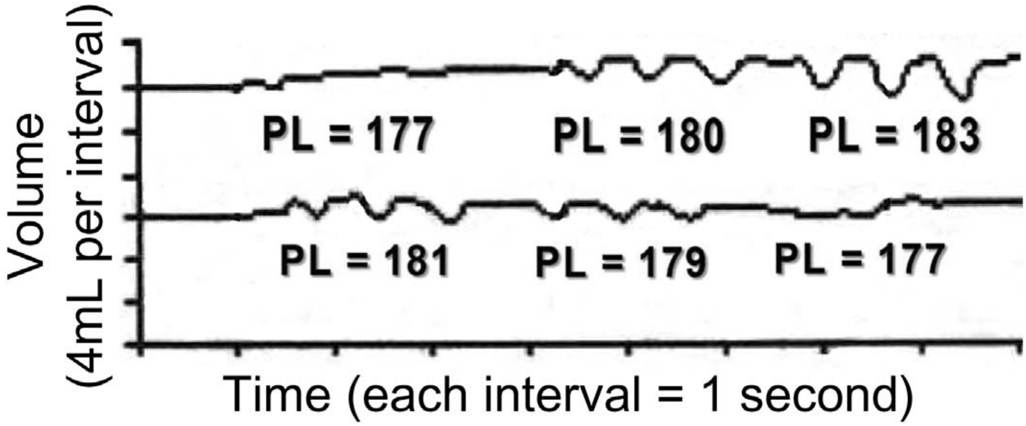

Figure 1. Example of eSRT measurement as obtained using GSI-33 Middle Ear Analyzer system. Note that as stimulus level (displayed below each response) decreases, so does the amplitude of the resultant deflection. When the deflection can no longer be visualized, the stimulation level is defined as eSRT.

electrodes utilizing NRT 3.0. For each electrode, optimal recording parameters were determined by utilizing the optimization feature of the NRT software. Once the optimal recording parameters were determined, NRT recording was commenced by starting 10 PL above C_{eSRT}. It should be noted that although the stimuli used for the NRT recordings were 10 PL above the maximum settings for each subject's MAP, the perceptual loudness did not exceed any subject's maximum comfortable levels due to the fact that the stimulation rate for NRT 3.0 used in this study (80 Hz) is much lower than the stimulation rates of the coding strategies (between 720 and 1200 Hz). If for some reason the NRT response was not clearly visible, the stimulus was then increased in steps of 5 PL until a clear response was obtained. The stimulus was then decreased in steps of 3 PL for a minimum of five averages. If the NRT response could still be visualized, more recordings were performed by decreasing the stimulus level in steps of 3 PL until the response could no longer be visualized. Once all of the recordings were obtained, the amplitude growth function feature of the NRT software was utilized to measure both NRT_{SLOPE} and the estimated NRT_T. All NRT recordings were stored to disk to enable off-line analysis if necessary. These procedures were repeated for all normally functioning electrodes that remained.

Table 1. Subject Demographic Data

Gender					
	Male	11			
	Female	10	Known Etiology (# of cases)		
				Diabetes	1
Age (years)				G. Measles	1
	Range	20.9 to 84.7		Genetic	1
	Mean	55.7		High Fever	1
	SD	18.97		Ménière's	1
				Meningitis	1
Duration of deafness (years)				Mondini	1
	Range	5.0 to 57.0		Noise Exposure	1
	Mean	27.1		Otosclerosis	1
	SD	16.3		Ototoxicity	2
				Sudden SNHL	1
Duration of cochlear implant use (months)				Unknown	9
	Range	3.6 to 76.8		Total	22
	Mean	22.8			
	SD	16.4			

Analysis

Due to the fact that variation in the profile of stimulation levels is common in cochlear implant recipients, it was necessary to treat each electrode individually. Also, it was felt that accuracy of predictions would be increased if electrodes were treated as individual entities. Thus, multivariate regression equations were developed for all 22 electrodes of the Nucleus 24 array. To determine which factors to utilize in these equations, multivariate regression analysis was performed using AGE, DUR_{DEAF}, DUR_{CI}, IMP_{MP1+2}, NRT_T, and NRT_{SLOPE} as factors. The factors found to be significant predictors of C_{eSRT} were included in the multivariate regression equations used for prediction of C levels, and the nonsignificant factors were discarded. To assess how well the regression functions predicted C_{eSRT}, a comparison between the C_{eSRT} and predicted C level (C_{REG}) was performed for each electrode. That is, the equations developed in the study were used to predict C_{eSRT} (the regression-predicted values will be referred to as "C_{REG}"), and then C_{REG} was compared to the actual measured C_{eSRT} to examine closeness of the predictions.

RESULTS

Subject Recruitment and Demographic Data

Of the approximately 60 adult Nucleus 24 patients that met all of the inclusion requirements for the study, 21 agreed to participate. Demographic data of these 21 subjects are presented in Table 1.

