Image Registration of Cochlear μ CT Data Using Heat Distribution Similarity

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Abstract. Better understanding of the anatomical variability of the human cochlear is important for the design and function of Cochlear Implants. Good non-rigid alignment of high-resolution cochlear μ CT data is a challenging task.

In this paper we study the use of heat distribution similarity between samples as an anatomical registration prior. We set-up and present our heat distribution model for the cochlea and utilize it in a typical cubic B-spline registration model. Evaluation and comparison is done against a corresponding normal registration of binary segmentations.

1 Introduction

Image registration and finding data correspondence is a well known challenge in biomedical image analysis. The choice and performance of the registration model depends highly on the involved imaging modalities, the anatomy of the object, the desired end-goal, etc. [9]. Larger and more complex deformations make it more challenging to set-up the optimal registration procedure. It becomes more difficult for the optimization to avoid local minima as the amount of parameters in the transformation model increases. To efficiently solve the problem it is often required to include additional data pre-processing, prior knowledge, regularization or constraints.

In this study we work with registration of μ CT images of the inner ear, which is the structure controlling hearing and balance. Establishing correspondences between samples is required to understand the anatomical/shape variability, which has uses in a range of interesting clinical applications regarding Cochlear Implants [13]. It can be in a patient-specific context, by advising recipients and surgeons to choose an electrode design suited for the anatomy of the user [12], and/or optimizing the CI-programming based on patient-specific physiological simulations [4]. Description of population-based anatomical variability further

allow manufacturers to explore the general implant design. The inner ear is terminologically divided into two parts - the spiral formed cochlea (for hearing) and the vestibular system (for balance) consisting of three semi-circular canals in a close to perpendicular configuration (see Figure 1). We will focus mostly on the cochlea part in this study, as this to our experience is the more difficult part to register. The challenge is mainly due to the relatively large observable differences compared to the compactness of the spiral. The spiral outer dimensions approximates to $10 \times 8 \times 4$ mm, and on average the cochlea winds 2.6 turns [5] but can approach up to three full turns. This corresponds to a difference in the order of 1-2 mm following the path of the spiral. The separation between the cochlear turns in the same region is typically one order of magnitude smaller. Further, the spiral lacks distinct features to identify corresponding locations. The whole spiral is a tube-like structure (see Figure 1) with a large degree of self-similarity in cross-sections.

Our aim is to set up an image registration procedure for cochlear data. Conventional practice is to start with a global alignment (rigid, affine etc.) followed by a non-rigid step consisting of very local deformations. The common global transformations cannot align cochlear shapes very well, as they cannot take into account the spiral nature of the data. This lack of global fit should be handled by the non-rigid registration instead. The desired non-rigid model should not just expand or reduce the apical part of the spiral to cope with variability in cochlea turning, but instead it should try to readjust the entire spiral. Essentially the model should be able to handle very local deformations while still adhering to a more global structure.

Fig. 1. Left: A slice from a μ CT dataset showing the segmentation of the inner ear. Right: A surface model of the inner ear constructed from the segmentation of a μ CT dataset.

There are different ways to modify the registration model to achieve this, and inclusion of prior-knowledge have been studied previously. An anatomical shape prior can be in form of a statistical shape model [2,6]. However, building shape models is in itself a labor intensive task rivaling if not surpassing the task of the registration, as the prerequisite for building the model is data that is already registered to have correspondences.

In the work of [1] an articulated skeleton model was pre-registered to intra-mouse data studies in order to recover large pose-differences between data acquisitions. Landmark correspondences of the skeleton model were then used to regularize the registration cost function. While in principle it is a useful approach to our case, corresponding landmarks are to our experience difficult to establish coherently and consistently for the cochlea.

It is also possible to do clever preprocessing of the data to obtain an image similarity measure more suited for the registration. In the work of [11] a selection of shape features were calculated from the objects and transformed into vector-valued 2D feature images, that were then registered using a classic image registration formulation. Skeletal features were used to provide the more global similarity between samples, while curvature and convexity features handles local similarity. The principle idea of processing the data to find a new similarity metric is sound and an approach that we follow. Instead of working from meshes and shape features we will work from the images and explore the use of a single image feature to improve our registrations - the heat distribution. Techniques for calculating volumetric maps of 3D heat distributions already exist, and have the potential to provide the required global context to the registration model. Since a heat map can be considered just another type of gray-scale image data, this approach would fit into already existing registration frameworks with little modification.

