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VERIFICATION OF COMPUTED TOMOGRAPHIC ESTIMATES OF COCHLEAR IMPLANT ARRAY POSITION: A MICRO-CT AND HISTOLOGICAL ANALYSIS

by

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A Capstone Project submitted in partial fulfillment of the requirements for the degree of:

Doctor of Audiology

Washington University School of Medicine Program in Audiology and Communication Sciences

May 20, 2011

Approved by: Richard Chole, M.D., Ph.D. Capstone Project Advisor Timothy Hullar, M.D., FACS, Second Reader

Abstract: We examine the efficacy two volume spatial registration of pre and postoperative clinical computed tomography (CT) imaging to verify post-operative electrode array placement in cochlear implant (CI) patients. To measure the degree of accuracy with which the composite image predicts in-vivo placement of the array, we replicate the CI surgical process in cadaver heads. Pre-operative, post-operative, micro CT imaging and histology are utilized for verification. copyright by

Jessica R. Teymouri

2011

Acknowledgements:

I would like to thank the following people for their support and guidance in the completion of this project:

Richard Chole, M.D., Ph.D., Capstone Project Advisor Timothy Hullar, M.D., FACS, Second Reader Timothy Holden, B.S.E. Patricia Keller, Histology Core Manager Human donors

This capstone project was supported by:

Department of Otolaryngology WUSM (Chole 2R01DC 000263-22) (Hullar K08)

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ABBREVIATIONS

2D Two dimensional

3D Three dimensional

AOS Advance off stylet

CI Cochlear implant

CNC Consonant-nucelus-consonant

CT Computed tomography

EAS Electro-acoustic stimulation

HINT Hearing in noise test

MMA Methamethacrylate

OPFOS Orthogonal-plane fluorescence optical sectioning

RW Round window

SIT Standard insertion technique

SM Scala media

SPEAK Spectral peak processing strategy

ST Scala tympani

SV Scala vestibuli

Introduction

Since the inception of the multichannel cochlear implant (CI), numerous factors have been identified that affect clinical outcomes and performance. One of those factors is variation of surgical technique and the resultant position of the electrode array. As a result, advancements have been made in electrode design and surgical techniques. Refinements of surgical techniques must be accompanied by refinements in objective, reliable clinical measures to verify that goals of the surgery have been realized. Clinical computed tomography (CT) scanning is one such applicable tool. In 2002, Skinner et al. described four main approaches to estimating the in vivo intra-cochlear position of the implanted electrode array, the first of which is the surgeon's report. The remaining methods are based on image analysis. Skinner, et al. (2002) created a technique utilizing spatial registration of a CI patient's pre and post-operative CT scans aligned with a cochlear atlas that defines intra-cochlear structure. The atlas is based on orthogonal-plane fluorescence optical sectioning (OPFOS) microscopy scan of a single, normal hearing donor (Voie, 2002). OPFOS is an imaging technique that yields quantitative measurements of the mammalian cochlea and facilitates three dimensional (3D) reconstructions of its intricate anatomy. The 3-D image that is derived from the CT volume registration is used to estimate medio-lateral and scalar position, and depth of insertion of the electrode array. Research suggests these variables are not only related to preservation of residual hearing, but may influence performance outcomes (Skinner, 2007; Finley, 2008).

The technique developed by Skinner, et al. (2007) addresses the issue of "bloom" artifact from the metal contacts in the array, which obscures visualization in the post-operative scan.

Metallic electrodes in the array are identified and refined using a pixel threshold technique in ANALYZE® software (Robb, et al. 1989). The resulting image is then translated to the

preoperative CT volume. Identification of scalar boundaries presents a challenge due to the limited spatial resolution and soft tissue detail available with clinical CT which images bone/tissue boundaries. This is addressed by overlaying the cochlear atlas onto the combined CT data to better visualize the scalar position of the CI array. However, only an approximation of the scalar divisions is available and there is no information as to how the implanted array is interacting with the intra-cochlear soft tissue structures. The aim of this study is to address these perceived limitations by replicating the clinical CI surgical process using non-fixed cadaver heads. Outcomes are verified using pre and post-operative CT scanning, as well as micro CT (Lane, et al. 2007) scanning and a histological analysis that serves as the gold standard.

Background

Conservation of cochlear anatomy and preservation of residual hearing have implications for traditional CI candidates, candidates for bimodal hearing, and future treatment options for cochlear implant recipients (Gantz, 2005; Balkany, 2006; Fraysse 2006; James, 2005; James, 2006). Patients with greater residual hearing also benefit from lower thresholds of stimulation, which are determined during device programming. This decreases power consumption of the external portion of the device. Maximization of surviving neural elements may also allow for finer frequency perception (Roland, 2005). Furthermore, CI recipients who have higher numbers of electrodes residing in the scala tympani (ST) and less insertion trauma obtain greater benefit from the device (Skinner, 2002; Aschendorff, 2007), as evidenced by their higher scores on open set word recognition testing.