Table 2. Summary Data for Clinical Measures

Measure	Grand Mean	Standard Deviation	Range
IMP_{MP1+2} (kΩ)	7.01	1.85	2.94 to 15.50
T_{COUNT} (PL)	140.52	16.35	104 to 184
C_{eSRT} (PL)	201.87	16.89	163 to 243

Table 3. Summary Data for NRT Measures

Measure	Grand Mean	Standard Deviation	Range
NRT_T (PL)	181.77	13.78	140 to 228
NRT_{SLOPE} (μV/PL)	11.84	8.13	1.69 to 57.3

Table 4. Factors Identified as Significant Predictors of C Levels by Electrode

Electrode #	n	Factor	t statistic	p value	Electrode #	n	Factor	t statistic	p value
1	17	NRT_T	3.629	0.005	11	22	NRT_T	4.203	0.001
2	17	NRT_T	2.297	0.044	12	22	NRT_T	3.681	0.002
3	22	NRT_T	5.375	0.001	13	22	NRT_T	3.139	0.007
4	22	NRT_T	3.247	0.005	14	22	NRT_T	3.763	0.002
5	22	NRT_T	4.096	0.001	15	22	NRT_T	2.867	0.012
6	22	NRT_T	3.333	0.005	16	22	NRT_T	2.734	0.015
7	22	NRT_T	5.471	0.001	17	22	NRT_T	3.094	0.007
		NRT_{SLOPE}	2.624	0.019	18	22	NRT_T	3.528	0.003
8	22	NRT_T	4.018	0.001	19	21	NRT_T	3.373	0.005
9	22	NRT_T	5.688	0.001	20	21	NRT_T	2.778	0.015
		NRT_{SLOPE}	2.425	0.028	21	22	NRT_T	3.607	0.003
10	21	NRT_T	4.663	0.001	22	21	NRT_T	3.112	0.008

Clinical Measurements

Table 1 includes three measures used in the study: AGE, DUR_{DEAF}, and DUR_{CI}. It is noteworthy that considerable variance is demonstrated by these three measures. Table 2 shows the grand mean, standard deviation, and range for IMP_{MP1+2}, T_{COUNT}, and C_{eSRT} across all electrodes for all 21 participants.

The values observed for IMP_{MP1+2} were within the clinical normative range, thus indicating that all electrodes used in the study had normal function. The values obtained for T_{COUNT} and C_{eSRT} are typical when compared to clinically obtained values. In addition, the difference between the mean T_{COUNT} and the C_{eSRT} means was approximately 60 programming levels, also typical for Nucleus 24 users programmed with the ACE processing strategy.

NRT Measurements

Descriptive statistics of the NRT measurements obtained for the 21 study participants are presented in Table 3. As

Table 5. Electrode-Specific Regression Equations for Prediction of C Levels from NRT Measures

Electrode #	Regression Equations Used for Prediction of C Level
22	$70.659 + (0.711 * NRT_T) + (0.381 * NRT_{SLOPE})$
21	$63.565 + (0.749 * NRT_T) + (0.393 * NRT_{SLOPE})$
20	$72.182 + (0.725 * NRT_T) + (0.208 * NRT_{SLOPE})$
19	$54.768 + (0.811 * NRT_T) + (0.250 * NRT_{SLOPE})$
18	$39.949 + (0.871 * NRT_T) + (0.535 * NRT_{SLOPE})$
17	$52.117 + (0.780 * NRT_T) + (0.773 * NRT_{SLOPE})$
16	$62.555 + (0.729 * NRT_T) + (0.760 * NRT_{SLOPE})$
15	$78.228 + (0.659 * NRT_T) + (0.504 * NRT_{SLOPE})$
14	$42.898 + (0.851 * NRT_T) + (0.382 * NRT_{SLOPE})$
13	$42.996 + (0.866 * NRT_T) + (0.216 * NRT_{SLOPE})$
12	$47.361 + (0.825 * NRT_T) + (0.399 * NRT_{SLOPE})$
11	$9.498 + (1.033 * NRT_T) + (0.199 * NRT_{SLOPE})$
10	$26.204 + (0.927 * NRT_T) + (0.408 * NRT_{SLOPE})$
9	$41.510 + (0.846 * NRT_T) + (0.550 * NRT_{SLOPE})$
8	$58.670 + (0.753 * NRT_T) + (0.475 * NRT_{SLOPE})$
7	$56.599 + (0.748 * NRT_T) + (0.764 * NRT_{SLOPE})$
6	$74.845 + (0.686 * NRT_T) + (0.0822 * NRT_{SLOPE})$
5	$63.844 + (0.733 * NRT_T) + (0.193 * NRT_{SLOPE})$
4	$82.415 + (0.623 * NRT_T) + (0.380 * NRT_{SLOPE})$
3	$48.646 + (0.817 * NRT_T) + (0.248 * NRT_{SLOPE})$
2	$96.907 + (0.532 * NRT_T) + (0.0649 * NRT_{SLOPE})$
1	$78.671 + (0.693 * NRT_T) - (1.462 * NRT_{SLOPE})$

Table 6. Statistical Data for Predictive Regression Equations

Electrode #	R	R^2	p statistic	power	Electrode #	R	R^2	p statistic	power
22	0.723	0.522	0.001	0.972	11	0.785	0.616	<0.001	0.996
21	0.713	0.509	0.001	0.974	10	0.818	0.669	<0.001	0.998
20	0.802	0.643	<0.001	0.997	9	0.789	0.623	<0.001	0.997
19	0.818	0.669	<0.001	0.998	8	0.831	0.691	<0.001	0.999
18	0.817	0.667	<0.001	0.999	7	0.877	0.769	<0.001	1.000
17	0.778	0.605	<0.001	0.995	6	0.834	0.695	<0.001	0.999
16	0.754	0.568	<0.001	0.990	5	0.795	0.631	<0.001	0.997
15	0.752	0.565	<0.001	0.989	4	0.825	0.681	<0.001	0.999
14	0.701	0.491	0.002	0.966	3	0.780	0.608	<0.001	0.995
13	0.708	0.502	0.001	0.971	2	0.625	0.391	0.031	0.783
12	0.775	0.601	<0.001	0.994	1	0.743	0.552	0.002	0.960

expected, the grand mean for NRT_T is approximately 65% of the dynamic range. The range of values for both NRT_T and NRT_{SLOPE} falls within the range typically seen clinically.