The purpose of this study is then to test and evaluate deformable registration using a B-spline transformation model on a series of inner ear/cochlear datasets with and without the use of heat distribution similarity in the registration model.

2 Materials and Methods

In this section we provide a more detailed description of the data and its processing, the set up and evaluation of registration models and the computation of heat distributions. In order to conceptualize and test the overall procedure we create and use some simple synthetic 2D images. This data is introduced in Section 2.1 and corresponding registration model described in Section 2.4. Details concerning the cochlear data and the initial processing are found in Section 2.2. The computation of the heat distribution in this data is described in Section 2.3. Finally, the registration models (for both data types) are detailed in Section 2.4 and their evaluation in Section 2.5.

2.1 2D Synthetic Data

Data Generation: Small synthetic 2D images are generated to demonstrate the concept of using maps of heat distributions in a registration model. Two binary 100x100 images, B_i , were created manually containing a foreground spiral region and a background. In order to create a classic gray-scale version of the images (I_i), random noise was added to each pixel. The noise models for both regions were Gaussian, $\mathcal{N}_j(\mu_j, \sigma_j)$. The corresponding volumetric heat distributions (H_i)

were generated simplistically; The apex of the spiral was manually selected as the source. Heat was propagated iteratively with a 4-neighborhood kernel. The heat spreads to previously untouched foreground voxels, and for each iteration the heat is decreased by 1. The synthetic data is presented in Figure 2.

Fig. 2. Synthetic 2D data with I_1 and I_2 showing the two gray-scale images, and H_1 and H_2 the corresponding heat map versions

Image Registration: In short, we initially calculate one rigid transformation that is applied to both of the moving images, i.e. I_2 and H_2 . This is followed by non-rigid registrations between respectively the pair of grayscale and heat map images. The formulation and details on the images registrations are described in Section 2.4. The result of the deformations are visually compared and evaluated.

2.2 Cochlear Data

A collection of $N=17$ dried temporal bones from the University of Bern were prepared and scanned with a Scanco Medical μ CT100 system. The data was reconstructed and processed to obtain image volumes of 48 micron isotropic voxel-sizes containing the inner ear (Figure 1, left).

Image Segmentation: The inner ear border was delineated semi-automatically to obtain a binary segmentation, B_i , of each dataset using ITK-SNAP [14]. The images contain some openings and non-anatomical artifacts that had to be manually handled to obtain comparable segmentations across datasets. A surface model was generated for each dataset using Marching Cubes followed by a surface reconstruction [10] to obtain a well-formed triangular mesh (Figure 1, right).

Initial Rigid Alignment: Before proceeding further we choose to perform an initial registration of the data to bring it into a common space and orientation. We use a rigid transform to remove translational and rotational differences between the datasets while retaining variation in size or scaling.

The initial registration is done with principal component transformations calculated from the extracted surface models. One dataset was chosen as the reference, to which the others were aligned. In short, the mean vertex position, $\bar{p}_i$, of the i -th dataset is subtracted from all vertices translating the center of mass to position (0,0,0). Finding the eigenvectors of the 3-x-3 covariance matrix of the mesh vertex positions (after the translation) provides a rotation matrix to

the principal axes. This essentially corresponds to fitting an ellipsoid to the point cloud of each dataset and aligning the ellipsoid axes, and it works consistently due to the asymmetry of the inner ear shape.

After the initial registration all images were cropped to contain only the cochlea region, since this is the structure of our focus. The first principal axis described above separates the cochlea from the vestibular region. Therefore, the cropping is accomplished easily by splitting each dataset at $x = 0$ (see Figure 1 and 3a).

2.3 Heat Distribution

The usage of heat distribution models for registration of complex anatomical shapes allows the generation of a global similarity between samples regardless of local differences in shape.

