Evaluating and Improving Cochlear Length Measurements on Clinical Computed Tomography Images

John E. Iyaniwura
The University of Western Ontario

Supervisor
Dr. Hanif M. Ladak
The University of Western Ontario

Joint Supervisor
Dr. Sumit K. Agrawal
The University of Western Ontario

Graduate Program in Biomedical Engineering

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Abstract

Cochlear implants provide the sensation of sound to deaf individuals. An accurate estimate of cochlear duct length (CDL) is required for pre-operative implant electrode selection and can be obtained from clinical computed tomography (CT) by measuring the “A-value”.

The objectives of this work were to estimate the accuracy and variability in manual A-value measurements, and to automate measurements.

Four specialists repeatedly measured the A-value on clinical CT images from which the inter- and intra-observer variability were calculated. Accuracy was assessed by comparison to measurements on higher resolution micro-CT images. Motivated by this study, software was developed to automate the A-value measurement by registering an annotated atlas to unlabelled images.

There was significant variability in manual A-value measurements made using either standard clinical or multi-planar reformatted views with the latter exhibiting higher variability but better accuracy. The automated approach eliminated variability and improved accuracy, enabling the correct selection of electrode length.

Keywords: Cochlear implant, cochlear duct length, A-value, intra-observer variability, inter-observer variability, accuracy, computed tomography, image registration
Co-Authorship

This master’s thesis is an integration of two articles, both of which formulate a chapter each. The first article, Chapter 2, is currently published in the Journal of Otology & Neurotology and the second article, Chapter 3, is submitted and currently under review by the Journal of Otolaryngology – Head & Neck Surgery.


The initial motivation prompting this study was presented by S. K. Agrawal and H. M Ladak. My contributions were to the development of the study procedure under the guidance of S. Riyahi-Alam, S. K. Agrawal and and H. M Ladak and to the implementation of the study and data analysis with guidance from Y. Bureau and M. Elfarnawany. I prepared the initial draft of the manuscript, which was edited by S. K. Agrawal and M. Elfarnawany and reviewed by all authors. L. S. Parnes, Z. Kassam, and M. Sharma were specialists who took part in the study. H. M Ladak and S. K. Agrawal were primary supervisors.

**Chapter 3:** Iyaniwura JE, Elfarnawany M, Ladak HM, Agrawal SK. An automated A-value Measurement Tool for Accurate Cochlear Duct Length Estimation. was submitted to *J Otolaryngol Head Neck Surg* on June 13, 2017, and is currently under revision.

My contribution to this study was to the development of the registration algorithm, under guidance of H. M Ladak and M. Elfarnawany, and the analysis of all data generated from testing the algorithm. I prepared the initial draft of the manuscript which was edited by S. K. Agrawal and M. Elfarnawany and reviewed by all authors. H. M Ladak and S. K. Agrawal were primary supervisors.
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List of Abbreviations

2D Two Dimensional
3D Three Dimensional
ANOVA Analysis of Variance
APD Auditory Processing Disorders
CDL Cochlear Duct Length
CHL Conductive Hearing Loss
CI Cochlear Implants
CT Computed Tomography
DOF Degree of Freedom
FFD Free Form Deformation
ICC Intra-class Correlation coefficient
micro-CT Micro Computed Tomography
MPR Multi-Planar Reconstructed
MSE Mean-Squared Error
NCC Normalized Cross Correlation
NMSE Normalized Mean-Squared Error
OC Organ of Corti
SM Scala Media
SNHL Sensorineural Hearing Loss
ST Scala Tympani
SV Scala Vestibuli
TM Tympanic Membrane
Chapter 1: Introduction

Hearing loss is considered the third most common chronic medical condition with adults over the age of sixty-five, preceded only by arthritis and hypertension [1, 2]. Reduced speech comprehension from hearing loss has significant ramifications, from social isolation to depression which can then subsequently progress to an overall general decline in health [2–4]. Cochlear implants are currently the most prevalent invasive intervention for individuals who are profoundly deaf or hard of hearing [2, 5]. Candidates for cochlear implants exhibit sensory deafness, whereby their lack of sense of sound is due to the reduced functionality of their cochlea, the end organ of hearing [5, 6]. As of 2012, approximately 324,200 registered cochlear implants have been implanted worldwide [7].

Furthermore, children, either from infancy or in their earlier years, are also reported to suffer from hearing loss in significant amounts. MED-EL GmbH (Innsbruck, Austria), in 2013, reported approximately 50,000 cochlear implants are manufactured yearly, far below the predicted demand of 130,000 required for children alone. This translates to approximately 1-3 newborns per thousand requiring cochlear implants for their type of hearing loss [8]. Current worldwide data shows an increase in demand for cochlear implants for both the child and adult populations, especially with the aging baby boomer generation beginning to experience age-related hearing loss [9–12]. With the increase in use of cochlear implants, there has been a renewed research interest in the cochlea [13–15]. This research has allowed for both the improvement of the implantation process and the advancement of the technology. However, there is still a need for further improvement of surgical guidance for cochlear implants.
1.1 The Auditory System

The human auditory system is conceptually divided into four compartments: the outer, middle, and inner ear and the central auditory nervous system; the first three compartments are illustrated in Figure 1.1.

![Diagram of the human auditory system](image)

**Figure 1.1**: First three compartments of the human auditory system (Image courtesy of MED-EL GmbH)

1.1.1 The Outer and Middle Ear

The outer ear is the point of contact for incoming sound waves. The primary structures of the outer ear are the pinna and the ear canal leading to the tympanic membrane (TM), commonly known as the eardrum. Incoming sound waves are focused towards the
ear canal by the pinna. Once in the ear canal, sound waves within frequency range of approximately 1.5 kHz to 7 Khz are amplified by a factor of 10 to 15 dB [16]. The amplified sound waves collide with the TM, stimulating its vibration. TM vibrations are transferred to the middle ear through anatomical connections. The middle ear consists primarily of a chain of three bones or ossicles: the malleus, the incus and the stapes (Figure 1.2). The vibration of the TM triggers the movement of these bones. The primary function of the middle ear ossicular chain is to provide an efficient means of delivering sound waves into the inner ear.

![Figure 1.2: Middle-ear structures (TM: Tympanic Membrane or eardrum) (Image courtesy of MED-EL GmbH)](image)

1.1.2 Inner Ear

The third compartment of the auditory system is the inner ear, which is divided into three parts: semicircular canals, vestibule, and the cochlea.
1.1.2.1 Cochlear Anatomy

The major inner ear structure of interest pertaining to sound is the cochlea, a fluid-filled snail-like structure. A normal cochlea, as illustrated in Figure 1.3, has two full turns (basal and middle), and an apical turn, in addition to two openings, the round and oval windows.