Unlike other factors affecting clinical outcomes such as etiology, length of auditory deprivation or surviving spiral ganglion cells, surgical placement of the electrode array is one

variable over which the surgeon may exert a considerable amount of control. Numerous studies demonstrate that by implementing an atraumatic, or soft surgical technique, patient outcomes may be positively affected due to the greatest number of electrodes inserted into and remaining in ST, a decrease in damage to the organ of Corti, and the greatest opportunity for preservation of residual hearing.

Atraumatic Surgery

It was once accepted that after cochlear implant surgery, the only transmission route of sound to the auditory nerve would be through electrical stimulation via the implant, as insertion trauma during the surgical process would destroy all residual hearing (Copeland, 2004).

However, recent studies and clinical trials have demonstrated the feasibility of hearing preservation following cochlear implantation in conjunction with refined surgical approach.

"Soft surgery" is a term used to describe surgical implantation of the electrode array that results in the least amount of disruption and damage to cochlear structures such as the basilar membrane, osseous spiral lamina, and the modiolar wall. Atraumatic insertions decrease sequela secondary to fibrosis and ossification after placement of the array (Berrettini, 2007).

Components of the technique include: anterior-inferior cochleostomy placement with respect to the round window (Balkany, 2006), cochleostomy size less than 1.2 mm, placement of the array in the ST, avoidance of suction of perilymphatic fluid, containment of bone dust (Lehnhardt, 1994; Friedland, 2009), a slow rate of insertion (Roland, 2005), as well as an insertion depth of less than 400 degrees (Fraysse et al., 2005).

Increased rates of conservation of residual hearing, in conjunction with improved surgical technique and CI technology have been reported (Gantz, 2005; Fraysse, 2006). For example,

Balkany et al. reported stable post operative pure tone thresholds in approximately one third of subjects tested in the 1980s. This rate increased to approximately 50% in the 1990s and, although quantification of residual hearing may differ among investigators, general hearing conservation rates exceeding 80% have been reported in recent literature (Balkany, 2006; Gstoettner, 2004; Kiefer, 2004; James, 2005). With advances in electrode array design, surgical technique, and speech processing, candidacy for cochlear implantation has correspondingly widened to include patients who would have formerly been excluded on account of having "too much" residual hearing, regardless of poor word recognition scores. Many patients with residual hearing are captured in this population. Of equal consideration is future therapy for recipients who may be less than 12 months old at the time of implantation. For these reasons, avoidance of the long-term consequences of insertion trauma has become increasingly important (Wardrop, 2005; Balkany 2006).

Electroacoustic Stimulation

Although preservation of residual hearing is desirable for all patients, it is critical for patients aiming to utilize a hybrid implant consisting of the combination of ipsilateral electrical and acoustic stimulation (EAS). This method stands in contrast to bimodal stimulation in which a CI user also wears a hearing aid on the contralateral ear. With EAS, low to mid-frequency information, where patients often have the greatest amount of residual hearing, is amplified with a hearing aid, transmitted acoustically and naturally encoded by the apical region of the cochlea, while high frequency information is transmitted electrically to the basal region of the cochlea via cochlear implant (Gantz, 2005) thus matching the tonotopic organization of the cochlea.

The combination of electrical and acoustic information plays a critical role in speech recognition in the presence of noise for some CI users (James, et al., 2006). Fraysse, et al. (2006), James (2005) and Gantz (2005) found that signal to noise ratios for speech recognition in multi-talker babble increased by 3-9 dB in the CI + ipsilateral hearing aid as compared to the CI alone condition. This translates to 30-40% increase in speech understanding as demonstrated by Eddington, et al. using the hearing in noise test (HINT) (House Ear Institute) sentence scores (1997). Moreover, CI users subjectively prefer the quality of sound with EAS. Those patients with a post-lingual onset of hearing loss often describe speech with a CI as sounding synthetic, mechanical, or "raspy." This complaint is likely due to the limited spectral resolution (the inability to reproduce the range of pitch perception present in normal hearing) available using a CI. Although limited pitch perception may not interfere with speech understanding in quiet, it is detrimental to the user when listening to speech in the presence of background noise which requires more acute pitch discrimination (Gantz, 2005).