Calculating a heat map, H_i , for each dataset is done after the initial registration and is initiated by the placement of a source and sink. The source was manually set at the cochlear apex (see Figure 3a) and the sink was chosen as the inner ear center of mass (i.e. position (0,0,0)). The heat values at the two extremes were fixed. The heat distribution over time in a region is governed by the Partial Differential Equation (PDE)

$$\frac{\partial u}{\partial t} - \alpha \Delta u = 0 \quad (1)$$

which describes the distribution of heat, u , over time, t , in a medium with thermal conductivity α . With Δ being the Laplacian operator $\Delta u \equiv u_{xx} + u_{yy} + u_{zz}$. Assuming α to be one and $t \rightarrow \infty$ we obtain the thermal equilibrium state solution described by the Laplacian equation

$$\Delta u = 0 \quad (2)$$

Solving this PDE (Eq. 2) implies solving a boundary value problem with boundary conditions [3]. Careful assignment of the boundary values can be positive for the registration process. Assigning Dirichlet boundary conditions f to specific anatomical sites $\mathcal{A}$ such as the apex and the center of the cochlea creates a shape metric image that can be used for steering the registration process to an improved solution.

Discrete Laplacian on a Closed Domain: We want to solve

$$\Delta u = 0 \quad u|_{\mathcal{A}} = f \quad (3)$$

for $f = f(x, y, z)$ the boundary values defined at anatomical sites $\mathcal{A}$. All the foreground voxels of a binary image segmentation, B_i , will constitute the domain Ω where the heat diffusion will be applied. By applying the Laplace discrete operator to all image voxels, Equation 2 can be written in matrix form as $\mathbf{A}u = 0$. The matrix $\mathbf{A}$, called the graph Laplacian or adjacency matrix, encodes the

(a) Heat distribution at the surface of the cochlear. The source point in the apex is marked in black.

(b) Discrete voxel lattice. Central voxel highlighted in red. Neighbors in x , y and z axis are at distances δx , δy , δz respectively.

Fig. 3. Heat distribution for 3D data

neighboring relations between voxels. This is because we in the voxel image lattice (see Figure 3b) can approximate the discrete Laplacian by computing the second order finite differences.

The solution to the Laplacian with Dirichlet anatomical conditions is obtained by solving the system of equations $\mathbf{A}u = \mathbf{b}$, with $\mathbf{b}$ being a row matrix encoding the boundary values at $\mathcal{A}$ given by:

$$f(x, y, z) = \begin{cases} 1, & \text{for } (x, y, z) \in \text{cochlear apex (source)} \\ 0, & \text{for } (x, y, z) \in \text{cochlea center of mass (sink)} \end{cases} \quad (4)$$

Although $\mathbf{A}$ and $\mathbf{b}$ are sparse by definition, solving the system of equations with standard techniques might be unfeasible. Given that $\mathbf{A}$ is symmetric and positive definite we can use the Preconditioned Conjugate Gradient method using the Incomplete Cholesky Factorization of $\mathbf{A}$ as a pre-conditioner [7]. This allows solving the system iteratively in a short time and with a low memory footprint. For the generation of the map to be useful, the cochlea segmentation must ensure that the cochlear turns does not intersect each other in the segmentation.

Two Step Heat Map Generation: When solving the entire 3D domain using just a sink and a source voxel the decay of the heat function is very fast to our experience. We obtain a very small heat gradient throughout the cochlea and the resulting heat map is too flat to be used properly. We improve the heat map by applying a two step process for the generation of the map. First, we compute the heat map with a single voxel sink and source point, but using only the boundary voxels of the cochlea segmentation as the diffusion domain. This ensures that heat spreads over a reduced number of voxels, generating a boundary heat map with better gradient and slower heat decay. Second, the resulting boundary heat

map is used as boundary condition for a second heat propagation over the entire cochlea segmentation domain.

2.4 Deformable Image Registration

The work-flow for non-rigid image registration is quite standard. The (N-1) moving datasets are registered to a chosen reference, following the formulation and framework of the `elastix` [8] toolbox.

The registration of the moving dataset, I_M , towards the fixed image, I_F , is formulated as a (parametric) transformation, T_μ , where the vector μ containing the p -parameters of the transformation model are found as an optimization of the cost function, $\mathcal{C}$.

$$\hat{\mu} = \arg \min_{\mu} \mathcal{C}(T_\mu, I_F, I_M) \quad (5)$$

The transformation model used in this paper is the cubic B-spline grid in a multi-resolution setting. The spacing between grid points follow a gradually decreasing schedule to start with a rough alignment that is slowly refined. The particular schedule used was (24, 16, 8) voxels.