![Cochlea Diagram](image)

**Figure 1.3:** The cochlea and its openings (Image courtesy of MED-EL GmbH)

There are three ducts (scalae) within the cochlear canal as depicted in Figure 1.4. The round window, enclosed by a thin membrane, is the entrance to the lower duct called the scala tympani (ST). The oval window, covered by the stapes footplate, is the entrance to the upper duct called the scala vestibuli (SV). Both ducts, ST and SV, are separated by the scala media (SM), which spans the length of the cochlea, barring a small section towards the apex of the cochlea called the helicotrema. The SM is enclosed on the bottom by the basilar membrane, on which rests the organ of Corti (OC), and on the top by the Reissner’s membrane. The OC itself, is populated by microscopic “hair cells” (sensory receptors) which are an important component of the hearing process [16].
1.1.2.2 Cochlear Physiology

The mechanical movement of the ossicular chain in the middle ear is translated to the cochlea by way of the stapes footplate which is connected to the oval window. The vibration of the oval window membrane by the stapes transmits a pressure wave, which in turn induces the movement of fluids within the cochlear ducts and consequently the bending of the hair cells located in the OC. The hair cells serve as transducers, essentially converting their mechanical movement to electrochemical signals, generating nerve impulses, which are then propagated along the auditory nerve and then to the brain [16, 17]. The hair cells in the OC, along the basilar membrane, map frequencies within the human hearing range, approximately 20 Hz to 20 kHz [16]. Higher frequencies are
stimulated around the lower turns of the cochlea (basal and middle turns) and lower frequencies are stimulated towards the apex [17], as illustrated in Figure 1.5.

![Figure 1.5: Frequency response of the human cochlea (Image courtesy of MED-EL)](image)

### 1.2 Hearing Loss

Hearing loss results from the reduced functionality of the auditory system. Such reduction can occur due to prolonged exposure to high levels of sound, consumption of drugs and chemicals detrimental to the auditory structures, aging, diseases and infection, personal injuries, or hereditary traits [18, 19]. There are four types of hearing loss, auditory processing disorders (APD), conductive hearing loss, sensorineural hearing loss, and mixed hearing loss. APD are difficult to diagnose, however they are attributed to the brain’s inability to properly interpret auditory information [20–22]. Conductive hearing loss (CHL) stems from any impediment in the outer or middle ear, hindering the transmission of sound to the cochlea. Sensorineural hearing loss (SNHL) is commonly due to degraded
functionality of the cochlea [23]. Mixed hearing loss is attributed to a combination of both CHL and SNHL.

### 1.2.1 Sensorineural Hearing Loss (SNHL)

Significant loss of the hair cells in the cochlea can result in individuals becoming profoundly deaf or hard of hearing [16]. SNHL is commonly attributed to poor performance of the hair cells within cochlea which subsequently results in the inefficient transmission of nerve impulses to the brain. Among other factors, the hair cells within the cochlea are the most susceptible to damage as a result of overstimulation by sound, aging or hereditary circumstances [16, 23].

### 1.3 Cochlear Implants

Cochlear implants (CI) are surgically implanted medical devices that are used to restore the sense of sound to individuals suffering from SNHL. They are composed of two parts, an external and internal portion as illustrated in Figure 1.6.
1.3.1 Functionality

The external portion of a CI is composed of a microphone/processor and a transmitter. The microphone receives and amplifies surrounding sounds which are in turn processed by the processor in order to isolate sound frequencies of interest. Typical frequencies pertaining to human audible speech are prioritized. The transmitter receives the processed signal from the processor and transmits the signal to the internal portion of the implant, in addition to supplying power to the internal portion, through electromagnetic induction. The internal portion of the implant consists of a receiver and an electrode array. The receiver converts the received signal from the transmitter to electrical impulses corresponding to the frequency of the signal. The electrode array is inserted in the cochlea and is stimulated by the receiver to inject current into the cochlea. The current is injected
at specific locations along the electrode based on the frequencies contained in the sound and through this, the signal/sound subsequently reaches the brain [7, 24–26].

### 1.3.2 Electrode Selection

An important preoperative step of CI surgeries is the selection of the electrode array length. This selection is dependent on the cochlear duct length (CDL), defined as the distance from the round window to the helicotrema along the spiral shape of the cochlea. Accurate estimation of the CDL allows for deeper insertion of the electrode, while avoiding surgical trauma or complication from incomplete insertions [27, 28]. Deeper electrode insertion allows for stimulation of lower frequencies in the cochlea. Significant benefits of lower frequency stimulation include tonal language discrimination, improved musical appreciation and an overall improvement in hearing outcomes [29, 30]. Postoperatively, the electrodes in the electrode array are mapped to the expected frequencies within the cochlea based on the CDL. With deeper insertions of the electrode array the lower frequency tonotopical regions of the cochlea can be stimulated allowing for the creation of improved patient-specific frequency maps [27, 31].

### 1.3.3 Frequency Mapping

As briefly alluded to in Section 1.3.2, an important postoperative step of CI surgeries is the generation of frequency maps, which is the mapping of frequencies to the electrode array that is inserted in the cochlea. This is required post-operatively to adequately program the inserted electrode array to include the possible range of frequencies of the patient’s particular cochlea [32–34]. The programming of frequencies is aided by the Greenwood
Equation; an equation used to help determine the distribution of frequencies along the CDL of a given cochlea [35, 36]. Therefore, inaccurate CDL estimates can generate poor frequency maps, leading to a less than desirable outcome for the CI user. In addition, deeper insertions allow for improved frequency mapping which facilitates a more natural tonotopical distribution of electrodes along the cochlea [28].

1.4 Measuring Cochlear Duct Length

The literature reports significant variability in the length of human cochleae [13]. The first measurements of human cochleae date as far back as the late 1800s [13]; however, pivotal work by Hardy in 1938 cataloged CDL variability with ranges from 25 to 35 mm [37]. Others studies measured CDL at approximately 46 mm [38]. Early measurements of the CDL were carried out through histological examinations, but with the dawn of computed tomography (CT), CDLs have been measured radiographically and with 3-dimensional (3D) models developed from medical images [13, 37, 39–41].

Histology-based CDL measurement is not clinical feasible for patient-specific surgical planning. Although 3D modeling from medical images could offer the possibility of robust and automated methods that can fit the surgical workflow, such methods have yet to be validated. From a clinical perspective, a simple approach that is gaining some traction is that proposed by Escudé et al., who expressed the relationship between CDL and a single measurement, the “A-value”, which can easily be measured by surgeons using two dimensional (2D) CT images of the cochlea [42]. Equation 1 expresses this relationship whereby A is the measured A-value and CDL the estimated cochlear duct length.
The A-value, as seen in Figure 1.7, is defined as the Euclidean distance of a straight line drawn from the round window passing through the apex at the modiolar axis to the furthest point on the contralateral wall in the basal turn [40].

Building on Escudé et al., Alexiades et al. [43] developed equations estimating the CDL using the A-value and linear regression techniques. In the literature, the CDL is commonly measured along the lateral wall or along the OC of the cochlea [13]; however, the electrode typically falls in between both locations. Therefore, Alexiades et al. [43], estimated the CDL along the lateral wall, along the OC, and along the expected electrode insertion point of the cochlea, as illustrated in the cross sectional image of the cochlea in Figure 1.8 [43].
Currently, A-values are measured manually by surgeons which introduces a potential for bias as well as intra- and inter-observer variability. A single attempt has been made to use image techniques to automate measurements of the cochlea [44]; however, this attempt was performed on low resolution images, synthetic data, and its robustness was not clear. It did however demonstrate the use of image registration techniques to calculate lengths of anatomical structures within the inner ear through the transfer of expert placed landmarks to a target image. In this thesis a similar technique using atlas image registration and the transfer of expertly placed landmarks on high resolution images and non-synthetic data was developed for the automatic measurement of the A-value. An automatic method would eliminate observer variability, improving the consistency of the A-value measurement. Since the method developed in this thesis utilized image registration, an overview of registration is given in the following section.
1.5 Image Registration

Image registration refers to the alignment, or mapping, of two or more images into a common spatial region. The images being registered are mapped to one another based on a common relationship. One popular relationship that is utilized is based on the respective intensity values of the images. Registration algorithms based on intensity relationships can be cast as an optimization task [45, 46]. A typical intensity-based image registration algorithm is illustrated in Figure 1.9.

