Available online at www.sciencedirect.com
SCIENCE DIRECT®
Hearing Research 205 (2005) 83–93
HEARING RESEARCH
www.elsevier.com/locate/heares

Histopathology of human cochlear implants: Correlation of psychophysical and anatomical measures

Aayesha M. Khan [a,b], Darren M. Whiten [a,c], Joseph B. Nadol, Jr. [b,c], Donald K. Eddington [a,b,c,d,*]

[a] Cochlear Implant Research Laboratory, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, MA 02114, USA
[b] Department of Otology and Laryngology, Harvard Medical School, 243 Charles Street, Boston, MA 02114, USA
[c] Speech and Hearing Bioscience and Technology Program, Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02369, USA
[d] Research Laboratory of Electronics, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02369, USA

Received 29 September 2004; accepted 3 March 2005
Available online 12 April 2005

Abstract

The cadavaric temporal bones of five subjects who underwent cochlear implantation during life (2 Nucleus and 3 Ineraid) were analyzed using two-dimensional (2D) reconstruction of serial sections to determine the number of surviving spiral ganglion cells (SGCs) in the region of each electrode of the implanted arrays. The last psychophysical threshold and maximum-comfortable sensation level measured for each electrode were compared to their respective SGC count to determine the across-electrode psychophysical variance accounted for by the SGC counts. Significant correlations between psychophysical measures and SGC counts were found in only two of the five subjects: one Nucleus implantee (e.g., $r = -0.71$; $p < 0.001$ for threshold vs. count) and one Ineraid implantee (e.g., $r = -0.86$; $p < 0.05$ for threshold vs. count). A three-dimensional (3D) model of the implanted cochlea was formulated using the temporal-bone anatomy of the Nucleus subject for whom the 2D analysis did not result in significant correlations between counts and psychophysical measures. Predictions of the threshold vs. electrode profile were closer to the measured profile for the 3D model than for the 2D analysis. These results lead us to hypothesize that 3D techniques will be required to asses the impact of peripheral anatomy on the benefit patients derive from cochlear implantation.

Keywords: Cochlear implantation; Spiral ganglion cells; Psychophysics

1. Introduction

The improvement in speech reception provided to the profoundly hearing-impaired by today's cochlear implants is striking for at least two reasons. First is the substantial benefit realized by most implanted patients in communication (e.g., Anderson et al., 2002; Osberger et al., 2000; Parkinson et al., 2002) that leads most analysts to assign very positive cost/utility ratios to unilateral implantation (e.g., Francis et al., 2002; Summerfield et al., 1997, 2002; Wyatt et al., 1996). Second (and most relevant to the focus of this report) is

Abbreviations: μs, microsecond; μm, micrometer; nC, nanoCoulomb; pps, pulses per second; r^2, coefficient of determination (squared correlation coefficient); *p*, level of significance; 2D, two-dimensional; 3D, three-dimensional; C, stimulus level eliciting maximum comfortable sensation level; CD, cochlear duct; *D*, distance between an electrode and Rosenthal's canal; DR, C–T; FT, fibrous tissue volume; I1, I2 and I3, three subjects with Ineraid implants; N1 and N2, two subjects with Nucleus implants; NB, volume of new bone; NU6, Northwestern University single-syllable word test #6; psEAM, patient-specific electroanatomical model; RC, Rosenthal's canal; SGC, spiral ganglion cell; T, stimulus level eliciting threshold sensation level

* Corresponding author. Tel.: +1 617 573 3766; fax: +1 617 573 3550.
E-mail address: dke@cirl.meei.harvard.edu (D.K. Eddington).

0378-5955/$ - see front matter
doi:10.1016/j.heares.2005.03.003

the wide range of benefit that is measured across individual patients. For instance, the median score for the reception of single-syllable words in our clinic population using the most recent devices approaches 40% with individual patient scores ranging from 0% to greater than 95%.

If the mechanisms responsible for this wide range of performance were identified, investigators could direct effort at overcoming the fundamental factors limiting speech reception. This would likely increase the pace at which the quality of hearing is improved. Also, once the factors limiting performance are identified, the development of methods for their presurgical evaluation would likely lead to better estimates of the degree to which individual patients will benefit from the implantation of specific devices. These important consequences (improved performance and better prognostication) have led investigators to expend considerable effort searching for factors that account for the large interpatient variance in implantee performance.