Subjective improvement in the aesthetic quality of sound (James, 2006) using EAS is also encouraging as it relates to music appreciation with a CI. Gantz et al. (2005) found that EAS users were substantially more accurate than traditional CI users in melody recognition, pure tone frequency discrimination, as well as timbre ratings for low frequencies. In addition, the mean score for EAS users in an open-set test of familiar melody recognition was 80.1% correct (1 year post hook-up) as compared to the mean score for 27 traditional CI users of 30.7%. Ability to perceive the fundamental frequency via residual acoustic hearing may account for the difference in scores and in the ability to enjoy both familiar and novel music.

Scala Tympani Placement

Real world benefit and preservation of cochlear structures are optimized placement of the electrode array into the ST. Physiologically, insertion into the ST places the electrode contacts in close proximity to excitable neurons of interest; those in the osseous spiral lamina and the ganglion cells within Rosenthal's canal. Also, the ST is bounded by both the basilar membrane and osseous spiral lamina, offering a natural protective mechanism during insertion, while the scala vestibuli (SV) and the scala media (SM) are separated only by Reissner's membrane, a fragile two-celled layered structure. The significance of this may be appreciated when considering that even minor intracochlear trauma to the osseous spiral lamina during insertion has been shown to correlate with increased thresholds and a decrease in response selectivity (Wardrop, 2005). Finally, the lumen of the ST has a slightly larger diameter than that of the SV for increased accommodation of the array.

Clinically, word recognition may also be affected by array placement. Studies have suggested that insertion, or migration, of the array from the ST into the SV may be detrimental to speech comprehension. Skinner, et al. (2002) observed a significant negative correlation between consonant-nucleus-consonant (CNC) (Lehiste & Peterson, 1959) word scores and the number of electrodes in SV, as verified by pre- and post-operative CT images registered three dimensionally. Conversely, the highest scoring subjects had the greatest number of electrodes in the ST. Skinner stated, "This finding suggests that when electrodes are not in their intended position in the ST, their stimulation of surviving nerve fibers is associated with poorer word recognition than might have been possible if they had been in ST." Similarly, in 2008 Finley, et al. deduced that a significant portion of outcome variance in user performance on CNC word recognition was attributable to scalar position of the electrode array. When an electrode contact

lies in the SV, rather than the ST, the likelihood of cross-turn stimulation is increased. In this scenario, a contact lying equidistant between spiral ganglion neurons located at ascending turns within the cochlea, when stimulated, would excite ganglion cells at various critical bandwidths (Greenwood 1961), creating perceptual pitch cues that are confusing for the user (Finley, 2008). In Finley's 2008 study, statistical analysis revealed that a significant estimated improvement in CNC word recognition scores could be obtained with optimized scalar placement of the array in the ST.

Cochleostomy

A cochleostomy located adjacent to the anterior-inferior portion of the round window (RW) decreases the risk of inadvertent entry into the SM or the SV (Lenhardt, 2009), and sets the stage for subsequent surgical outcomes such as placement in the ST and preservation of the lateral wall and osseous spiral lamina (Finley 2008). Studies comparing locations have found that the highest rates of residual hearing preservation correspond to cochleostomy placement anterior-inferior to the RW, as opposed to entry through, or inferior to, the RW (Garcia-Ibanez, et al., 2008; Berrettini, 2008; Adunka, et al., 2007; Gantz, 2005). Finley, et al. (2008) observed in a group of fourteen subjects that in cases where the majority of contacts were located in SV, as verified by CT scan, that cochleostomy sites appeared to have been made too high along the lateral cochlear wall. They noted, "...cochleostomy placement antero-inferior to the RW annulus appears critical to consistent and desired placement in ST...."

Insertion Force

Components of force acting on the outer wall of the cochlea during array insertion include tension introduced by the surgeon, frictional force, relaxation force of the array, and adhesion forces (Todd, 2007). Combined, these forces exert pressure on the spiral ligament and in excess, may cause trauma. Implant manufacturers have attempted to remediate this issue in electrode array design and insertion techniques. For example, the "advance off stylet" (AOS) (Cochlear Corporation®, Sydney, Australia) is a technique in which the Nucleus 24 Contour Advance® electrode array is held in a straight position by an internal wire during insertion, until the point at which a white marker on the carrier site is aligned with the cochleostomy. The stylet is held in place while the array is advanced to its final intracochlear position where it resumes its preformed shape around the modiolus (Roland, 2005; Wardrop, 2005). In contrast, when the standard insertion technique (SIT), or partial withdrawal method, is performed with the Nucleus 24 Contour® the array is advanced into the cochlea while the stylet is held in place and withdrawn after full insertion (Todd, 2007). In 2005 Roland, et al. employed an Instron 5543 Universal Force Measurement System to quantify the force exerted on the intracochlear outer wall during CI electrode array insertion using both techniques. The measurements were made in cochlear models, and in formalin-fixed cadaveric temporal bones. Insertions using the AOS technique were made with fewer points of contact with the outer wall and significantly less force. Results were similar to those reported in other studies (Berettini, 2008; Todd, 2007; Stover, 2005). In their comparison of AOS and SIT, Todd, et al. (2007) noted a marked reduction in force application using the AOS technique, particularly at the basal turn, which historically has been the most vulnerable to insertion trauma (Biedron, 2010). They attributed the more desirable outcome to a combination of improved trajectory along the medial wall of the ST and an overall reduction in rigidity of the electrode.