![Image Registration Diagram](image.png)

**Figure 1.9**: Generic intensity-based image registration algorithm

In order to successfully register two images, a typical registration algorithm contains the components listed in Figure 1.9, whereby the goal is to register the moving image \((I_m)\) to the target image \((I_{targ})\). A transform \(T\) is applied on \(I_m\), to register it to
After the transformation occurs, the transformed image \((I_e)\) is compared to \(I_{targ}\) using an objective function \((O)\). The objective function computes a value which indicates how accurately the two images are registered. If the computed value is greater than a user-defined threshold, \(\epsilon\), an optimization technique is used to update the transform towards the direction of an ideal situation. This process is repeated by the optimizer until a transformation which produces an objective function value below \(\epsilon\) is reached; indicating a successful registration, i.e., optimal overlap of the two images. Therefore, three important factors that are considered in an image registration algorithm are the transform type, objective function, and the optimization mechanism [46, 47].

### 1.5.1 Transformation Type

Transforms are used to align the moving image to the target image, and these transforms are divided into two categories: linear and non-linear.

#### 1.5.1.1 Linear Registration

Linear registration techniques use linear transformations to align images. Linear registration can be separated into two categories, rigid and affine registration. Rigid registration attempts to register two images by addressing any differences in translation and rotation (Figure 1.10a).
Figure 1.10: (a) Rigid registration addressing translation and rotation differences (b) and affine registration addressing translation, rotation, scaling, and shearing differences

It is considered the simplest useful form of registration and for 3-dimensional (3D) images it provides 6 degrees of freedom (DOF): translation along $x, y, z$ and rotation about the $x, y, z$ axes.

Although rigid registration provides the simplest transformation, a more robust linear transformation can be achieved with affine registration. Affine registration attempts to register two images by addressing differences in translation, rotation, scaling and shearing, in $x, y, z$, therefore providing 12 DOF for 3D images. Figure 1.10b provides a 2D representation of affine registration. However, linear registration is limited because it can only capture global differences between images, but not local differences in shape [47, 48].

1.5.1.2 Non-Linear Registration

Non-linear registration techniques use transformations that permit image deformation. The deformable characteristics allows for local differences between images to be accounted for. Free-form deformation (FFD) registration is a type of non-linear
registration that allows for local deformation of images through the manipulation of a mesh of control points (Figure 1.11) [49].

![Figure 1.11](image.png)

**Figure 1.11:** Non-linear deformable registration, allowing for local deformation of the moving image to register to target image.

The number of control points determine the DOF. For example, a $4 \times 4 \times 4$ neighbouring mesh of control points in 3D, translates to a DOF of 64.

In FFD registration, after the movement of the control points, the corresponding movement of the image’s intensity values must be interpolated. B-spline registration is a type of FFD registration that uses B-spline functions to interpolate image intensity values after the movement of the respective control points [50, 51]. FFD registration has two noteworthy challenges: long computation times due to high DOF, and the potential for unnatural deformations in the final image. Therefore, the mesh and registration parameters must be carefully selected to allow for realistic registration results and an optimal computation time [52, 53].
1.5.2 Objective Function

The objective function provides a numerical score on the degree of overlap of the moving and target images. Commonly used objective functions measure either the similarity or dissimilarity between the intensity values of images, and are either maximized (if measuring similarity) or minimized (if measuring dissimilarity) to determine the optimal transformation that produces the best overlap.

When the intensity values between the images are similar, or are linearly related, with zero mean Gaussian noise, the mean-squared error (MSE) in the intensity values can be used as a dissimilarity measure. Equation 2 shows how the MSE is calculated between images $I_1$ and $I_2$, where $N$ is the number of pixels per voxels and $I_1(x, y)$ and $I_2(x, y)$ are the intensity values at location $(x, y)$ for each respective image:

$$MSE(I_1, I_2) = \frac{1}{N} \sum_{x} \sum_{y} (I_1(x, y) - I_2(x, y))^2$$  \hspace{1cm} \text{Equation 2}

The ideal (and minimal) value for MSE is zero when there is perfect overlap and the two images are identical with no noise. In practice, the presence of noise, artifacts, and structural differences in the images result in an ideal overlap not being achievable and rather the transformation that minimizes the objective function is accepted.

If there is still a linear relation between intensity values in the moving and target images, normalized mean-squared error (NMSE) can be employed; however, normalized cross correlation (NCC) is often preferred due to its steeper gradient that allows for faster convergence, compared to NMSE [47]. NCC is computed using Equation 3 where $\sigma_1$ and
\( \sigma_2 \) are the standard deviation of the intensity values in \( I_1(x, y) \) and \( I_2(x, y) \), respectively, and \( I_1 \) and \( I_2 \) are the mean intensity of \( I_1 \) and \( I_2 \) respectively. NCC is a measure of similarity that is maximized to an ideal value of one.

\[
NCC(I_1, I_2) = \frac{1}{N-1} \sum_x \sum_y \frac{(I_1(x, y) - \bar{I_1})(I_2(x, y) - \bar{I_2})}{\sigma_1 \sigma_2} \quad \text{Equation 3}
\]

Mutual information, which is based on Shannon entropy, is used as a stochastic approach for deriving an objective function if the corresponding intensities of the two images are not linearly related [50]. In practice, intra-modality images typically exhibit a linear relationship while inter-modality images do not [47]. For this thesis work, all images were CT and therefore mutual information was not considered as an objective function. Instead NCC was used because the CT images that were registered were of different resolutions and therefore a zero mean Gaussian noise was not expected. In addition, its steeper gradient, compared to NMSE, NCC allowed for quicker convergence.

1.5.3 Optimization

To iteratively solve for the optimal solution (maximal overlap of the two images) as defined by the objective function, an optimizer is required. The optimizer estimates the objective function value at the current location of \( I_m \) and compares it to its previous location (or the initial location if the optimizer is on its first iteration) to decide a better value for the transformation. Gradient ascent and descent are common simple optimizers and are used to find local maxima and minima of an objective function, respectively [47,
This optimizer takes a step in the direction of the gradient until the best local solution is reached or the user defined iteration limit is reached.

The challenge with optimization is ensuring that a global optimum is reached. Typically, in the initialization process, the amount of initial overlap between the moving and target images is maximized before running the registration algorithm. This increases the likelihood of the gradient optimizer reaching a local optimum that is indeed the global optimum [47, 55, 56]. For this thesis work, a gradient ascent optimizer was maximized in order to achieve the optimal overlap of the images and a hierarchical approach was used for the step sizes.

1.5.4 Atlas-Based Measurements

Atlas-based approaches are often used in image analysis and require a registration framework [57]. As noted before, an atlas-based approach has been used previously to estimate cochlear dimensions [44]. In this thesis, an atlas consisting of an exemplar image is annotated with points that define dimensions of interest. The atlas forms the moving image and is mapped to a target image on which measurements are required of the dimensions of interest. The mapping transforms the annotations to corresponding locations in the target image, and as such, distances between points can then be measured.