Predictive Factors

Multivariate linear regression analysis with AGE, DUR_{DEAF}, DUR_{CI}, IMP_{MP1+2}, NRT_T, and NRT_{SLOPE} defined as factors indicated that only NRT_T and NRT_{SLOPE} were statistically significant predictors of C_{eSRT} (Table 4).

Regression Equations

Using only NRT_T and NRT_{SLOPE} as factors, individualized regression equations were generated for each electrode (Table 5). R^2 ranged from 0.391 to 0.769, and all regressions were statistically significant at the p = 0.05 level (Table 6). Electrode number two was the only electrode that did not achieve the desired power of 0.80 (actual value, 0.783).

Comparison of Prediction from Regression versus Correction Factors

Figure 2 shows the means and standard deviations for C_{eSRT} and C levels predicted from regression (C_{REG}) for all electrodes. These data were obtained from all 21 participants and demonstrate that C_{REG} are close to C_{eSRT} across the entire electrode array. The method of estimating C level by global application of a correction factor to NRT_T is revisited in Figure 3, which shows that a correction factor of +20 closely approximates C_{eSRT} for basal electrodes but underestimates for the apical electrodes.

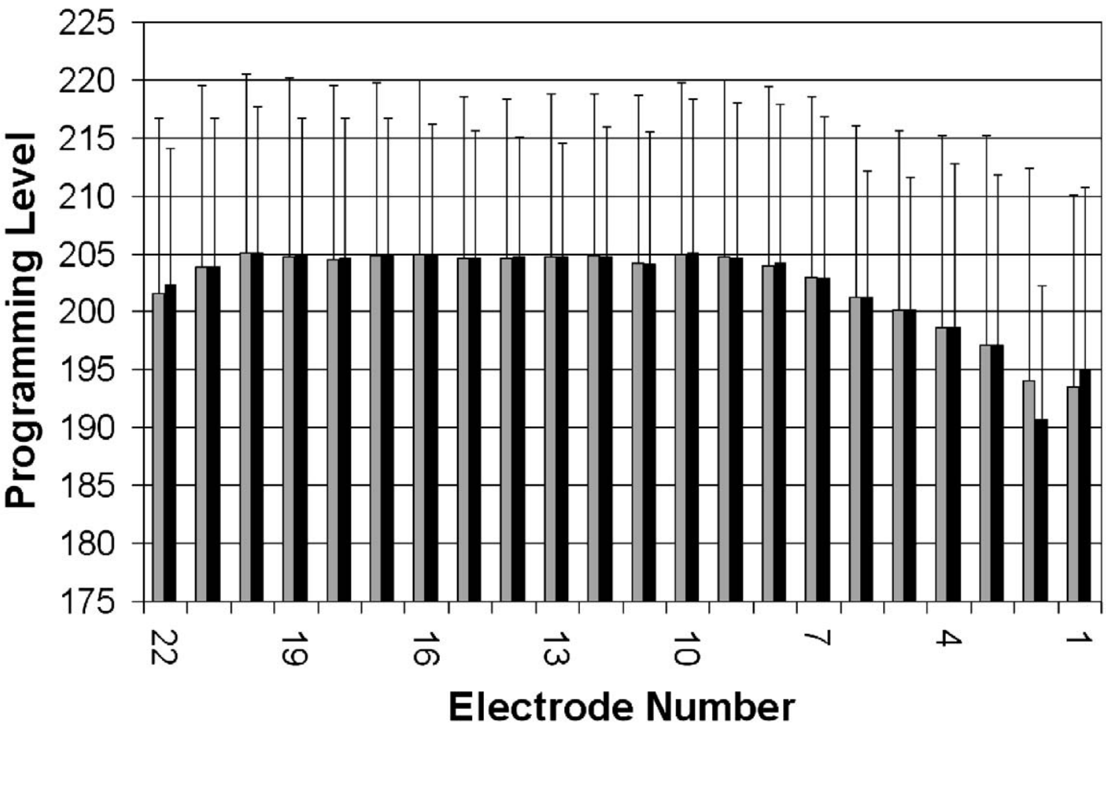

Figure 2. Mean C_{eSRT} and C_{REG} for all electrodes. Light and dark bars represent C_{eSRT} and C_{REG} means, respectively. Data demonstrates that C_{REG} is similar to C_{eSRT} across the electrode array when considering means and standard deviations.