Binary Set-up: We make a 'normal' registration between the segmentation volumes, to have something to compare our proposed usage of heat distributions against. The registration is done between the binary segmentation volumes, B_i , rather than the gray-scale volumes, I_i , for two reasons. First, the μ CT data contain smaller artifacts and certain weakly contrasted edges, that were dealt with during the segmentation (Section 2.2). Secondly, the registration should not be influenced by the anatomical differences in the surrounding bone structure. The following cost-function was used for the registration:

$$\mathcal{C}_1 = \alpha \cdot \mathcal{S}_{\text{Sim}}(\mu, B_F, B_M) + (1 - \alpha) \cdot \mathcal{P}_{\text{BE}}(\mu) \quad (6)$$

where α is a weight parameter in the interval [0,1], here chosen to 0.9 by means of experimentation. For the similarity term, $\mathcal{S}_{\text{Sim}}$, the sum of squared differences (SSD) is chosen. The term $\mathcal{P}_{\text{BE}}$ is the energy bending regularization used to penalize strong changes and foldings in the transformation.

Heat-map Set-up: In order to use the similarity of heat distributions in the registration, the cost function can essentially remain the same, simply replacing the underlying image data from the segmentations, B_i , to the heat maps, H_i . By experimentation we set $\alpha = 0.1$, while all other settings remains un-altered in order to provide a fair comparison between the two set-ups.

$$\mathcal{C}_2 = \alpha \cdot \mathcal{S}_{\text{Sim}}(\mu, H_F, H_M) + (1 - \alpha) \cdot \mathcal{P}_{\text{BE}}(\mu) \quad (7)$$

Table 1. Statistics of registration evaluation metrics, reported as the mean $\pm$ 1 std. Model 1 and 2 refers respectively to Eq. 6 (binary) and Eq. 7 (heat).

Metric	Dice Score	Mean Err. [mm]	Max Err. [mm]	Apex Err. [mm]
Model 1	$0.96 \pm <0.01$	$0.07 \pm <0.01$	0.54 ± 0.13	0.97 ± 0.58
Model 2	$0.99 \pm <0.01$	$0.05 \pm <0.01$	0.43 ± 0.12	0.66 ± 0.58

Registration Model - 2D Synthetic Data: The two registrations models described above (Eq. 6 and Eq. 7) are also applied in the case of synthetic 2D data with some minor modifications. The cost function terms remains unaltered, i.e. the SSD was used for the similarity metric with added bending energy regularization. However, the weighting parameter was set to $\alpha = 0.7$ in both cases, and only a single resolution was used with no smoothing and a B-spline grid point spacing of 3 pixels.

2.5 Evaluation

We are interested in comparing the registration results, $\hat{\mu}_j$, from using either model 1 (Eq. 6) or model 2 (Eq. 7) with different metrics. For a voxel based score we calculate the Dice Coefficient between the deformed binary volume, $B_i(T_{\mu_j})$, and the reference, B_{Ref} . The ground truth mesh, M_i , can be compared to the deformed reference mesh, $M_{\text{Ref}}(T_{\mu_j})$, from which we calculate the two-sided mean surface error and Hausdorff distance.

Since the above mentioned evaluation metrics are very generic and global we also use the apex error. A landmark is manually placed in the apex in all datasets, and we calculate the euclidean distance between the anatomical correspondence.

3 Results

2D Synthetic Data: The results with the synthetic data are shown in Figure 4. The 'normal' intensity registration (model 1), μ_I , was unable to fully capture

Fig. 4. Registration results on the synthetic 2D data. From left to right: The reference heat distribution H_1 , The moving heat map, H_2 , after transformation using the registration results, i.e. $H_2(T_{\mu_I})$ and $H_2(T_{\mu_H})$. Finally, the difference between the results, i.e. $|H_2(T_{\mu_I}) - H_2(T_{\mu_H})|$.

the full spiral with the given settings. When comparing the subtraction image of the two deformed heat maps, it should be noted that there is a difference throughout the entire spiral - suggesting that the registration based on the heat maps, μ_H , provides a more global twist of the spiral.