For this thesis, image registration techniques were utilized to address the challenges with estimating the CDL as discussed in section 1.4. Moreover, an atlas with points annotating the A-value was selected as the moving image for the registration process. The details of the atlas-based CDL measurement algorithm are discussed in Chapter 3 of this thesis.
1.6 Objectives

1.6.1 Objective 1

At the outset of this thesis work, the intra- and inter-observer variability, and accuracy in manual measurements of A-value were not well quantified. As variability and accuracy of A-value measurements directly affect CDL estimates, and in turn appropriate electrode length selection for a particular patient, the first objective of this thesis was to evaluate the intra- and inter-observer variability, and accuracy of manual A-value measurements in a clinical setting. The methodology and results of this evaluation are reported in Chapter 2.

1.6.2 Objective 2

Based on the results from the first objective, it was decided that the second objective would be to develop an automated method for measuring the A-value. This would eliminate observer variability and potentially improve on the accuracy reported in the first objective. An atlas-based approach was developed and evaluated for accuracy and is described in Chapter 3.
References


Chapter 2: Intra- and Inter-Observer Variability of Cochlear Length Measurements in Clinical CT

2.1 Introduction

The advent of cochlear implants (CI), has garnered renewed interest in variable size and shape of the human cochlea. The literature reports considerable variations in the cochlear duct length (CDL) [1–5]. In 1938, Hardy catalogued the variability in 68 human cochleae and found the CDL to vary between 25 and 35mm [6]. This variability can impact cochlear implant electrode selection [1, 7]. Studies have shown that apical stimulation may provide low-frequency response to patients [8–10], improve musical sound perception [8], improve tonal language discrimination [11] and potentially provide better hearing outcomes for CI users [10]. However, selecting the longest electrode in a small cochlea could potentially lead to an incomplete insertion and/or apical trauma [9].

In addition, the CDL can be used to create a personalized frequency map of the cochlea, using the Greenwood equation [12]. These customized frequency maps have the potential to reduce frequency-place mismatch [13], and initial results with image-guided programming have shown clinical benefit [14–17].

Escudé et al. proposed a method of preoperative CDL estimation by describing the correlation between a single measurement, the A-value, and the CDL [18]. The A-value measurement is defined as the length of the straight line between the middle of the round window, passing through the modiolar axis and reaching the furthest point on the basal turn.
Alexiades et al. (2014), derived an equation using linear regression methods to model this relationship [19].

The A-value was described as being measured in a multi-planar reconstructed (MPR) view through the cochlea [18, 20, 21], which allows ideal visualization through the round window and basal turn. This post-processing step can easily be performed on radiology workstations [22], however, these post-processing tools may not be readily available to surgeons using web-based viewers. In the standard clinical views of the temporal bone, typically only axial, coronal, and sagittal slices are provided. With this standard clinical view, it is difficult to observe the full basal turn of the cochlea in one slice of any of the three respective slices [18].

The first objective of this study is to evaluate the intra- and inter-observer variability in A-value measurements performed by cochlear implant surgeons and fellowship trained radiologists. The second objective is to compare the accuracy of A-value measurements from standard clinical views (axial, coronal, and sagittal) and MPR views with a gold standard obtained from high resolution micro-CT images.

### 2.2 Materials & Methods

#### 2.2.1 Image Acquisition

Ethics approval was obtained from the Department of Anatomy at the Schulich School of Medicine and Dentistry. Twenty fixed cadaveric temporal bone specimens were acquired for the study.
2.2.2 Clinical CT Images

The specimens were scanned at clinical resolution using the GE Medical Systems (GE Healthcare, Chicago, US), Discovery CT750 HD Clinical Scanner, equipped with GE’s Gemstone CT detector. Slice thickness was set to 0.625mm with the scanner operating at an x-ray voltage of 120 kV. The resolution of each sample’s scan was approximately 0.6mm and the acquisition time for each of the 20 samples was approximately 20 seconds.

2.2.3 Micro-CT Images

High resolution micro-CT images were used to obtain the gold standard A-values for each specimen. In order to fit within the micro-CT scanner bore, a cylindrical drill bit, with a diameter of 40mm and a height of 60mm, was used to cut out the region of interest from the temporal bone. The specimens were scanned using the GE Healthcare eXplore Locus μCT scanner. The scanner was set at a voltage of 80kV and a working current of 0.45mA. Approximately 900 views were captured, with an incremental angle of 0.4 degrees. Using a modified cone beam algorithm [23] the data was reconstructed into a 3D image with a voxel size of 20µm.

2.2.4 A-Value Measurements

Four specialists, two fellowship trained otolaryngologists who routinely perform cochlear implant surgery (SKA, LSP), and two fellowship trained radiologists (ZK, MS), volunteered as experts to perform A-value measurements. They were familiarized with A-
value measurements and given background literature by Escudé et al. [18] and Alexiades et al. [19] as reference. A free medical image viewing software, Synedra View Personal (Synedra information technologies GmbH, Austria) [24] was used to make the measurements. At the beginning of the measurement session, each specialist was given unlimited time to familiarize themselves with the software and post-processing tools.

The order of the specimens was randomized for each trial using Research Randomizer [25]. The images were initially presented in the standard clinical view (axial, coronal and sagittal slices), and the experts then made their first A-value measurement on these slices. (Figure 2.1a).

![Standard Clinical Measurement and MPR Measurement](image)

**Figure 2.1:** (a) Sample A-value measurements using the standard clinical view and (b) the multiplanar reconstructed view.

For their second measurement, the specialists used post-processing tools to create an MPR view as described by Escudé et al. [18]. A reconstruction plane through the basal turn of the cochlea was selected, and this was displayed using a 1.0-mm layer, minimum intensity projection. The A-value measurement was taken by measuring from the round window to the furthest point on the basal turn, passing through the modiolar axis (Figure 2.1b). The
time taken to make the first measurement, and the time taken to use the post-processing tools to acquire the MPR view and make the second A-value measurement, was recorded.

To assess intra-observer variability, each of the specialists repeated their measurements 3-4 weeks after their first session. Therefore, a total of 80 measurements were made by each observer; 20 in standard clinical and MPR views respectively per session, with two sessions in total. The images were again presented in a random order, and no identifiers on the images were present to minimize recall bias. Accuracy of these measures were assessed by comparing them against the gold standard A-value measurements made on micro-CT scans of the same specimen.

2.2.5 Statistical Analysis

2.2.5.1 Samples size and repetitions per observer

The sample size calculation was performed using the protocol outlined by Walters et al [26] for reliability studies. The protocol requires determining the minimum acceptable Intra-class correlation coefficient (ICC) in order to perform the calculation. The ICC values were interpreted using the following scale: Poor (<0.40), Fair (0.40 – 0.59), Good (0.60 – 0.74), and Excellent (0.75 – 1.00) based on Cicchetti [27]. Therefore, using a statistically acceptable $\alpha$ value of 0.05 and $\beta$ of 0.8 with the available participants (n=4), and a minimum acceptable ICC in the “good” range (ICC = 0.6), the necessary sample size for this study was 20 cadaveric scans and 2 repetitions per participant.
2.2.5.2 Inter-observer and intra-observer variability of A-values

Inter-observer variabilities were evaluated by averaging each specialist’s measurements from the two sessions and then calculating the intra-class correlation coefficient (ICC) of those measurements between all specialists. One-way ANOVA was performed to evaluate the variance between the A-value measurements made by the four specialists. The average absolute and relative differences of the specialists’ measurements were calculated. Pair-wise comparison between the individual specialists was performed with ICC values and paired t-tests.