Insertion Depth

Linear and angular insertion depth of the electrode array insertion have been suggested as variables that may correlate with hearing preservation and word recognition using a CI (Adunka, 2006; Gani, 2006; Finley, 2008). Therefore, a delicate balance between sufficient stimulation and conservation of cochlear structures must be struck. Linear insertion depth is length of insertion of the array in millimeters, and angular insertion depth represents degrees of rotation from a reference point, for example, the RW, vestibule or other anatomical landmark. Both may vary due to individual cochlear dimensions, and type of electrode array (Radeloff, 2008; Escude, 2006). However, some general guidelines have emerged. For example, advancing the array past the point of first resistance, which generally occurs between 17- 20 mm (Adunka, 2006) may cause rupture of the basilar membrane, fracture of the osseous spiral lamina and/or ligament, and buckling of the array (Adunka, 2006; James, 2005; Wardrop, 2005).

Over insertion of the array (past the point of first resistance) may result in insufficient stimulation of the basal region due to a void in electrodes. This results in diminished high frequency cues needed for speech understanding. Meanwhile, the risk of mechanical trauma increases with depth of insertion due to the anatomy of the cochlea and its limited ability to accommodate force as the radius of curvature increases and canal cross section area decreases as the apex is approached. Using human temporal bones Adunka et al. (2006) witnessed a positive relationship between insertion depth and cochlear trauma, particularly when the array was advanced past the point of first resistance which was, on average, reached at 20 mm.

Furthermore, over insertions are unnecessary as the region of the cochlea with the greatest density of spiral ganglion cells is the mid-portion of the basal turn (Nadol, 1988). A study by Ariyasu et al. (1989) which used computer-generated three-dimensional reconstructions of the organ of Corti, showed that spiral ganglion cells extend 1 ¾ turns along the organ of Corti and reach no higher than the middle of the second turn. Therefore, they concluded that electrode arrays need not be inserted beyond 1 ¾ turns.

Not only do deep insertions correlate with intra-cochlear damage, but they have also been associated with subjective reports of decreased sound quality, and poorer consonant and vowel identification (Gani, 2006). Electrical signals from CIs are faithful to the tonotopicity of the cochlea. Therefore, misalignment between the natural acoustic frequency regions of the cochlea (Greenwood, 1961) and the filter frequencies of the array result in unusable pitch percepts for the user, or "tonotopic warping" (Goupell, 2008; Faulkner, 2003). Misalignment may be a product of both surgical placement of the array and/or manipulation of frequency filters in CI mapping. In 1999 Fu, et al. examined the effects of both electrode location and filter bank spacing using SPEAK processing strategy (Cochlear Corporation®, Sydney, Australia), and concluded that, "... spectral cues, as represented by vowel recognition and consonantal place of articulation, were strongly affected by changes in electrode location and spacing. Both spectral and temporal phoneme cues were strongly affected by the degree of tonotopic warping, created by altering both the location and spacing of the activated electrodes."

Angular insertion depth

Xu, et al. (2000) asserted that angle of insertion depth may be a better reference for the position of the electrode array than linear insertion depth since variation in the distance between

the modiolus and the array is not a factor in the former metric. Similar to linear insertion depth, there appears to be a negative correlation between increased angular insertion depth and patient outcomes. Both James et al. (2005) and Fraysse et al. (2006) demonstrated that insertion depth angles exceeding 400° resulted in poorer preservation of residual hearing. Finley et al. (2008) found that angular insertion depths of select basal electrodes were significantly related to an increase in the number of electrodes migrating to SV, the demerits of which are aforementioned.

In 2006 Kos et al. reported the results of the withdrawal of electrode arrays that were deeply inserted in two patients with subjective reports of poor sound quality due to excessive low pitch sound, echoes, and poor word discrimination, despite sufficient adaptation time and fine tuning of their maps. After partial withdrawal of arrays, insertion angles decreased from 720° to 485° for one patient and from 675° to 433° for the second patient. Following partial withdrawal, word recognition scores improved for both patients, as did the subjective quality of sound. Both patients reported hearing more high frequency sounds and decreased echo. In their 2002 study on the relationship between word recognition scores and electrode array placement Skinner, et al. noted that the subject with the deepest angular insertion depth (655°), and no basal electrodes until 142°, obtained a low word recognition score of 24%. This score improved significantly when the 4 most apical electrodes were deactivated. Several other subjects without electrodes in the basal turn until greater than 90° (as a result of a deep insertion) also performed poorly on word recognition tasks, with the highest performing subject scoring less than 50%. Subjects in Gani's 2007 study received the Med-El Combi40+ CI that was designed to be deeply inserted to two full turns around the cochlea. Similar to results from Skinner's study, Gani et al. found that consonant and vowel identification performance increased for all five of their subjects when their three most apical electrodes were deactivated, as did the subjective quality of the sound.