We find it useful to group sources of intersubject performance variance into five categories: the implantee, the device, the sound-processing strategy, the procedure used to adjust the device/strategy to the patient, and the measure used to evaluate performance. Because use of appropriate methodology can minimize and characterize the variance associated with the last four categories, the sources of variance associated with the implantee have received the most attention.

The individual patient's anatomy and physiology will play a fundamental role in the benefit he/she derives from implantation. Until recently, however, the lack of histopathologic and physiological data from a substantial number of multichannel cochlear implantees has led most investigators to concentrate on what Blamey et al. (1996) termed "secondary factors": measures or characteristics that may reflect the state of the more fundamental anatomical/physiological factors in an individual patient. For instance, because the number of surviving spiral ganglion cells is related to the duration of hearing impairment and etiology (Incesulu et al., 1998; Nadol, 1997; Nadol et al., 1989; Otte et al., 1978), many investigators have examined the relationship between performance and these two secondary factors. Blamey et al. (1996) reviewed 13 such studies conducted before 1996 and noted that 9 found a significant negative correlation between speech-reception performance and duration of deafness. For instance, the study examining the largest number of subjects to date ($N = 808$) found duration of deafness, age at onset of deafness and etiology together accounted for only 20% of the intersubject performance variance. This is about the same percentage of performance variance explained by measures of cognitive function (e.g., Knutson et al., 1991), electrode threshold (Blamey et al., 1992) and electrode-array insertion depth (Marsh et al., 1993; Skinner et al., 2002). To date, investigators have not identified combinations of the abovementioned factors that explain substantially more than the approximately 20% of the performance variance explained by each individually.

Measures of basic psychophysical performance that characterize a patient's ability to receive cochlear place information (Collins et al., 1997; Dawson et al., 2000; Donaldson and Nelson, 2000; Henry and Turner, 2003; Henry et al., 2000; Nelson et al., 1995; Throckmorton and Collins, 1999; Zwolan et al., 1997) and temporal information (Cazals et al., 1994; Collins et al., 1994; Fu, 2002; Hanekom and Shannon, 1998) have been more successful in accounting for variance (40–97%) in at least small groups of subjects ($3 \leqslant N \leqslant 21$). The correlation between speech reception and modulation detection documented by Fu (2002) and accounting for 97% of the variance in consonant reception and 72% of the variance in vowel reception is remarkable. Results like these show that the spatial and temporal cues known to be important for speech reception in normal hearing also account for a significant portion of the performance variability in electric hearing. They may also identify parameters of sound-processing strategies that should receive attention when adjusting devices for patients and suggest regimes of auditory training (Fu, 2002). But these relationships have not identified specific anatomical or physiological limitations that future devices should target.

The histopathological analyses of cadavaric temporal bones from users of multichannel cochlear implants during life include studies that examine the degree to which variation in the peripheral anatomy accounts for variance in psychophysical and speech-reception measures (Clark et al., 1988; Fayad et al., 1991; Johnsson et al., 1979, 1982; Kawano et al., 1998; Linthicum et al., 1991; Linthicum and Galey, 1983; Marsh et al., 1992; Nadol et al., 2001; O'Leary et al., 1991; Terr et al., 1989; Zappia et al., 1991). Clark et al. (1988) reported the temporal-bone histopathology and psychophysical/speech-reception performance of one Nucleus implantee. These results support the biocompatibility of both the device materials and two years of electric stimulation, but their rather coarse spatial characterization (averaged over 5 mm segments) of spiral-ganglion cell (SGC) survival was not suitable for correlation with psychophysical measures made at individual electrodes. While Marsh et al. (1992) reported SGC survival using even larger segments, a sentence in Section 4 suggests estimates were also made at a finer (but not specified) spatial resolution that led to an unspecified negative correlation between psychophysical threshold and SGC survival. Fayed et al. (1991; see also Linthicum et al., 1991) reported total spiral-ganglion cell counts and percent survival of dendrites for the temporal bones of two multichannel users (one Ineraid and one Nucleus) and 14 single-channel users. While the