Intra-observer variability was assessed using ICC values and paired t-tests between the first and second measurement sessions for each specialist. The average difference, in units and percentages, of the first and second measurements within specialists was calculated.

The statistical analyses were performed on both the clinical and MPR view measurements. P-values less than 0.05 were considered significant.

2.2.5.3 A-value measurement accuracy

The accuracy was measured by comparing the clinical measurements against the gold standard micro-CT values. The absolute mean percentage difference was computed for each specialist for their clinical and MPR measurements. A paired t-test was used to compare the accuracies of the clinical and MPR views. The overall accuracy was calculated by averaging the absolute mean percentage differences of all specialists for both sessions.
2.3 Results

2.3.1 Inter-observer Variability

The ICC values, their confidence intervals, ANOVA and t-tests results for inter-observer variability are summarized in Table 2.1.

Table 2.1: Pair-wise and overall comparison of Inter-observer ICC values and their confidence intervals, t-test and ANOVA value

<table>
<thead>
<tr>
<th></th>
<th>Specialists</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 versus 2</td>
<td>1 versus 3</td>
<td>1 versus 4</td>
<td>2 versus 3</td>
<td>2 versus 4</td>
<td>3 versus 4</td>
<td></td>
</tr>
<tr>
<td>Clinical ICC</td>
<td>0.713**</td>
<td>0.792***</td>
<td>0.749**</td>
<td>0.443*</td>
<td>0.462*</td>
<td>0.590*</td>
<td>0.626**</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.412 –</td>
<td>0.549 –</td>
<td>0.409-</td>
<td>0.027-</td>
<td>0.046 –</td>
<td>0.201-</td>
<td>0.421 –</td>
</tr>
<tr>
<td>p value</td>
<td>0.332</td>
<td>0.535</td>
<td>0.017</td>
<td>0.250</td>
<td>0.017</td>
<td>0.025</td>
<td></td>
</tr>
<tr>
<td>ANOVA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.046</td>
</tr>
<tr>
<td>MPR ICC</td>
<td>0.489*</td>
<td>0.556**</td>
<td>0.472*</td>
<td>0.764 ***</td>
<td>0.659**</td>
<td>0.626**</td>
<td>0.569*</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.493 -</td>
<td>0.803</td>
<td>0.328 –</td>
<td>0.238 -</td>
<td>0.836</td>
<td>0.792</td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.087</td>
<td>&lt;0.001</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>ANOVA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ANOVA indicates analysis of variance; CI, confidence interval; MPR, multiplanar reconstructed
ICC: interclass correlation coefficient (single measure values)
*Fair ICC, **Good ICC, ***Excellent ICC

When comparing data from all 4 specialists ICC values of 0.626 and 0.569 were obtained for standard clinical and MPR views, respectively. The ICC value was good for the clinical views (0.626) and fair for the MPR views (0.569). However, the ANOVA revealed there was a significant difference between the acquired values by the 4 specialists on the clinical view ($p = 0.046$) and the MPR view ($p < 0.001$). Pair-wise comparison of the specialists revealed ICC values which ranged from fair (0.443) to excellent (0.792) on the clinical views, and fair (0.472) to excellent (0.764) on the MPR views.
On clinical views, the A-value measurement difference averaged 0.77mm (11%) between observers, with the variations ranging from 0.1mm (1%) to 2.2mm (31%). On the MPR measurements, the average variation was 0.90mm (12%) between observers, with the variation ranging from 0.20mm (2%) to 1.50mm (21%).

2.3.2 Intra-observer Variability

A summary of the ICC values and t-test results for intra-observer variability are summarized in Table 2.2. For the standard clinical views, ICC values ranged from fair (0.519) to excellent (0.867) within all four specialists. The A-value measurements varied significantly ($p=0.017$) between the two sessions for only one of the specialists. The ICC values for MPR view ranged from fair (0.405) to excellent (0.902) with significant differences observed between A-value measurements by two of the specialists. The intra-observer variability of the MPR value measurements worsened for 3 out of the 4 specialists, compared to their standard clinical measurements.

Table 2.2: Intra-observer ICC values and t-test results

<table>
<thead>
<tr>
<th>Observers</th>
<th>Clinical</th>
<th>MPR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC</td>
<td>Paired T-test</td>
</tr>
<tr>
<td>Specialist 1</td>
<td>0.855 ***</td>
<td>$p = 0.082$</td>
</tr>
<tr>
<td>Specialist 2</td>
<td>0.595 *</td>
<td>$p = 0.082$</td>
</tr>
<tr>
<td>Specialist 3</td>
<td>0.519 *</td>
<td>$p = 0.017$</td>
</tr>
<tr>
<td>Specialist 4</td>
<td>0.867 ***</td>
<td>$p = 0.691$</td>
</tr>
</tbody>
</table>

ICC: interclass correlation coefficient (single measure values); MPR, multiplanar reconstructed
*Fair ICC
***Excellent ICC
On average, each observer had an absolute difference of 0.31 mm (4%) between sessions for standard clinical measurements and 0.38 mm (5%) for MPR measurements. The range of variability between the two sessions was from 0 mm to 1.50 mm (19%) for standard clinical measurements and 0 mm to 1.40 mm (17%) on MPR measurements.

2.3.3 Accuracy

Compared to the gold standard micro-CT, the mean absolute percentage difference in A-value measurements made by each specialist using clinical and MPR views is summarized in Figure 2.2.

Figure 2.2: Absolute mean percentage difference of clinical standard (grey) and MPR (black) views compared to micro-CT gold standards. Paired t-test. **** p<0.0001, ***P<0.001, **P<0.01 *p<0.05

The A-value measurements recorded by all four specialists, in the MPR view had a lower absolute mean percentage difference from the gold standard than the measurements made in the standard clinical view. This trend was significant for all four specialists,
specialist 1 ($p < 0.001$), specialist 2 ($p < 0.001$), specialist 3 ($p < 0.001$), and specialist 4 ($p < 0.05$). The overall accuracy, calculated as the absolute mean percentage difference from all specialists in both sessions, was $14.5 \pm 5.4\%$ and $9.5 \pm 4.3\%$ for the standard clinical views and MPR views respectively. On average, it took an additional $51.3 \pm 23$ seconds per sample, to use post-processing tools to acquire the MPR view and measure the A-value.

### 2.4 Discussion

The inter-observer variation for A-value measurements was good on the clinical views, but only fair on the MPR views. The increased variability in the MPR results was likely introduced due to the additional step of using post-processing tools. The ideal oblique slice through the round window and basal turn was selected by the expert, and despite using a 1.0 mm minimum intensity projection, there were differences in the reconstructed views between experts. The ANOVA did reveal significant differences between the experts on both views, and the average difference of 11-12% could be clinically significant in terms of electrode selection and frequency mapping [13].

Intra-observer variability for each expert was less, with an average difference of 4-5% from the first session to the second session. However, the experts varied with 1 expert (25%) having an excellent correlation between sessions, and 3 experts (75%) only having a fair correlation. The maximum measurement difference was 17-19% on intra-observer variability, which was less than the 21-31% seen with inter-observer variability. This is consistent with each expert using a similar measurement and post-processing technique between sessions, however this technique varied between experts. This finding also
corresponds with other studies examining intra-observer and inter-observer variability in radiographic interpretation [28, 29].