For anatomical reasons, stimulation of overlapping populations of neurons is most likely to occur in the apex of the cochlea and induce deterioration of performance for CI users.

Existing studies on subjective and objective outcomes with overly deep CI insertions, while limited, seem to indicate a trend towards decreased performance as both linear and angular insertion depth extend beyond 20 mm and 400°.

Cochlear implant surgical techniques have evolved and contributed to the high levels of success realized by many current CI users. Critical assessment of the results of alterations of surgical techniques and electrode array design depend upon our ability to assess the position of the array in patients post-operatively. The use of CT and 3-D composite imaging to verify electrode position is critical to future advances in this field. CT scanning alone offers limited soft tissue information needed for the most accurate assessment. Our research group has created a technique to overcome this limitation, the merits of which have been demonstrated in previous studies which utilized highly detailed OPFOS and micro CT images for verification (Skinner, 2002). By replicating the surgical process in fresh, unfixed cadavers and affirming the position of the arrays by micro CT and histological analysis we endeavor to analyze the correspondence of our clinical CT analysis and the *in vivo* position of implanted arrays.

Methods

Six fresh cadaver heads underwent CT scanning first using the Siemens Volume Zoom® (Siemens Medical Solutions, Forchheim, Germany). The Volume Zoom® has four detector rows with the smallest detectors being 0.5 mm and can yield reconstructed images with voxel edge lengths of 100 µm. Although the Volume Zoom® machine is still in use, it is likely to be replaced in the future with the Siemens Sensation® as technology advances. For this reason,

images were obtained using both of these scanners. The heads were then scanned using the Siemens Sensation® which has 64 detector rows, the smallest detectors being $0.6 \, \text{mm}$, and can also reconstruct images at $100 \, \mu \text{m}$ voxels. In the pre-operative condition, heads were tilted backwards to obtain images in a modified Stenver's angle. Heads were positioned such that the scan plane was parallel to a line that traversed the inferior orbital rim and petrous apex, and were secured in place using surgical tape.

All surgeries were performed by two experienced otologists, Drs Richard Chole and Timothy Hullar of the department of otolaryngology at Washington University. Six ears were implanted with a straight array, and six ears were implanted with a contoured array. A standard trans-mastoid facial recess approach was used for all specimens under direct microscopic guidance. While "soft surgeries" were performed in some specimens, in some specimens, intentional trauma was introduced in order to produce varied outcomes. For example, in some specimens the array was inserted beyond the point of first resistance. The electrode arrays were cut approximately one inch outside the cochleostomy and were fixed with polyurethane adhesive (Gorilla Glue, Cincinnati, OH). Incision flaps were sutured and heads underwent post operative CT scanning. In the post-operative condition, heads were positioned with chins tilted downward to mimic clinical positioning that avoids having the receiver-stimulator in the scan plane. Great care was taken to avoid air trapped within the calvarium; when necessary, water was injected under the flaps to avoid this. Temporal bones were subsequently removed from the heads and reduced in size with an otologic drill (Anspach Effort®, Palm Beach Gardens, FL) to a core approximately five cm in diameter and ten cm in length. Despite care taken not to disrupt the implanted arrays, the array became dislodged in one specimen and the otic capsule was damaged in another. These two specimens were excluded from further analysis. The remaining specimens were fixed in formalin.

Micro-CT scanning of all temporal bones was performed with a Scanco μCT 40 (Scanco Medical AG, Basserdorf, Switzerland) to create images with higher spatial resolution and reduced metal artifact bloom, as compared to clinical scans. Reconstructed voxel resolution size of 18 μm is possible with micro-CT as opposed to 100 μm for the Sensation and Volume Zoom.

Labyrinths were dehydrated in a graded series of alcohols (50, 70, and 100%). Six bones were embedded with methamethacrylate (MMA; Osteo-Bed; Polysciences, Inc.) and four were embedded with LR White Hard Resin (London Resin Co; London, England). Standard infiltration protocol was used for MMA embedding. The specimens were infiltrated with 1.4 grams of benzoyl peroxide (catalyst) to 100 ml of Osteo-Bed and were refrigerated for two weeks. 3.5 grams of benzoyl peroxide to 100 ml of Osteo-Bed was added to harden the material. Glass containers were placed in a 37° C water bath for 48 hours. Containers were moved to a freezer for 45 minutes and consequently broken out of the glass. Following dehydration labyrinths embedded with resin infiltrated using a vacuum to extract all air. Resin filled molds were then accelerator cured for 24 hours.

