Journal of Medical Imaging

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Abstract. Cochlear implants (CIs) are surgically implanted medical devices used to treat individuals with severe-to-profound sensorineural hearing loss. Although these devices have been remarkably successful at restoring audibility, many patients experience poor outcomes. Our group has developed the first image-guided CI programming technique where the electrode positions are found in CT images and used to estimate neural activation patterns, which is unique information that audiologists can use to define patient-specific processor settings. Currently, neural activation is estimated using only the distance from each electrode to the neural activation sites, which might be less accurate than using high-resolution electro-anatomical models (EAMs) to perform physics-based estimations of neural activation. We propose a patient-customized EAM approach where the EAM is spatially and electrically adapted to a patient-specific configuration. Spatial adaptation is done through nonrigid registration of the model with the patient CT image. Electrical adaptation is done by adjusting tissue resistivity parameters, so the intracochlear voltage distributions predicted by the model best match those directly measured for the patient via their implant. We found that our approach, demonstrated for $N = 7$ patients, results in mean percent differences between direct and simulated measurements of voltage distributions of 10.9%. © 2017 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.4.2.025003](https://doi.org/10.1117/1.JMI.4.2.025003)]

Keywords: cochlear implant; image-based modeling; image-guided cochlear implant programming.

Paper 17058PR received Mar. 6, 2017; accepted for publication May 22, 2017; published online Jun. 14, 2017.

1 Introduction

Cochlear implants (CIs) are neural prosthetics that are used to treat severe-to-profound sensory-based hearing loss. Each CI has an electrode array with a number of electrodes, ranging between 12 and 22, dependent upon the manufacturer. These electrodes are situated in a silicone electrode array that is surgically inserted into the cochlea. The electrodes stimulate the spiral ganglion (SG) auditory nerve cells to create the sensation of sound. After implantation, each CI is programmed by an audiologist to attempt to optimize CI settings that will lead to better hearing outcomes. The programming process includes determining which electrodes will be activated or deactivated, assigning stimulation levels to each electrode, assigning a sound frequency band for each electrode, and a number of other settings. Optimal settings depend on many factors, including the location of the electrodes within the cochlea.^{1,2} The cochlea is composed of three principal intracochlear cavities called the scala tympani (ST), scala vestibuli (SV), and scala media (SM). The ST and SM are separated by the basilar membrane (BM), and the SM and SV are separated by Reissner's membrane (RM).

Inserted CI electrode arrays lie within either the ST or SV or can cross the thin membranes separating the two and lie in both cavities. The placement of the array in the scalas and the distance from each electrode to the SG nerve cells that they stimulate are positional factors that affect hearing outcomes.^{1–3} SG cells are located in the modiolus (MO), around which the cochlea spirally wraps. The segmentation of the ST, SV, and MO surfaces in conventional CT was achieved using a previously

published method.⁴ Briefly, an active shape model was semiautomatically created from 9 μ CT images of cochlea specimens and was fit to the partial information that was available on conventional CT images. The preparation protocol used for the specimens that were μ CT imaged to construct the active-shape model did not include steps necessary to preserve RM, and thus the separation between SV and SM is not visible in our images and not represented in our model. Instead, our SV surface represents a combined volume of both the SM and SV. The fitting allowed us to estimate the position of the structures not visible in the conventional CT images. A segmented CT image of a specimen along with its corresponding registered μ CT are shown in Fig. 1. As can be seen in this figure, the registered μ CT confirms that our CT segmentation approach allows accurate estimation of intracochlear structures that are not directly visible in CT images.

The intracochlear positioning of the electrodes is usually unknown since the electrode array is surgically inserted into the cochlea through a small opening and its intracochlear position cannot be seen. Lacking knowledge of the location of the electrodes, the audiologists have to entirely depend on patient feedback when trying to optimize CI settings. As patients require weeks or months of experience with given settings for the hearing performance to stabilize, many programming sessions are required over the course of years and they may not result in optimal settings for many patients.

We have developed several image processing techniques that permit localization of CI electrodes in CT images with high accuracy.^{5,6} Using these techniques, our group has developed

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Fig. 1 (a) The segmentation of the ST, SV, and MO in a μ CT image, (b) a conventional CT image and (c) the 3-D meshes of these structures are shown. ST is shown in blue, SV in yellow, and MO in red.

the first image-guided CI programming (IGCIP) technique where electrode position is used to estimate the neural activation patterns created by the electrodes, which is unique information that audiologists can use to define patient-specific CI processor settings. It has been shown in a large clinical study that using IGCIP leads to improved hearing outcomes.³ Even though the clinical studies have shown that our IGCIP method leads to better hearing outcomes, it is possible that the method could be improved with a better estimate of the electrodes' neural activation patterns. In our current system, neural activation is estimated using only the distance from each electrode to the neural activation sites. This approach might be less accurate than a high-resolution electro-anatomical model (EAM) of the electrically stimulated cochlea.