The accuracy of the measurements compared to micro-CT was significantly worse on clinical views as compared to the MPR views. On the standard axial, coronal, and sagittal slices, it was difficult to find a single slice that visualized both the round window and the furthest point along the basal turn. This resulted in the experts under-estimating the A-value on the clinical scans. Although there was higher variability using the post-processing tools to create the MPR view, the A-value measurements were still significantly more accurate than the clinical views ($p < 0.001$). Considering the minimal time taken to create the MPR views, the necessary post-processing tools should be available when measuring A-value.

The significance of the variability and accuracy can be assessed by examining their effect on the calculated CDL. On the MPR views, the average intra-observer difference was 5%, inter-observer difference was 12%, and accuracy difference was 10%. Using the Alexiades’ equation [19, 30] and an average CDL value of 32.9mm [19], there could be a variation of ±3.9mm in the total CDL of the cochlea. This difference could impact cochlear implant electrode choice [31], and could lead to a significantly different individualized frequency map using the Greenwood equation [12, 13].

Although the A-value measurement on MPR views is the simplest method to estimate the CDL, clinicians should be aware of the variability when using these results in practice. The development of automated A-value measurement tools may help to alleviate the intra- and inter-observer variation, and possibly increase the accuracy of calculated CDL estimates in the future.
References


Chapter 3: An Automated A-Value Measurement Tool for Accurate Cochlear Duct Length Estimation

3.1 Introduction

Cochlear implants (CI) are now commonly used worldwide to restore hearing in patients with severe to profound sensorineural hearing loss (SNHL) [1–3]. The literature has described significant variation in the human cochlear duct length (CDL) [4–8], which may have an impact on CI electrode selection for patients [9, 10]. There is some evidence that apical stimulation can positively affect low-frequency response, tonal language discrimination, music appreciation, and provide an overall improvement in hearing outcomes [10–13]. In addition, with the aid of the Greenwood equation, the CDL can also be used to create patient-specific frequency maps [14, 15].

The CDL can be estimated using the A-value, a measurement defined as the length of the straight line between the middle of the round window, passing through the modiolar axis, and reaching the furthest point on the basal turn [16]. This measurement was proposed by Escudé et al, who utilized the correlation between the A-value and the CDL [16]. Alexiades et al.[17] proposed an equation to determine CDLs using the A-value, and these equations were further modified using high resolution imaging by Koch et al. [18]. However, despite the simplicity of this method and its relevance, there is significant inter-observer and intra-observer variability associated with the A-value measurement on clinical CT scans [19, 20]. The development of an automated tool to measure the A-value could alleviate this user variability.
The primary objective of this study is to develop an automated algorithm using atlas-based registration techniques on an open-source platform. The secondary objective is to compare the accuracy of the automated tool against manual measurements by experts. A set of micro-CT images of the same sample set was used as the gold standard for measurement.

3.2 Methods

3.2.1 Image Acquisition

Twenty fixed cadaveric temporal bone specimens were obtained for the study. Ethics approval was acquired through the Department of Anatomy at the Schulich School of Medicine and Dentistry at Western University, Ontario Canada.

3.2.2 Clinical CT Images

All twenty specimens were scanned at a clinical resolution of 600µm using the Discovery CT750 HD Clinical Scanner (GE Healthcare, Chicago, IL), equipped with GE’s Gemstone CT detector. The Scanner was set to a slice thickness of 0.625mm and an x-ray voltage of 120kV. The acquisition time for each of the twenty specimens was approximately 20 seconds.

3.2.3 Micro-CT Images

High resolution micro-CT images were acquired for all twenty specimens. The temporal bone specimens where trimmed using a cylindrical drill bit, with a diameter of 40mm and a height of 60mm. Special care was taken to ensure the region of interest was preserved. The trimmed specimens could then be imaged with the eXplore Locus µCT
scanner (GE Healthcare, Chicago, IL), which was set at 80kV and 0.45mA. Using an incremental angle of 0.4 degrees, approximately 900 views could be captured. A modified cone beam algorithm [21] was used to reconstruct a 3D image with a voxel size of 20μm.

3.2.4 Gold standard values

A fellowship trained neurotologist (SKA) measured the A-value on a set of twenty high resolution micro-CT images. These images were reconstructed at an oblique angle that enabled the full basal turn of the cochlea to be visualized. The reconstructed views were subsequently displayed with an appropriate minimum-intensity projection as described by Escudé et al.[16]. The A-value for all twenty specimens served as the gold standard reference values [19].

3.2.5 Atlas generation

The specimen with the median gold standard A-value was selected to be used as the single atlas for the automated algorithm. The atlas was mirrored to ensure that models were available for both right and left cochleae. To facilitate accurate registration, the atlas was cropped to only contain the region of interest in 3D Slicer [22]. Two fiducials were then placed; one on the centre of the round window and the other on furthest point on the basal turn as shown in Figure 3.1.

![Atlas with two fiducials on the right and left cochleae](image)

Figure 3.1: Atlas with two fiducials on the right and left cochleae
3.2.6 Registration Algorithm

The registration algorithm was developed on an open source software platform, 3D Slicer [22, 23]. The algorithm components are illustrated in the flowchart (Figure 3.2). The atlas (source image) was loaded along with the clinical CT (target) image. Fiducials were placed on the following landmarks: the cochlear apex, modiolus, round window and oval window. Landmark registration was then used to ensure the source and target images were in the same spatial region. Finally, the target image was cropped to extract the region of interest (i.e., the cochlea and immediate surrounding structures).

Figure 3.2: Automated A-value registration algorithm
3.2.7 Affine Registration

Affine image registration is a form of linear registration that incorporates translation, rotation, scaling, and shearing. The dimension of the image determines the degrees of freedom in the registration [24]. The CT images were 3-dimensional, which resulted in a total of 12 degrees of freedom (DOF) (translation, rotation, scaling, and shearing were performed in each of the x, y, and z axis). Affine registration is restricted in that it only captures global differences between images, therefore, it is typically used as a technique to align a set of images before non-linear registration techniques are applied [24, 25]. To capture global differences alone, only 0.1 percent of the clinical CT (target image) was considered by the algorithm. Normalized cross correlation (NCC) was used as the image similarity comparison metric, which defined the registration’s objective function. Table 3.1 outlines the complete set of parameters used.

3.2.8 B-spline Registration

A free-form deformation (FFD) model based on B-splines, was used to address local differences between the images. FFDs allows for local deformation of an image through the manipulation of a mesh of control points [25]. After the movement of the control points, a B-spline function is used to interpolate the corresponding movement in the image and the degrees of freedom for B-spline registration is determined by the number of control points [26]. After the affine registration addressed global differences, B-spline registration was then used to address local differences between the images. The parameters used for the B-spline registration in Table 3.1 were based on Elfarnawany et al.[27]. A 3D mesh of control points (4x4x4) allowed for a total of 81 DOF and NCC again was used as
the image similarity metric used to define the objective function. The whole clinical sample (100%) was used in the registration process in an attempt to capture all the local differences between the clinical CT and atlas images. The generated B-spline transform matrix was applied to the atlas and its corresponding A-value fiducials, and the new distance between the fiducials was computed as the A-value of the target image.