Following embedding procedures labyrinths were further trimmed to approximately one inch in diameter and 2.5 inches in length and the resulting blocks were sectioned using a Buehler IsoMet (Beuhler; Lake Bluff, IL) low speed diamond circular saw using a 5 inch wafering blade by the same manufacturer. Blocks were aligned so that the modiolus was parallel to the plane of the saw blade. Sections were spaced approximately 500-600 µm thickness, including the kerf of the saw (200 µm). Sections were fixed onto slides, without staining. Slides were viewed using an Olympus BH2-RFCA (1.25x) microscope (Olympus America, Inc; Center Valley, PA).

Images were obtained with a Sony DKC-5000 (Sony Electronics, Inc; San Diego, CA) digital camera and were aesthetically retouched using Photoshop CS to better display histology.

Slides were analyzed independently by the author and two otologists to ascertain the degree of accuracy with which the CT model predicts the scalar location of the electrode array. A form was created to document the mid-modiolar degrees around the cochlea for pertinent slides, and to record scalar placement of the array for each individual slide (Figure 1). Researchers who analyzed the histology were blinded to all images including the 3-D composites, pre-, post-operative, and micro CT scans. The researcher who rendered the images was blinded to the histological analysis and judged scalar placement using the 3-D CT composite technique alone.

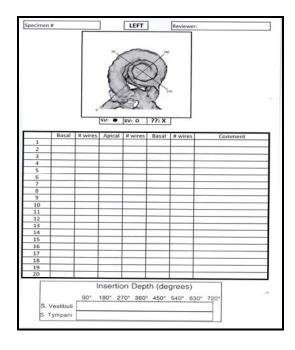


Figure 1: Reviewer's form for histological analysis

Results

The intracochlear electrode position was determinable by CT analysis in all bones, and was judged as residing in the ST, the SV, or the SM. During histology analysis the authors observed that the electrode array in four bones had originally been inserted into the ST but was residing in the region of the SM. For example, in Figures 5-6 the electrode in the apical turn is in contact with the lateral cochlear wall, displacing the basilar membrane superiorly. This led to the creation of a third category to document not only the scalar placement of the array, but also its interaction with the basilar membrane.

The CT technique gives a volume based on registration of pre and post-operative CT imaging. Using histology we are able to ascertain within two dimensions (2D) where individual electrodes are positioned and how they interact with soft tissue structures within the cochlea. However, for us to validate the CT registration method a comparison between 3-D images must be made. Therefore, a 3-D composite image using high resolution micro CT imaging was performed and revealed a high degree of accuracy and correlation of electrode position with the clinical CT analysis. Figures 2 and 3 show a 2D slice from each of the post operative CT volumes of cochlea 255 (left) and how the electrode array segment in this slice was marked. Figure 4 shows the same 2D slice in the pre operative CT volume with the 3D objects marking the array position translated from the two post operative CTs. It clearly shows the position of the electrode markers from the clinical CT analysis to lie within the array outline from the micro CT. This level of agreement was seen in all the samples, with the exception of one in which there appeared to have been movement of the array. This likely happened after the head underwent clinical CT scanning, during the temporal bone removal and drill down process to allow the bone to fit into the micro CT specimen holder. For the 214 electrodes in all samples, only 14

electrodes as marked by the clinical CT analysis were found to be more than 50% outside the boundary marked by the micro CT. If the sample with the suspected array movement were to be excluded, the number of electrodes outside the 50% criteria would decrease to four out of 198 electrodes.

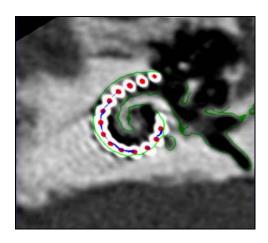


Figure 2: Post operative clinical CT scan of cochlea 255 L. The green line represents the outline of the cochlear wall, as identified by the preoperative clinical scan. The red dots identify the centroid of the metal artifact bloom generated by the electrode contacts in this section of the array.

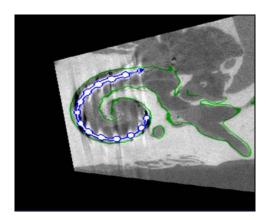


Figure 3: Post operative micro CT scan of cochlea 255 L. The green line represents the outline of the cochlear wall, as identified by the preoperative clinical scan. The dark blue line represents the outline of this segment of the electrode array.