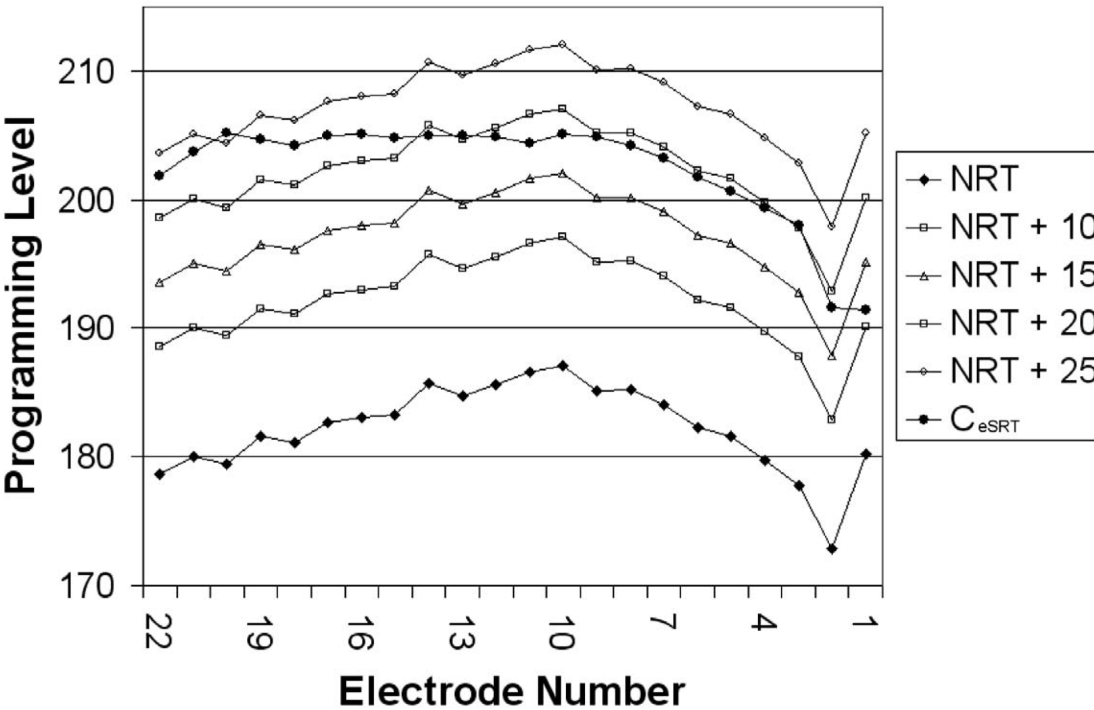

Figure 3. Addition of correction factors to NRT_T has been used to estimate C level. Note: Correction factor of +20 (NRT_{T+20}) appears to approximate C_{eSRT}; however, the NRT_{T+20} contour does not match that of C_{eSRT}, especially for the apical electrodes.

To determine which correction factor would best approximate C_{eSRT}, the absolute value of the difference between NRT_T plus correction factor (NRT_{T+CF}) and C_{eSRT} was averaged across all electrodes using the integer range of 18 through 25 for correction factor values (i.e., NRT_{T+18} through NRT_{T+25}). The absolute value of differences was used to correct for the artificial shrinkage of the mean values that would result from the averaging of positive and negative values. These mean absolute value differences were compared to the mean absolute value difference of C_{REG} and C_{eSRT} (Figure 4). Results showed that a correction factor of +21 programming levels provided the closest prediction of C_{eSRT} using the NRT_{T+CF} method; however, paired t-test indicated that the C_{REG} technique resulted in a significantly smaller mean absolute value difference: $t\ (490) = -7.217$, $p \leq 0.001$.

Accuracy of Predictions

The individual mean absolute value differences between C_{eSRT} and C_{REG} for all 22 electrodes is shown in Figure 5. The grand mean of the absolute value difference across all 22 electrodes was seven programming levels with a standard deviation of five levels. It must be pointed out that since the differences were converted to absolute values, the mean differences reported in Figure 5 are reflective of both understimulation (C_{REG} is less than C_{eSRT}) and overstimulation (C_{REG} is greater than C_{eSRT}).

Prevalence of Predictions Resulting in Overstimulation

The data in Figure 5 represent a total of 443 electrodes. Of these, 44 electrodes (9.9%) had predicted values (C_{REG}) greater than C_{eSRT} by more than ten programming levels, which we consider to be a clinical definition of overstimulation. It was observed that the majority of cases of these overstimulations occurred in subjects who had more than 20 years of profound hearing loss prior to cochlear implantation. When these subjects were excluded, the grand mean of the absolute value difference across all 22 electrodes was reduced to six programming levels with a standard deviation of five levels (Figure 6). The prevalence of overstimulation