Several groups have used EAMs to study intracochlear voltage distribution and its effect on neural activation. Since one of the first volume conduction models created from an unrolled human cochlea using a finite-element method,⁷ several methods have been adopted by different groups. Frijns et al.^{8,9} used a rotationally symmetric model of a guinea pig cochlea and human cochlea¹⁰ to solve for the voltage distribution using a boundary element method (BEM). Whiten¹¹ and Kalkman et al.¹² created EAMs of human cochlea from histological images using finite difference method and BEM, respectively. Although these models have been shown to be useful, they cannot be applied *in vivo*; thus, patient-specific differences cannot be incorporated into these models. It has been shown that human cochleae differ not only in volume but also in shape, number of turns, length, etc.^{13,14} Considering these anatomical differences, Malherbe et al.¹⁵ used CT images acquired from three patients to construct three-dimensional (3-D) patient-specific EAMs of CI users. However, the model relies on manual point selection on the two-dimensional (2-D) CT image slices. Manually determining points using CT images alone is not only arduous, it is also difficult if not impossible with fine scale intracochlear structures, such as the modiolar wall or the partition between the ST and the SV, because they are not directly visible due to the lack of adequate resolution of the CT. To overcome this, Malherbe et al. used a high-resolution photomicrograph of a single cochlea and rigidly registered it to the patient CT image to approximate the dimensions of such fine scale patient-specific structures, which we have shown to be a less accurate approach than a high-resolution nonrigid model for estimating patient-specific anatomy.¹⁶

In a previous study, we developed a high-resolution EAM created using μ CT images of cochlea specimens.¹⁷ Preliminary

tests were conducted to show that the model is stable¹⁷ and can be made patient-specific by spatially adapting the model to patient CT data.¹⁸ However, this model does not account for patient-specific electrical characteristics, i.e., the resistivity of different tissue types. This is important because the ultimate goal of the model is to use it to estimate neural stimulation patterns and to do so accurately will require accurately estimating the voltage distribution in the cochlea. Thus, in this study, our goal is to develop a modeling approach that permits not only spatial adaptation but also electrical adaptation. This requires a sampling of the voltage distribution in the patient's cochlea. In the CI community, such a measurement is termed electrical field imaging (EFI). In this process, one electrode at a time is activated while voltage at each of the remaining electrodes in the cochlea is measured, thus sampling the intracochlear potentials at the sites where the electrodes sit. In this work, we propose a modeling approach that uses CT imaging to spatially adapt the model and EFI to electrically adapt the model to the patient. We demonstrate our approach for $N = 7$ patients. Since our eventual goal is to estimate neural activation caused by the injected current, agreement between measured and simulated results in terms of voltage values at the electrodes would provide strong evidence that the estimated neural activations may be accurate.

2 Methods

2.1 Data

The μ CT images of nine cadaveric cochlea specimens that were used to create our model were acquired using a ScanCo scanner. These images had a voxel size of ~ 0.036 mm isotropic. $N = 7$ patients, with six unilateral and one bilateral implants, who had undergone CI surgery were preoperatively scanned using conventional radiological scanners with temporal bone imaging protocols and having a voxel size of $\sim 0.3 \times 0.3 \times 0.4$ mm³ and postoperatively scanned using a Xoran XCAT fpVCT scanner. The voxel dimensions in these images were 0.4 mm isotropic.

In addition, EFI measurements were performed for the same patients using software provided by the CI manufacturer—Advanced Bionics (Valencia, California). The EFI measurements were recorded for all of the 16 electrodes. Stimulation was performed at 32 μ A of current. The CI patients each had at least 6 months experience with their implants prior to the EFI measurements.