3D Cochlea Data: The quantitative evaluation is presented in Figure 5a and Table 1. The visual differences between the two registration models are illustrated in Figure 5b for a single case. In three cases the deformations resulted in an anatomically incorrect warping, where for instance the separation of the cochlea turns was not preserved. It is not apparent from the evaluation metrics, but very clear from a visual inspection of those samples.

(a) Graph of the sample wise improvement between model 2 (heat) and model 1 (binary) in evaluation scores.

(b) Comparison of deformations. Left: Model 1 (binary) Right: Model 2 (heat). Blue transparent surface is ground truth and gray is the fitted surface.

Fig. 5. Results of the registration of 3D data

4 Discussion and Conclusion

The contribution of this study is a presentation and evaluation of using heat distribution similarity as a way of aiding image registration of cochlear samples. For now we have demonstrated its ability to add flexibility to the transformation and to improve registration accuracy. However, there are other important aspects to consider. Introducing additional pre-processing obviously adds more computations and processing time. It is likely to involve extra parameters to tune and it may contribute with noise and uncertainty to the registration. Our approach rely heavily upon a good segmentation of the data, which required a lot of manual labor. The additional processing time for calculating the heat-distributions were not a substantial issue considering the observed benefits. There are some factors that may affect the usage of the heat distributions. First, the manual placement of the source landmark inherently carries some uncertainty, but it is not immediately considered problematic. Secondly and more importantly, is the effect of the heat gradient throughout the cochlea. If the change in heat is too small, it might not have the desired guiding effect upon the registration, and too much change might force very strong deformations. Finding the right balance should be part of our future work. It is further important to note that the transformation model remains the same with this pre-processing strategy. The registration between the original images (segmentation or gray-scale) have the potential to find the same transformations as with the heat maps included. Without the heat distributions, the convergence rate may be slower and more levels of resolution and tweaking of registration parameters is required. The data pre-processing can have the added benefit of easing the registration set-up.

Our evaluation of the method is based mostly on global metrics. Their usefulness is limited, as they are hardly able to show whether a registration is successful or not. For that we need more anatomically meaningful evaluation metrics like the apex error. This error is very local, so it does not reveal if the desired deformation throughout the cochlea is achieved. The lack of consistent landmarks or uniquely identifiable locations on the cochlear makes it challenging to perform better quantitative evaluation of the registration. It would require setting up larger elaborate methods, exceeding the scope of this study. What we conclude from the results, is that heat distribution similarity adds flexibility to the registration, thereby allowing turning of the cochlea apex to be captured in a more anatomically correct manner.

Considerations can also be made to the chosen registration model. We work with the B-spline grid as the transformation model which has some limitations. Choosing a fluid- or optical flow-based model [9] could potentially be more suited for this kind of spiral anatomy.

Working on the binary data, better registrations were achieved with little regularization ($\alpha = 0.9$) in order to allow larger deformations. But since there is nothing to guide the transform to the anatomical correct place, then the method falls short. The maps of heat distributions provide global similarity to the otherwise locally defined B-spline transformation. It adds a lot of flexibility to the procedure - in fact too much. Strong regularization ($\alpha = 0.1$) was required

to ensure reasonable deformations. Even though the results look very positive, our experience is that the procedure is not stable. It is likely to run into very large unreasonable deformations, that for instance goes across the separation of the cochlea turns. Essentially, we have a difficulty in applying enough and/or correct regularization. This is a problem to be addressed in future work. Additional regularization could for instance be forcing local rigidity in the bony structures surrounding the cochlea.

Of the 16 tested registrations, we observed three failed cases where deformations were unreasonable. These datasets are the cases least similar to chosen reference data. The issue is therefore not only lack of regularization, but part of the solution could also be by introducing coarser resolution levels in the registration. Further, this study was run on down-sampled data. The data is originally in a higher resolution, where the separation between cochlea turns is more clear. Using this data may help prevent the unreasonable deformations.

To conclude, we have presented a data pre-processing strategy for aiding non-rigid image registration using similarity of heat distributions. We have tested the idea on synthetic 2D data and on μ CT of the cochlea, and demonstrated its ability to provide a global guidance and flexibility to the registration procedure.

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