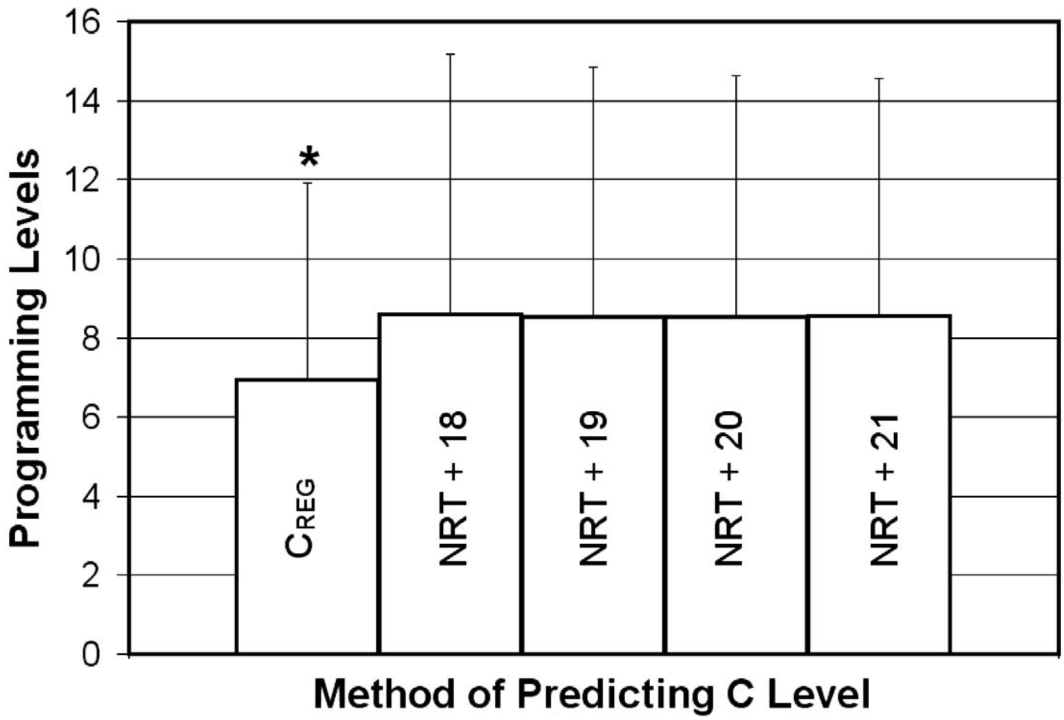

Figure 4. Mean absolute value differences for two methods of predicting C level (NRT_{T+CF} and C_{REG}). Results indicated that NRT_{T+21} was the best estimator for the NRT_{T+CF} method. Paired t-test indicated that C_{REG} more closely predicted C_{eSRT} than NRT_{T+21}; t (490) = -7.217, $p \leq 0.001$.

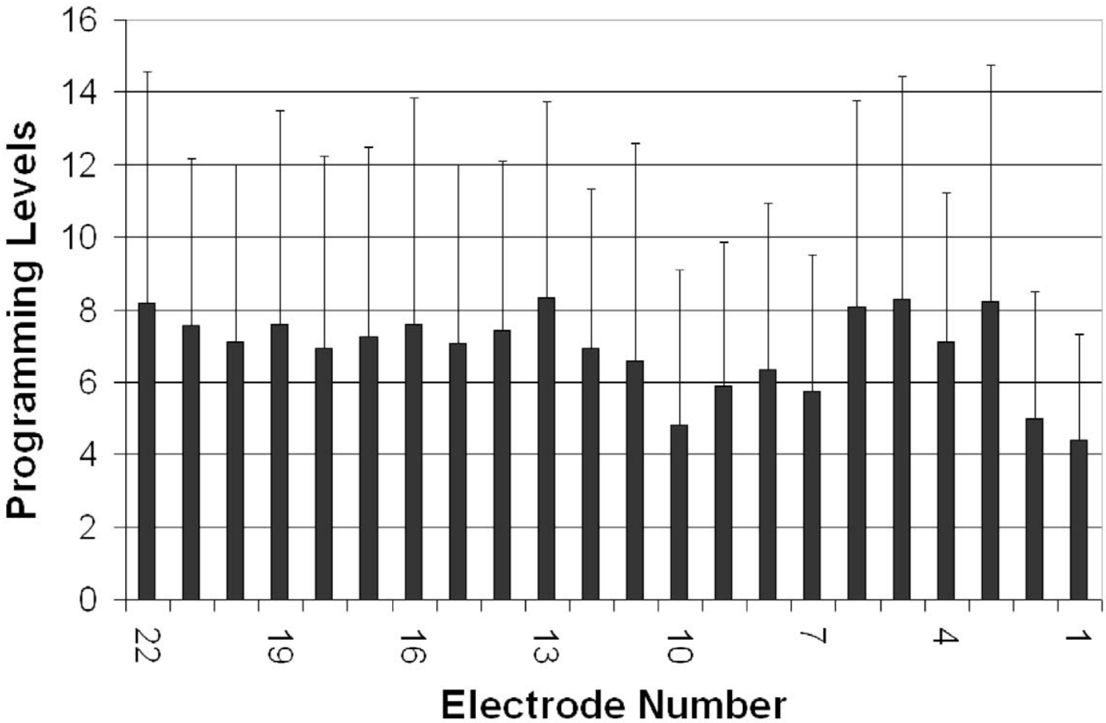

Figure 5. Mean absolute value differences between C_{eSRT} and C_{REG} for all 22 electrodes. The grand mean across all electrodes was seven programming levels (SD = five levels). Due to the use of absolute values, these results are reflective of both positive and negative differences between the two measures.

in these subjects with a history of less than 20 years of profound deafness prior to implantation dramatically dropped to 2 electrodes out of a total of 228 (0.9%).

DISCUSSION

Obtained Measurements

The mean dynamic range for MAPs created with C_{eSRT} (61.35) matches the dynamic ranges typically seen clinical at the University of Miami Cochlear Implant Program. The mean NRT_T (181.77) was equivalent to 67.2% of the mean dynamic range when eSRT was used to set C levels, which is consistent with data presented in the literature (Stephan et al, 1988; Stephan et al, 1990; Van den Borne et al, 1994; Hodges et al, 1999; Bresnihan et al, 2001; Allum et al, 2002).

Significance of Variables in C Level Prediction

Multivariate regression analysis indicated that only the NRT_T (all electrodes) and NRT_{SLOPE} (electrodes seven and nine, only) measures were significant predictors of C level. The factors IMP_{MP1+2}, AGE, DUR_{CI}, and DUR_{DEAF} were not found to be significant predictors of C level. It was expected that NRT_T would be a good predictor of C levels as investigators have reported modest to good correlations between both measures (Brown et al, 2000; Hughes, Abbas, et al, 2000; Zimmerling and Hochmair, 2002; Polak et al, 2003, Polak et al, 2004). Reports of significant correlations between NRT_{SLOPE} and C level could not be found in the literature; however, NRT_{SLOPE} has been modestly correlated with performance with the cochlear implant (Hall, 1990; Gantz et al, 1994; Franck and Norton, 2001). It is not understood why only electrodes seven and nine showed a strong correlation between