2.2 Patient-Specific EAM

2.2.1 Spatial customization

For each patient, pre- and postimplantation CT images were automatically segmented using previously published techniques⁴⁻⁶ to localize the position of the electrodes and the anatomical structures that we used to create EAMs, including ST, SV, and MO. As previously mentioned, our segmentation algorithm prevents us from segmenting SM and RM. While RM is an important structure for natural hearing, its width is finer than the resolution of the μ CT images, so ignoring it does not affect the electrical simulations achieved by our model; thus, segmentation of the RM was not considered critical in this study. The 3-D meshes of the anatomical structures are surfaces composed of a set of points, and they were created using an active-shape model approach.¹⁹ High-resolution EAMs were created using μ CT images of nine cochlea specimens as previously described.¹⁷ In brief, for each specimen, a uniform 3-D grid of nodes with spacing of 0.072 mm was defined over the field of view of the μ CT image. Each node was assigned to a tissue class, including air, bone, soft tissue, neural tissue, and electrolytic fluid. Nodes that were enclosed by either ST or SV were assigned to the electrolytic fluid tissue class, and nodes enclosed by MO were classified as neural tissue. For the remaining nodes, a simple thresholding of the μ CT was applied to decide among air, bone, and soft tissue. The tissue classes correspond to different electrical resistivity values. The default values for these tissue classes are: $\infty \Omega\text{cm}$ for air, 5000 Ωcm for bone, 300 Ωcm for soft tissue, 600 Ωcm for neural tissue, and 50 Ωcm for electrolytic fluid.²⁰

We warped each individual μ CT to match the shape of the patient cochlea and combined the tissue segmentations using a voting scheme. To do this, the patient CT image was nonlinearly registered to each of the high-resolution μ CTs using thin-plate splines (TPS).²¹ The TPS formulation presented in Eq. (1) is limited to 2-D, but extension to the 3-D formulation we used in this work is straightforward. TPS define a nonrigid transformation that minimizes the bending energy, which is given by

$$I_f = \iint_{R^2} (f_{xx}^2 + 2f_{xy}^2 + f_{yy}^2) dx dy. \quad (1)$$

The surface points of the segmented ST, SV, and MO were used as landmarks in the patient CT image. For a one-to-one point correspondence to exist between these surfaces and the manual segmentations of the ST, SV, and MO in the μ CT images, the active shape model was registered to each of the μ CT images. This was done in a semiautomated fashion where, first, the active shape model was fit to the image, then visible errors between the active shape model and the manual segmentations were manually corrected using software designed for this purpose, and finally the closest points on the manual segmentation surfaces were found. These points were used as the landmarks in the μ CT images for the TPS transformation. The TPS registration between the low-resolution patient CT image and high-resolution μ CTs allowed us to create a high-resolution resistivity map for each patient. The TPS mapping between two different spaces defined by two corresponding landmark point sets (x_i, y_i) and (x'_i, y'_i) has the form

$$f(x, y) = a_0 + a_1x + a_2y + \sum_{i=1}^n w_i U[|(x'_i, y'_i) - (x, y)|], \quad (2)$$

where $U(r) = r^2 \log r$ is the radial basis function, a_0 , a_1 , and a_2 are the affine coefficients, and w_i is the weight vector. The coefficients and the weight vector are determined such that total bending energy, e.g., total curvature, is minimized while providing an exact transformation between the two sets of landmark points.

The patient resistivity map was created in the region around the patient's cochlea and with the same resolution as the grids defined on the μ CTs. The TPS registrations provided the non-linear mapping between the patient space and μ CT spaces and were used to label each node in a new high-resolution patient resistivity map. For each node x in the patient resistivity map, the corresponding point y in a μ CT can be found using the TPS registration. The tissue class of y was then stored as a candidate assignment for the tissue class of x . This procedure was followed for each μ CT image, resulting in nine different tissue candidates z_i $i = [1, 2, \dots, 9]$, for each node. A final resistivity map was achieved using a majority voting scheme among all of the nine tissue candidates

$$Z = \operatorname{argmax}_l \left(\sum_{i=1}^9 z_i = l \right), \quad (3)$$

where Z is the final tissue class. Once the resistivity map was created, we used the position of the electrode array and electrodes found using postimplantation CT images to determine the location of the 16 stimulating electrodes and the silicone electrode array in the high-resolution resistivity maps. This was achieved by first rigidly registering the postoperative CT image to the preoperative CT image of the same patient, and then using this registration to transform the electrodes and the electrode array from postoperative CT image space to the preoperative CT image space. In Fig. 2, the silicone electrode array, the stimulating electrodes, and the MO are shown in gray, black, and red, respectively. The silicone electrode array was modeled as a perfectly resistive material. The electrodes on the other hand were modeled as 2-D plates located on the surface of the electrode array facing the neural stimulating sites. In CIs, the ground electrode is located near the surface of the skull adjacent to the ear to which the electrode array is implanted. Thus, the ground electrode is located relatively far from the stimulating electrodes and the SG nerve cells. Since our model only includes 5 mm of space around the

Fig. 2 The 3-D meshes of the MO, the silicone array, and the stimulating electrodes, in red, gray, and black, respectively.