Table 3.1: Automated method parameters for Landmark, Affine and B-spline registration

<table>
<thead>
<tr>
<th>Registration</th>
<th>Initialization</th>
<th>Objective Function</th>
<th>Degrees Of Freedom (DOF)</th>
<th>% of Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Landmark</td>
<td>Fiducial Placements</td>
<td>Least Squares</td>
<td>6 DOF</td>
<td>N/A</td>
</tr>
<tr>
<td>Affine</td>
<td>Geometric Alignment</td>
<td>Normalized Cross Correlation (NCC)</td>
<td>12 DOF</td>
<td>0.1</td>
</tr>
<tr>
<td>B-spline</td>
<td>Affine Transform</td>
<td>Normalized Cross Correlation (NCC)</td>
<td>64 DOF</td>
<td>100</td>
</tr>
</tbody>
</table>

3.2.9 Evaluation of Automated method

The registration algorithm was implemented on nineteen specimens, as the atlas was excluded from the analysis. Depending on whether the target image was a right or left cochlea, the registration algorithm was applied using the corresponding atlas. The results of the automated method applied on the clinical CT images were compared to the gold standard A-values from the micro-CT images of the same samples. Additionally, the automated method results were compared to the A-values manually acquired by experts on the same set of clinical CT images in a previous study [19].
3.2.10 Qualitative Evaluation

3D models of the atlas and a clinical CT image sample were created. The overlap of the models and the A-value fiducials were qualitatively evaluated before and after the registration algorithm. The deformation grids of the atlas, before and after each registration step, were also generated and visualized.

3.2.11 Quantitative Evaluation

A-values obtained using the automated registration-based method were compared to the gold standard reference values by calculating the absolute percentage difference. The mean percentage difference of the automated method from the gold standard was compared to the difference of the manual method reported in Iyaniwura et al. [19]. The automated and manually measured A-values were tested for normality using the Shapiro-Wilk test. Based on this result, the Wilcoxon matched pairs test was used to compare these values against the gold standard. The correlation between the two sets (automated and manual) of A-values and the gold standard A-values were evaluated using the Spearman correlation.

Lastly, Bland-Altman plots were used to display the differences between the A-values from clinical CT (automated method and manually measured) and the gold standard A-value measurements. A clinically acceptable A-value error range of ±1.05mm was calculated based on the revised cochlear length equations published by Koch et al. [18] and is indicated on the derived Bland-Altman plots.
3.3 Results

3.3.1 Qualitative results

The cochlear models generated from the micro-CT (atlas), clinical CT (target), and the corresponding deformation grids were analysed. In all cases, affine registration successfully aligned the atlas and clinical CT images, addressing the majority of the global differences between the two images. Subsequently, the B-spline registration further improved the alignment addressing the local difference between the two images.

Figure 3.3 provides a specific example where the target image was larger than the atlas. Affine registration globally expanded the atlas as shown by the deformation grid, and this achieved a partial overlap with the target (Figure 3.3b). B-spline registration was then able to deal with the local differences, and the individual protrusions can be visualized on the deformation grid (Figure 3.3c).
3.3.2 Quantitative results

The absolute percentage difference (mean ± standard deviation), Wilcoxon test, and Spearman correlation were used to analyze manual and automated A-value measurements. Table 3.2 summarizes these results as compared to the gold standard measurements from micro-CT. The automated method had a 2.7 ± 2.1% absolute difference from the gold standard compared to a difference of 9.5 ± 4.3% for the manual method reported in Iyaniwura et al. [19]. Using the Wilcoxon test, the automated method was not significantly different from the gold standard ($p = 0.061$, ns), but the manual method was significantly different from the gold standard ($p < 0.0001$). Comparing the automated method against the manual method, the results were significantly different from each other ($p < 0.0001$).
Both the automated and manual methods had significant Spearman correlations of \( r = 0.70 \) \((p < 0.01)\) and \( r = 0.69 \) \((p < 0.01)\), respectively, when compared to the gold standard measurements.

### Table 3.2: Percentage Difference, Spearman correlation & Wilcoxon test comparison of manual and automated method

<table>
<thead>
<tr>
<th></th>
<th>% Difference</th>
<th>Wilcoxon</th>
<th>Spearman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual</td>
<td>9.5 ± 4.3%</td>
<td>( p &lt; 0.0001 )</td>
<td>( r = 0.69^{**} )</td>
</tr>
<tr>
<td>Automated</td>
<td>2.7 ± 2.1%</td>
<td>( p = 0.061 ) (ns)</td>
<td>( r = 0.70^{**} )</td>
</tr>
</tbody>
</table>

\( ** p < 0.01 \)

Bland-Altman plots were generated as shown in Figure 3.4. A comparison of the automated method against the gold standard revealed that all measurements fell within the acceptable range (Figure 3.4a). The manual measurements by experts underestimated the true A-value, and 26% of them were outside of the acceptable range (Figure 3.4b).
3.4 Discussion

As discussed, there is significant variation in cochlear size and morphology described in the literature [4–8, 28]. To develop a robust algorithm, fifty cochleae were initially scanned and a subset of twenty cochleae were chosen to represent a wide range of A-values. An additional strength of the study was the availability of micro-CT images, which allowed for a gold standard validation of the algorithm.

Overall, the quantitative results revealed a statistically significant $6.8 \pm 4.8\%$ improvement in accuracy using the automated method. This algorithm also corrected the
26% of values that fell outside the clinically acceptable range using the manual method as observed on the Bland-Altman plots. The type of error on these plots was also different between the automated and manual methods. The automated algorithm had a random error centred on the origin, whereas the manual measurements consistently underestimated the true A-value (Figure 3.4). The error observed in Figure 3.4b can be described as a systematic error in the manual measurements. This error is most likely attributed to both the poor visibility of the round window in clinical CT images, and the variability associated with the selection of an oblique plane for the multiplanar reconstruction of each clinical CT image; however, a similar study with a larger $n$ (participants) would need to be conducted[19].

Intra- and inter-observer variability between specialists also has been identified as a major source of error when measuring A-values on clinical CT [19, 20]. Iyaniwura et al [19] reported intraclass correlation (ICC) coefficients for inter-observer variability (ICC = 0.57) and intra-observer variability (ICC range = 0.54 to 0.90). Rivas et al. [20] reported a mean absolute difference as high as 8 mm for CDL estimates calculated from manual A-value measurements. The automated algorithm described eliminates this observer variability.

The clinical significance of improved accuracy and consistency can be assessed by examining its effect on electrode selection and on the frequency mapping of the cochlea via the Greenwood equation. [15, 17, 29]. With regards to electrode selection, Iyaniwura et al [19], using an average CDL value of 32.9 mm, derived an average CDL variation of ±3.9mm with the manual method. Cochlear implant manufacturers have off the shelf implants available in 15mm, 17mm, 20mm, 24mm, 25mm, 28mm and 31mm variants,
therefore, a variation of ±3.9mm could lead to improper electrode selection preoperatively [30–34]. In terms of customized frequency maps, Koch et al [18] calculated that a 6mm error in CDL would result in a frequency-place mismatch of 400 Hz at the apical turn and 1100 Hz along the basal turn of the cochlea. These discrepancies could translate into discernible effects on cochlear implant performance [14, 35].