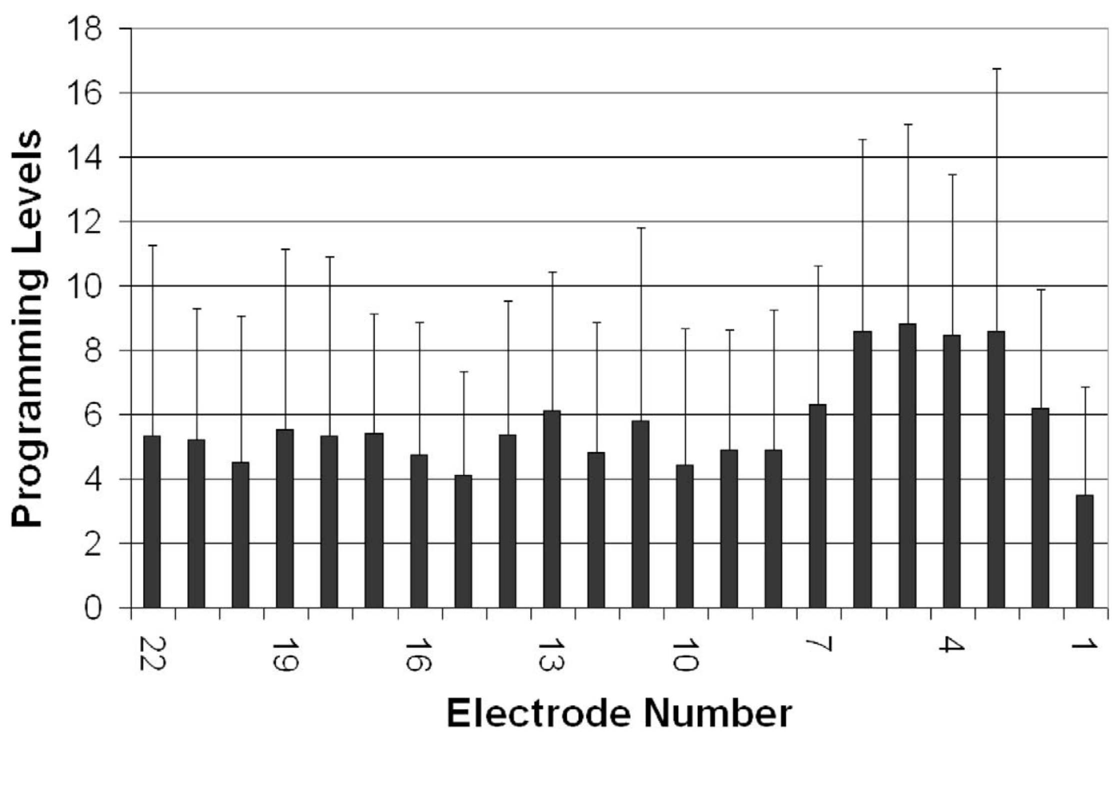

Figure 6. Mean absolute value differences between C_{eSRT} and C_{REG} for all 22 electrodes for subjects with fewer than 20 years of profound hearing loss prior to cochlear implantation. The grand mean across all electrodes was six programming levels (SD = five levels), indicating that predictions were closer to actual C levels for this population of subjects.

NRT_{SLOPE} and C level as no systematic variation of the predictive strength of NRT_{SLOPE} could be discerned as a function of electrode position. This was surprising because NRT_{SLOPE} has been demonstrated to vary as a function of recording electrode location and is suspected to provide information regarding the density of surviving spiral ganglion cells (Polak et al, 2004). Consequently, it was hypothesized that the spiral ganglion cell density dictated the programming level requirements, thus the expectation that NRT_{SLOPE} would contribute significantly to the prediction of C levels. The decision was made to incorporate NRT_{SLOPE} into the regression equations despite the statistical data because this measure still provides some degree of predictive information. In addition, by making a clinically based decision to retain NRT_{SLOPE} in the equations, uniformity of the equation structure is preserved across electrodes.

Electrode impedance provides indication of both electrode and electrode-tissue interface status (Hughes et al, 2001). Since changes in the electrode impedance may reflect changes in the electrode environment that can affect the ability of the electrode to be stimulated as well as record the NRT response, it was felt that the IMP_{MP1+2} variable might interact with the relationship between the NRT measures and C levels and thus provide predictive data for estimation of C levels. Further, Hughes et al (2001) reported that electrode impedance varied systematically and on average was lowest for basal electrodes and highest for apical electrodes. It was reasoned that a systematic variance in electrode impedance would influence the C level depending on electrode position. One possible reason for the lack of a significant relationship between IMP_{MP1+2} and C level may be due to the fact that the C level is dependent not only on the electrode impedance but also the degree of nerve survival. In other words, the influence of electrode impedance on the amount of current required to stimulate a particular region of the cochlea may be negated by the fact that someone with larger nerve survival will