cochlea, to simulate a distant ground, we defined the entire border of the model to be ground. Then, one of the stimulating electrodes was chosen as a current source whose current sinks to ground. We then defined the system of linear equations defined by Poisson's equation for electrical current at each node

$$\nabla^2 \phi = f, \quad (4)$$

where ϕ is the voltage and f is a constant. Solving this system of equations using the biconjugate gradient method,²² the final output of the model is the voltage map V , which contains the voltage at each of the nodes. This follows the approach proposed by Whiten.¹¹

2.2.2 Electrical customization

The second step of the approach we propose to create patient-specific EAMs includes optimizing the resistivity values of different tissue classes to match the patient-specific values. Given that *in vivo* measurements of the resistivity values of different tissue classes are not possible, a different approach was taken to try to adjust these parameters. This approach is as follows: intracochlear potentials were calculated for a given patient with default tissue resistivity values for each of the 16 electrodes injecting 32 μA of current into the system. The simulated voltage distribution was then compared to the actual measured voltage distribution acquired from the patient, and new tissue resistivity values were selected to try to improve the agreement between the two. We designed a heuristic search approach that leverages our knowledge of how changes in the resistivity values of different tissue types affect the simulated voltage distribution. We found that a change in the electrolytic fluid resistivity has negligible effects, whereas a change in the resistivity values of soft tissue and neural tissue have different effects as shown in Fig. 3. The principal effect when changing the soft tissue resistivity value is a change in the average value of the voltage distribution across electrodes while the shape of the voltage distribution maintains the same slope. Changing neural tissue resistivity value on the other hand sharpens or flattens the curve, i.e., a decrease in the neural tissue resistivity value will result in a flattening of the curve and vice versa.

Fig. 3 The effect of the change in the different tissue resistivity values.

Algorithm 1 Optimizing tissue resistivity values.

Input: V_{EFI} = Patient EFI measurement, V_S = Simulation results, R_{NT} = Neural tissue resistivity, R_{ST} = Soft tissue resistivity, $\text{Slope}_{\text{EFI}}$ = Slope of the EFI measurement, Slope_S = Slope of the simulation