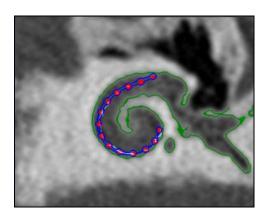


Figure 4: Pre-operative clinical CT scan of cochlea 255 L. The green line represents the outline of the cochlear wall. The red and dark blue objects are translated from the post operative clinical and micro CT volumes respectively and mark the position of the array segment in this slice.

261 L	Histology	Histology	Histology	CT Technique	CT Technique	CT	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Technique	
						Basal	
4	T	T		T	T		100%
5	T	M(T)		T	M		100%
				_			
6	T	M(T)	M(T)	T	M		67%
	_	1.1 (1)		_			
7	T	M(T)	M(T)	T	M		67%
/	_			1	141		0770
8	T	M(T)	M	T	NA		67%
o	L	M(T)	IVI	T	M		07%
			T. C. C. D.	 			6501
9	I	M(V)	M(V)	T	M		67%

Table 1: Histology and clinical CT correlation for a left, resin embedded cochlea.

261 R	Histology	Histology	Histology	CT Technique	CT Technique	CT	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Technique	
						Basal	
1	T	T		T	T		100%
2	T	T		T	T		100%
3	T	T		T	T		100%
4	T	M (T)		T	T		100%
5	T	M (V)		T	M		100%

Table 2: Histology and clinical CT correlation for a right, resin embedded cochlea.

255 L	Histology	Histology	Histology	CT Technique	CT Technique	CT Technique	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Basal	
3	M	M (T)		T	M		100%
5	M (T)	M (T)		T	M		100%
6	M (T)	T	M (T)	T	M		67%
7	M (T)	M (T)	M (T)	T	M		67%
8	M(T)	M (T)	M (T)	T	M	M	100%
9	M(T)	M(T)	M (T)	T	M	M	100%

Table 3: Histology and clinical CT correlation for a left, resin embedded cochlea.

255 R	Histology	Histology	Histology	CT Technique	CT Technique	CT	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Technique	
						Basal	
2	T	M(T)		T	T T		100%
	_			_	_		
3	M(T)	M(T)		T	T		100%
				_	_		
4	M(T)	M(T)		T	T		100%
	(-)	(-)		_	_		10070
6	M(V)	T		T	T		50%
0	IVI(V)	-		1	<u> </u>		3070
7	T 7			<u></u>	T.		00/
/	V			I	T		0%

Table 4: Histology and clinical CT correlation for a right, resin embedded cochlea.

108 L	Histology	Histology	Histology	CT Technique	CT Technique	CT Technique	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Basal	
2	T	T		T			50%
	_	•		_			
5	T	V	V	T	M	V	67%
	_	_	_	_		_	
6	T	V	V	T	V	V	100%
	_	_	_		_	_	
7	T	V	V	T	V	V	100%
	_	_	_	_			

Table 5: Histology and clinical CT correlation for a left, MMA embedded cochlea.

108 R	Histology	Histology	Histology	CT Technique	CT Technique	CT Technique	Agreement
Histology Section	Basal	Apical	Basal	Basal	Apical	Basal	
6	T	T		T	M		50%
8	T	V	V	T	M	V	67%
	_	_	_				
9	T	V	V	T	M	V	67%
	_	_	_				
10	T	V	V	T	M	V	67%
		_	•	*		•	0770

Table 6: Histology and clinical CT correlation for a right, MMA embedded cochlea.

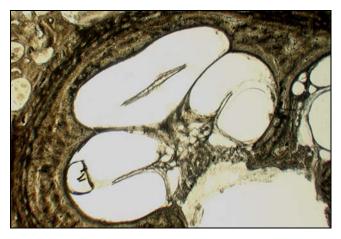


Figure 5: Apical view of midmodiolar section. The electrode has displaced the basilar membrane upward.

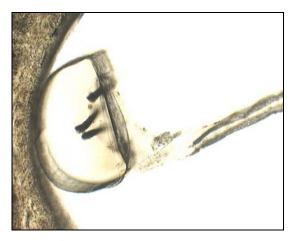


Figure 6: Close view of apical electrode from Figure 6.

Analysis for specimens embedded with MMA (Tables 5-6) was adapted for swelling artifact that obscured electrode placement. Due to the degree of swelling, histological analyses of these cochleae were more subjective. In most cases, displacement of the basilar membrane by individual electrodes was used to judge the originally inserted position of the array (Figure 7). In some instances it was impossible to determine the original electrode position (Figure 8).

Additionally, swelling artifact affected the validity of the CT analysis due to the morphological displacement of the array, which altered linear insertion depth, as well as judgments regarding scalar placement.