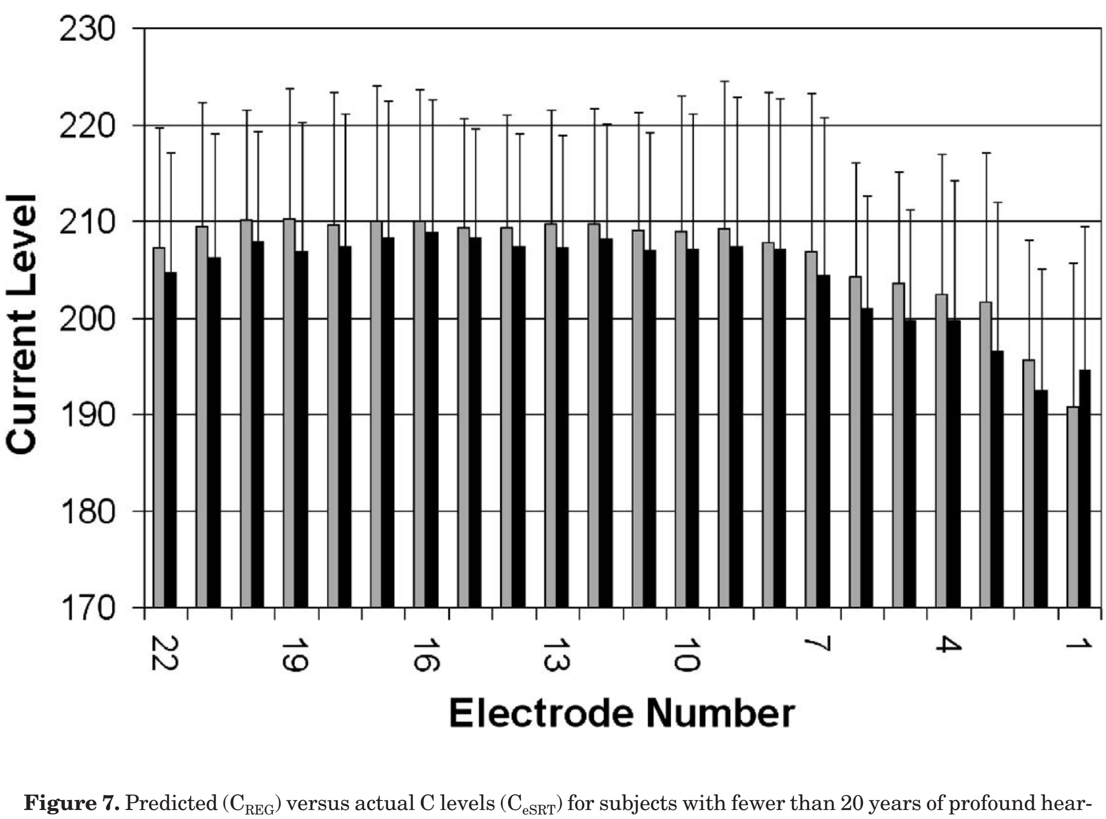

Figure 7. Predicted (C_{REG}) versus actual C levels (C_{eSRT}) for subjects with fewer than 20 years of profound hearing loss prior to cochlear implantation. Light and dark bars represent C_{eSRT} and C_{REG} means, respectively. Generally, the means of the predicted C levels were lower than the means of actual C levels, suggesting that minimal overstimulation occurred.

require less current to reach C level than someone with poorer nerve survival.

Blamey et al (1996) reported that age at the time of cochlear implantation was associated with a slight negative effect on performance with the cochlear implant. Biological age-related changes in the auditory system pathways, specifically the spiral ganglion cells, have been reported (Nadol, 1997; Syka, 2002). Consequently, it was felt that AGE would be of predictive value. It is possible that AGE might have been significant if children were included in the study as differences in both NRT and programming measures have been reported for adults versus children (Spivak and Chute, 1994; Hughes, Abbas, et al, 2000; Hughes et al, 2001; Gordon et al, 2002; Morita et al, 2003; Gantz et al, 2004). The number of subjects over the range of age groups was probably insufficient to determine if AGE was a significant predictor of C level. Another factor that must be taken into consideration is that both the NRT and programming measures were obtained with monopolar stimulation, which is known to result in broader excitation of spiral ganglion cells (Brown et al, 1996; Dillier et al, 2002). The stimulation of more spiral ganglion cells may effectively nullify the ability of AGE to predict C levels. It would be interesting to compare the predictive ability of AGE for C levels for monophasic versus biphasic stimulation modes.

When deafness is significant, effects on survival of the spiral ganglion cells have been reported (Hardie, 1998; Geier et al, 1999; Shepherd and Hardie, 2001; Syka, 2002). Shepherd et al (1993) stated that the extent of cochlear pathology generally increases with duration of deafness and that the survival of peripheral dendrites and spiral ganglion cell has a direct relation with cochlear status. Thus, it was anticipated that the expected decline in cochlear status and the resultant decline in neural survival secondary to duration of deafness (DUR_{DEAF}) would account for some of the variance in stimulation level requirements. As discussed earlier, the broader excitation pattern of monopolar stimulation utilized during NRT and programming measurements may have confounded the relationship between DUR_{DEAF} and C level in these subjects. It also must be acknowledged that the DUR_{DEAF} variable probably lacks precision in measurement because it relies on the ability of the subjects to accurately recall the onset of their deafness. In addition, further inaccuracies in this variable were likely present in the subjects with long-term progressive deafness since it is not always clear when the degree of their deafness reached the point of being profound.

Questions have been raised regarding the importance of spiral ganglion cell survival on performance with cochlear implants. Shepherd et al (1993) noted that postmortem studies have shown that spiral ganglion cell survival in humans with hearing loss ranged anywhere from 20 to 70% of that in persons with normal hearing. In their study, only one animal exhibited eABR responses that were clearly affected by spiral ganglion cell loss; however, it was estimated that the spiral ganglion survival was less than 5% in this animal, much lower than that typically observed in humans with hearing loss. As a result, Shepherd et al postulated that the position of the cochlear implant electrode in the lumen of the scala tympani was likely more critical than spiral ganglion cell survival. It is unknown how the results reported by Shepherd et al translated to our results because the generator site of their eABR wave IV measure is higher up in the auditory pathway than the generator site of the NRT response (spiral ganglion cells). That is, the survival of the spiral ganglion cells could have a greater effect on the eCAP response of the auditory nerve than the later potentials typically recorded during eABR acquisition.