There have been a number of registration techniques that have been described in the medical imaging literature. In structures with significant variability, FFD (non-linear/non-rigid) registration like B-spline, as well as atlas-based registration techniques, are typically used [25, 27, 36–42]. In this study, a single atlas with B-spline registration was sufficient in improving the accuracy of A-value measurements, which are based upon the basal turn of the cochlea. However, the apical turn of the cochlea exhibits significant additional variation between patients [5, 17, 18, 29]. If the apical turn was to be directly modeled in the future, this variability could be addressed using multi-atlas registration techniques whereby atlases with variation in their apical turns are used [42–44].

Other studies have attempted to register inner ear structures for a variety of purposes. Christensen et al. used a deformable atlas based registration technique to measure shapes within the inner ear [45], however they did not measure the A-value or the CDL. Rivas et al [20] developed a sophisticated algorithm for measuring the CDL, however no high-resolution micro-CT images were available to validate their results.

The implemented automated algorithm will be made available as an open-source software extension to 3D Slicer. This would allow for further development by other groups and validation of the methodology on a wider variety of cochleae.
3.5 Conclusion

An automated method to estimate cochlear length based on the A-value was developed using open-source atlas-based registration tools. The automated method produced more accurate results than the manual method, and eliminated the observer variability between experts. This improved accuracy may be clinically important for electrode selection and patient-specific frequency mapping of cochlear implants.
References


Chapter 4: Conclusions and Direction for Future Work

4.1 Conclusions

The purpose of this thesis was first to evaluate clinical methods of estimating the CDL, and second to improve on those methods through automation by using image registration techniques. The thesis was therefore divided into two chapters based on the objectives stated in section 1.6. The conclusion of both chapters are discussed hereafter.

In Chapter 2, four specialists measured the A-value, a clinically accepted metric used for estimating the CDL [1, 2] from standard clinical CT images and MPR CT images. Results showed high inter-observer variability with ICC values of 0.626 and 0.569 for standard clinical and MPR images, respectively. Similarly, intra-observer variability exhibited ICC values that ranged from 0.517 to 0.857 and 0.405 to 0.902 for standard clinical and MPR images, respectively. Although higher observer variability was exhibited when using MPR views, the accuracy obtained with MPR views was better than when using standard clinical views with the accuracy measured as the average mean percentage difference being $9.5 \pm 4.3\%$ for MPR images compared to $14.5 \pm 5.4\%$ for standard clinical images. These errors are clinically significant as they imply a strong likelihood of an inappropriate electrode length selection. The recommendation drawn from this study was that clinicians should use MPR CT images when possible with the manual method, however the study suggested that the best approach to eliminate the variability altogether was to automate the A-value measurement.
In Chapter 3, an automated measurement tool was developed to measure the A-value. The algorithm implemented by the measurement tool utilized image registration techniques to transfer points denoted by an expert on an atlas micro-CT image to clinical CT images. The Euclidean distance between the denoted points represented the A-value. The automated method had a mean error of 2.7 \( \pm 2.1\% \) and was more accurate than the manual method which had a mean error of 9.5 \( \pm 4.3\% \). This result is clinically significant because the automated method increases the chances of appropriate electrode length selection. Moreover, the automated method eliminated observer variability in the process. Importantly, the algorithm was developed on an open-source platform to allow for public access.

The importance of this work hinges on the current trend of manufacturers providing electrode array lengths in varying discrete sizes and with the current recommended method for estimating the CDL for implant electrode selection. The current recommended method is based on manual measurement of the A-value [1–3]. Prior to this thesis, few studies had extensively assessed the clinical feasibility of A-value measurement as a means for estimating the CDL. In particular, data on intra- and inter-observer variability in A-value measurements were lacking. However, the need for a reliable method of estimation is increasing as both the demand for cochlear implants increases and the current trend in research tends towards the personalization of cochlear implants [4–6]. Therefore, the development of an automated method provides manufacturers and clinicians alike with a tool addressing variability and accuracy.
4.2 Future Directions

Visualization of intracochlear anatomy has improved significantly in the last decade due to advancements in medical imaging [5, 7–9]; however, these visualization techniques are currently only applicable to cadaveric ears. With an increased interest in developing variable-length electrode arrays and patient-specific frequency maps, such visualization could prove to be valuable in patient-specific implant programming if simultaneous visualization of an implanted electrode relative to the basilar membrane is possible [4, 10, 11]. Therefore, using these high resolution micro-CT images to infer features in clinical CT images via registration is an effective way to take advantage of micro-CT images.

One conceivable future direction for this thesis is the annotation of other anatomical structures of the auditory system, and the use of the developed algorithm to transfer those annotations to lower resolution clinical CT images. For example, annotation of the CDL can allow for direct measurements of the CDL, circumventing the need to estimate the A-value. This can be done by having a user create an atlas in which many points are selected along the entire length of the cochlea to estimate its length. However, the challenge with this approach is addressing the large variability in the length and shape of apical turn of the cochlea [9, 12, 13]. The use of multiple atlases which represent the variability in the apical turn can be a potential avenue to explore in addressing the variability in the apical turn. Essentially, each atlas would be registered to an image to be analyzed with the one producing the best overlap being used to calculate CDL. Two critical issues in using multi-atlas registration are (1) selection of images to use as atlases and (2) computational time [14]. The first issue of image selection for atlases has been addressed in our laboratory by
building a large repository of micro-CT images of human cochleae and selecting exemplar images that span the observed variation in CDL. The second issue of speed arises from the fact that non-linear registration is computationally expensive and multiple registrations must be done. Instead, one can potentially improve performance by simply doing a linear registration of multiple atlases to a target clinical CT image and select the atlas that results in the best overlap for the more computationally expensive step of non-linear registration. Furthermore, the linear registration could be performed on coarsened versions of both the atlases and the target image with the final non-linear registration being performed at the full resolution. Of course, hardware solutions based on graphical processing units (GPUs), field programmable gate arrays (FPGAs) or applications-specific integrated circuits (ASICs) are also a possibility to improve computation speed.

To date, many of the software tools in the hearing literature tend to be inaccessible to users outside the laboratory in which they were developed. All things considered, an open-source software development approach such as that utilized in this work allows for further testing, development, and adaptation by the scientific community at large. In addition, it provides a publicly available tool which clinicians can potentially use to acquire accurate CDL estimates. A future direction for a multi-atlas CDL estimation approach will utilize an open-source approach.
References


Curriculum Vitae

Name: John Enioluwa Iyaniwura, B.Eng.

Education:

2015 – Present MEng (Biomedical Engineering) Western University London, Ontario, CA

2007 – 2011 B.Eng. (Biomedical & Electrical Engineering) – high distinction Carleton University Ottawa, Ontario, CA

Honours and Awards:

2016 – Present Otolaryngology Graduate Research Scholarship Recipient
2015 – 2016 Mitacs Accelerate Internship
2007 – 09,11 Carleton University Dean’s List
2007 – 10 Nortel Scholarship for Excellence

Related Work Experience:

2017 Graduate Teaching Assistant (Introduction to Electrical Engineering – ECE2238)
2016 Graduate Teaching Assistant (Introduction to C++ Programming for Engineers – ES 1036) Western University London, Ontario, CA

2014 – 2015 Software Engineer II
2011 – 2014 Software Engineer I Rockwell Collins Canada Kanata, Ontario, CA

Publications:


### Conferences and Presentations:

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