Figure 7: Example of swelling artifact seen with polymethamethacrylate embedding material in the basilar turn of a midmodiolar section. The basilar membrane is displaced superiorly therefore the researchers concluded that its original position was the ST.



Figure 8: Example of swelling artifact seen with polymethamethacrylate embedding material in the basilar turn of a midmodiolar section. Original position of the electrode is indeterminable.

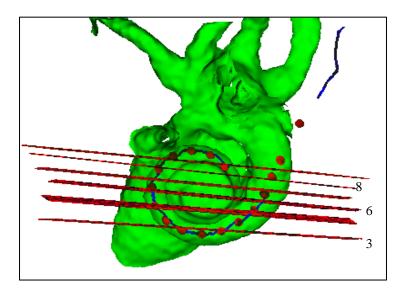


Figure 9: 3-D rendering of boundary between soft tissue and bone from the preoperative cochlea. The electrode array object from the post operative clinical CT scan has been imported. Red dots represent the center of each electrode. The blue line represents lead wires of the array. Location of histology sections 3, 6, and 8 are identified.

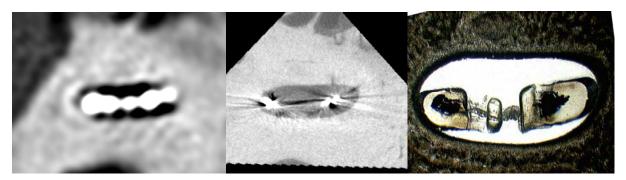


Figure 10: Left cochlea clinical and micro CT images with corresponding histology image #3.



Figure 11: Left cochlea clinical and micro CT images with corresponding histology image #6.

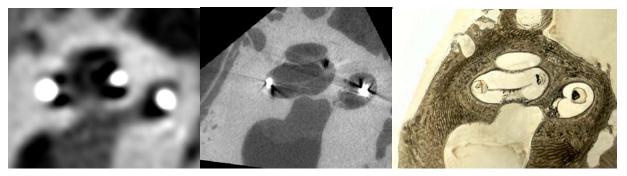


Figure 12: Left cochlear clinical and micro CT images with corresponding histology image #8.

Discussion

A. Effects of embedding material

Unexpectedly, we found a significant degree of swelling artifact in bones embedded with polymethamethacrylate, which was a confounding variable in the analysis of six bones. To our knowledge, the only report of swelling artifact seen with methamethacrylate is Adunka, 2006. In the majority of these cases, the original placement of the array could be deduced by scrutinizing the ruptured basilar membrane (Figure 7). However, in cases where swelling was excessive (Figure 8) the position of the array became significantly displaced, which decreased validity of results. Since there was no array swelling in the L.R. White embedded cochleae, this technique resulted in significantly fewer artifacts.

B. Imaging and Histological Correlation

Surgical technique and resulting position of the electrode array are principal factors in the avoidance of intracochlear trauma, preservation of residual hearing, and optimization of clinical outcomes for CI patients (Friedland, 2009; James, 2005; Skinner, 2007; Kiefer, 2004; Skinner, 2002). The purpose of this study was to determine the degree of accuracy

with which a patient's CI electrode image, based on clinical CT scans, predicts the in vivo position of the array. Information derived from the technique may assist in studying effects of electrical stimulation, as it relates to the *in vivo* array position. We found that histological analyses highly correlated with imaging techniques in identification of scalar placement, as well as distinguishing where the array transitioned from ST to SV. Results from MMA embedded bones were convoluted by swelling artifact. However, bones embedded with resin yielded illustrative corroboration between the CT technique, micro CT, and histology images. For example, in specimen 255 (left cochlea) the transition of the CI array from the ST to the SV agrees with the CT imaging technique (Table 1; Figures 9-12). As with all cadaveric studies, a limiting factor in the present study is the lack of cellular repair mechanisms and tissue perfusion seen in the living cochlea. Future studies may consider increasing both the sample size and number of arrays from various manufacturers. Considering the high number of electrodes observed to be residing in the region of the SM, investigation as to how the array interacts with the soft tissue structures of the cochlea, and its effects on clinical outcomes is warranted. How the array stimulates spiral ganglion elements while in this medio-lateral position may be of particular interest.

Conclusion

Information obtained using our CT method (Skinner, et al 2007) provides valuable insight into the efficacy of surgical techniques and has proven particularly useful for optimizing patient performance in conjunction with fine tuning of the CI processor, or when deciphering subjective percepts of CI users (Whiting, 2008). Furthermore, CT imaging is a viable tool that

can easily be incorporated into the management of cochlear implant recipients (Xu, 2000; Whiting, 2008). The results of this study suggest that a composite, 3-D image using a patient's pre and post-operative CT scan images accurately portrays the position of the electrode array as determined by micro CT scanning and histology.

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