Blamey et al (1996) indicated that the spiral ganglion cell population may continue to decline following cochlear implantation or stabilize due to neuro-protective effects of the electrical stimulation provided by the device. Other investigators have reported positive effects of chronic electrical stimulation in deafened animals and humans (Truy et al, 1995; Hartmann et al, 1997, Hardie, 1998; Klinke et al, 1999; Ponton et al, 2000; Kral et al, 2001; Sharma, Spahr, et al, 2002, Sharma, Dorman, et al, 2002). Hence, it was be expected that DUR_{CI} would also provide predictive information regarding stimulation requirements of the surviving spiral ganglion cells. This is a difficult variable to consider because it is closely related to DUR_{DEAF} since the benefit of electrical stimulation depends on the degree of neural degeneration at the initiation of stimulation. Thus, for an individual with long-term deafness, the benefits of electrical stimulation may be minimal if the degree of degenerative change is too great. Further, the situation is muddled by AGE since it has been demonstrated that the plasticity of the neural auditory pathway declines as a function of aging (Ponton et al, 1996; Ponton et al, 1999).

Prediction of C Levels from NRT_T and NRT_{SLOPE}

When NRT_T and NRT_{SLOPE} are used as copredictors of C levels, the R values ranged from 0.625 to 0.877 with a mean of 0.775 and were similar to correlations observed between NRT_T and C levels by others (Hughes, Abbas, et al, 2000; Polak et al, 2004). Stated in a different way, depending on electrode, the use of NRT_T and NRT_{SLOPE} as predictive factors was able to capture between 39.1% and 76.9% of the variance present in the C levels. With an observed power of 0.783, electrode number two was the only one in which these two cofactors did not result in a desired power of 0.80. This is likely due to the fact that electrodes one and two are typically not utilized in adults, as they prefer to wear the smaller 3G processor that has a limited ability to stimulate only 20 of the 22 electrodes due to power supply issues. Studies have demonstrated differences in electrical stimulation properties of electrodes that are inactive when compared to active electrodes (Hughes et al, 2001).

Comparison of Predicted versus Measured C Levels

When the predicted C levels were compared to the C levels set using eSRT in the 21 subjects, the means were very close. It was determined that the overall prevalence of overstimulation by more than ten programming levels using the regression equations was less than 10% of all electrodes when all subjects were considered. By removing subjects with greater than 20 years of deafness, the prevalence was dropped to less than 1%. This suggests that using regression equations to predict C levels can be fairly accurate; however, it may be necessary to take the subject population into account when using the equations (e.g., having separate equations for different populations of cochlear implant users).

Comparison of Prediction Methods

As no other objective methods for prediction of C levels have yet been proposed, no other data are available for comparison. The methods that have been proposed thus far that are the closest to being totally objective require some subjective feedback while the estimated C levels are globally increased or decreased (Franck and Norton, 2001; Franck, 2002; Seyle and Brown, 2002). Using the NRT_T data obtained from the 21 subjects used in this study, it was determined that a correction factor of 21 was the closest approximation of C level when added to NRT_T. Comparison of mean differences between actual and predicted C levels indicated that the regression method developed in this study was significantly more accurate than the global addition of a correction factor of 21.

Since different subject populations do not always exhibit the same variance in parameters, it is expected that the accuracy of C level predictions may vary for different populations. This can easily be determined by applying the regression functions to predict C levels for a separate sample population and comparing the predicted C levels to the measured C levels for this separate population of subjects. It is not expected that a significant difference will be found between the results of a separate sample population and the current study as long as the sample population has adequate size to ensure that sample variance is equivalent to the overall population variance.

Limitations of the Prediction of C Levels from NRT_T and NRT_{SLOPE}

Although the use of NRT_T and NRT_{SLOPE} as regression factors to predict C level has demonstrated considerable promise, several limitations must be taken into consideration. First, the parameters used to obtain the NRT responses are not clinically standardized. Investigators have shown that alteration of NRT stimulating and recording parameters can result in significant changes in the NRT measures (Brown et al, 1998; Abbas et al, 2000; Cullington, 2000; Dillier et al, 2002; Zimmerling and Hochmair, 2002). In addition, altering the NRT stimulating parameters can affect the relationship between the NRT and programming measures. While it was demonstrated that the use of the regression method of prediction can be applied to different subject populations with reasonable success, this was possible because the same parameters and techniques were utilized in obtaining the NRT and programming measures. Second, the regression functions developed in this study were designed to predict C levels as set using electrically evoked stapedial reflex thresholds. Thus, the predicted C levels may differ when compared to C levels that are obtained via means other than reflexes, such as using subjective loudness rating scales. Third, the regression functions were developed using data obtained from adults. Consequently, the accuracy of predictions may be different for children. Due to the variety of factors and constraints discussed, it is recommended that normative data be obtained and personalized regression functions developed by persons interested in using this technique of predicting C levels to maximize accuracy of predictions. Further investigation is clearly needed to determine the applicability of this approach with pediatric subjects.

CONCLUSIONS

Despite the fact that only two of the six variables were significant predictors of C level, the study was successful in developing regression functions capable of estimating C levels based on eSRT. This was especially true when the regression equations were applied to subjects with fewer than 20 years of profound hearing loss. It was therefore concluded that prediction of C levels without the use of subjective responses is feasible when using NRT measures. This method has the potential for clinical use in assisting in the setting of programming levels in difficult to test subjects, provided that the same parameters and techniques utilized in this study are utilized. Otherwise, normative data should be obtained for the purpose of development of new regression functions to take into account any changes in parameters or techniques that are present. Further research is necessary to determine the impact of utilizing predicted C levels using this technique on speech perception performance, as well as application to different populations of patients (e.g., children).

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