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1 Initialize threshold, maxIteration,  $R_{\text{NT}}$ ,  $R_{\text{ST}}$  values
2 while  $\Delta|\text{average error}| > \text{threshold}$  and  $\text{counter} < \text{maxIteration}$  do
3   Run simulation with  $R_{\text{NT}}$  and  $R_{\text{ST}}$ 
4   for each electrode  $i = 1:16$  do
5      $\text{error}[i] = \text{mean}\{(V_{\text{EFI}}[i] - V_S[i])/V_{\text{EFI}}[i]\}$ 
6   end
7    $\text{average error} = \text{mean}(\text{error})$ 
8   if error has the same sign for all 16 electrodes then
9      $R_{\text{ST}} = R_{\text{ST}} * (1 + \text{average error})$ 
10  else
11    Find 6 closest ( $\text{Closest}_6$ ) and 6 furthest ( $\text{Furthest}_6$ ) electrodes to the active electrode
12     $\text{Slope}_{\text{EFI}} = (V_{\text{EFI\_Closest}_6} - V_{\text{EFI\_Furthest}_6})/V_{\text{EFI\_Closest}_6}$ 
13     $\text{Slope}_S = (V_{S\_Closest_6} - V_{S\_Furthest_6})/V_{S\_Closest_6}$ 
14     $R_{\text{NT}} = R_{\text{NT}} * (\text{Slope}_{\text{EFI}}/\text{Slope}_S)$ 
15  end
16  counter++
17 end

```

Using this knowledge, we developed an automatic heuristic search as shown in Algorithm 1. In this algorithm, the resistivity values of the soft and neural tissues are adjusted based on average error, which is the average normalized mean difference between simulation results and the acquired patient data

Fig. 4 Normalized change, with respect to the default values, in soft and neural tissue resistivity values, as well as absolute value of the average error over number of iterations.

Table 1 Patient-specific neural and soft tissue resistivity values are shown for each ear. In addition, initial and final (average error $\times 100\%$) values and number of iterations that the heuristic search algorithm ran are shown.

	Average error default tissue resistivity (%)	Average error adjusted tissue resistivity (%)	Number of iterations	Neural tissue resistivity (Ωcm)	Soft tissue resistivity (Ωcm)
Ear 1	33.3	22.1	20	46	300
Ear 2	59.1	9.0	18	128	83
Ear 3	63.5	10.6	16	148	78
Ear 4	47.5	7.0	28	92	118
Ear 5	59.7	12.8	24	89	121
Ear 6	28.6	9.2	22	98	216
Ear 7	49.1	10.6	15	306	59
Ear 8	19.4	5.7	30	84	300
Average	45.0	10.9	22		

computed as shown in the pseudocode. The algorithm first calculates the error, the normalized mean difference between the simulation voltage distribution vector and the voltage distribution vector acquired from the patient for a stimulating electrode, for each of the 16 electrodes. It then checks whether those values have all the same sign, i.e., whether simulation results are either bigger or smaller than the acquired patient data for all of the 16 active electrodes. If they all have the same sign, then it adjusts the soft tissue resistivity value by multiplying it by 1 plus the average error. If the signs are different, then it calculates the slope of each curve and adjusts the neural tissue resistivity value by multiplying it by the ratio of the two slopes. The heuristic search runs until the change in the absolute value of the average error is less than a threshold value or a maximum number of iterations are completed. This heuristic search, rather than a generic search scheme, was adopted because the heuristic search uses *a priori* knowledge of the effect of the two parameters to converge more quickly than a generic search could, which is important due to the high computation time required for each iteration in the search.

2.3 Evaluation

A threshold value of 10^{-3} and a maximum number of iterations of 50 were used in the heuristic search. All the simulations were run on a computer cluster, where the voltage distribution for each of the active electrodes can be calculated in parallel. We evaluated the accuracy of our EAM approach both qualitatively and quantitatively, in terms of the absolute value of the average

Fig. 5 Comparison between the acquired patient data and the simulation results for ear 1.

error. A large difference between the initial and the final absolute value of the average error would indicate that the electrical customization method provides a better fit between the simulation results and the EFI measurements.

3 Results

Each iteration takes, on average, an hour and a half to complete. The heuristic search algorithm was able to converge in 22 iterations on average. In Fig. 4, the change in soft and neural tissue resistivity values and the absolute value of average error over number of iterations are shown.

Final soft and neural tissue resistivity values, initial and final absolute values of the (average error $\times 100\%$), and the number of iterations for each ear are shown in Table 1. As can be seen in this table, the mean error when default resistivity values are used is 45.0%, and it drops to 10.9% when tissue resistivity values are customized, indicating that optimizing tissue resistivity values leads to more accurate simulations of the EFI measurements and that our patient-specific EAM is able to estimate patient EFI data with a high accuracy. The maximum absolute value of (average error $\times 100\%$) when tissue resistivity values are optimized is 22%, as shown in this table. The algorithm was unable to find better resistivity values that will match the patient data for ear 1 due to the noisiness of the acquired patient data (see Fig. 5).

In Fig. 6, a comparison between the acquired patient data and the simulation results is shown for ear 8. As shown in this figure, the simulated and measured results show a very similar trend; however, the model tends to overestimate the width of the region

of high-voltage gradient at neighboring electrodes near the stimulating electrode for certain active electrodes.

4 Conclusion

To the best of our knowledge, this work presents the first high resolution patient specific model that has been created for live CI recipients and compared to *in vivo* measurements. This represents a crucial step toward developing and validating the first *in vivo* patient-specific EAMs. Quantitative analysis of the results has shown that tuning resistivity values of different tissue types for each patient increased the accuracy of our patient-specific EAMs by around 34% points. However, it is important to note that currently we do not have an independent way to verify whether the simulation results are accurate or rather good fits. In the future, we plan to include a nerve model into which estimated voltage values will be input. Then, acquired electrically evoked compound action potential measurements will be compared to the simulated action potentials to verify our results. Accurate *in vivo* patient-specific EAMs will permit more accurately estimating neural stimulation patterns and lead to the selection of better CI mapping parameters, which will ultimately lead to better hearing outcomes with CIs.

Disclosures

This research was performed under an IRB protocol for human data approved by Vanderbilt University. No conflicts of interest, financial or otherwise, are declared by the authors.

Fig. 6 Comparison between the acquired patient data and the simulation results for ear 8.

Acknowledgments

This research was supported in part by Grant No. R01DC014037 from the National Institute on Deafness and Other Communication Disorders. The content is solely the responsibility of the authors and does not necessarily represent the official views of this institute. This work was conducted in part using the resources of the Advanced Computing Center for Research and Education at Vanderbilt University, Nashville, Tennessee. We would like to thank Advance Bionics for providing the research software package that allows patient EFI data measurements.

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Jack H. Noble received his BE, MS, and PhD degrees in electrical engineering from Vanderbilt University, Nashville, Tennessee in 2007, 2008, and 2011, respectively. Since 2011, he has been a research assistant professor in the Department of Electrical Engineering and Computer Science, Vanderbilt University. His primary research interests include medical image analysis, image segmentation, registration, statistical modeling, and image-guided surgery techniques, with emphasis on methods for image-guided cochlear implant interventions.