Julie Shade
Computer Integrated Surgery II
Critical Review/Seminar Presentation
March 9, 2017

Deformable Registration of Organic Shapes via Surface Intrinsic Integrals: Application to Outer Ear Surfaces
Authors: Sajjad Baloch, Alexander Zouhar, and Tong Fang

<u>Introduction</u>

In our project, we aim to identify corresponding regions of non-contoured soft tissue in all patients in a database of head and neck CT images for refined dose-toxicity analysis. We will first implement a deformable registration method to register contoured anatomical regions between patients, then create a statistical atlas of the "average patient" by iterative bootstrapping or another method as appropriate, validate the predictive power of this atlas, and finally use the atlas to identify arbitrary corresponding regions in all patients. We assume that we can extrapolate the necessary information about anatomical correspondences by determining geometric correspondences between surfaces. However, this may not always be true, as the authors of the first paper I chose to review point out. This paper, *Deformable Registration of Organic Shapes via Surface Intrinsic Integrals: Application to Outer Ear Surfaces* by Baloch et al. proposes a novel method of deformable registration that addresses several of the challenges in registering organic surfaces, then validates the proposed method via registration of outer ear surfaces. The second paper I will review, *Sparing the Region of the Salivary Gland Containing Stem Cells Preserves Saliva Production After Radiotherapy for Head and Neck Cancer* by Luijk et al., presents an example of the type of question we hope to be able to answer with our framework. I will not go into much detail about the methods, as they are not relevant to our project, but will discuss how our project could be used to validate a hypothesis like the one presented in the paper.

<u>Summary</u>

Deformable registration methods have been developed for registration of organic surfaces, but Baloch et al. are unhappy with their limitations. Primarily, they point out that anatomical correspondences are not necessarily the same as geometric correspondences and that the current popular methodologies do not take into account the topology of the surface as well as they should. They propose a novel deformable registration method based on a complex geometric and anatomical surface descriptor and suggest that this method will address some of the challenges of anatomically relevant, detailed registration of organic surfaces. In the second paper, Luijk et al. suggest via animal and human studies that a specific area of the parotid gland contains stem cells and may be critical to avoid in radiotherapy to avoid decreased saliva production (xerostomia).

<u>Technical Approach</u>

Baloch et al. propose a deformable registration method that begins with rigid registration between two surfaces, then progressive deformation of the registered surface based on several different types of anatomical and geometric landmarks. The overall objective is to find a diffeomorphic transformation h such that $M_s \rightarrow h(M_T)$ where M_s represents the source anatomy and M_T represents the target anatomy. The transformation h should minimize the bending energy, $E(h) = \omega_e E_e(h) + \omega_i E_i(h)$ where $E_e(h)$ represents the external energy and $E_i(h)$ represents the internal energy. The external energy is defined as:

$$E_e(h) := \gamma_G E_e^G(h) + \gamma_F E_e^F(h)$$

γ_G, γ_F are weights (if $\gamma_F = 0$, only consider geometric features) and E_e^G, E_e^F are energies of geometric and anatomical components. E_e^G has 2 components: global shape $E_e^S(h)$ and local/regional geometry $E_e^F(h)$. The first component, $E_e^S(h)$, uses Geodesic Distance Integrals (GDI) to describe the global shape/topology. They are defined at each point on the surface as:

$$S(u) := \int_{x \in \mathcal{M}} g(u, x) d\mathcal{M}.$$

The second, $E_e^F(h)$, is a feature vector, which is defined at each point as:

$$u \in M : \boldsymbol{\alpha}_l(u) : (\kappa_\mu(u), \kappa_G(u), \kappa_{pc1}(u), \kappa_{pc2}(u))$$

In which κ_μ = extrema of mean curvature, κ_{pc1} = minima of minimum principal curvature, κ_{pc2} = maxima of maximum principal curvature, κ_G = minima of Gauss curvature. Each feature in this vector gives a different type of information. For example, κ_G helps capture saddle points. This is calculated at multiple scales to give $A(u) = [\boldsymbol{\alpha}_r(u; s_1), \ldots, \boldsymbol{\alpha}_r(u; s_k), S(u)]$, which helps resolve conflicts between the anatomy of the source and the target.

After definition of these features, the registration is performed in four stages. In the first stage the source is rigidly registered to the target. The following three stages involve anatomical information from *Canonical Ear Surfaces,* the GDIs, and the feature vectors. In each stage, components $\sum \|h(l_S^i) - l_T^i\|$ are identified (initial guess h is output of previous stage, l is landmark of interest) and the following steps are carried out:

1. Landmarks on source surface are identified ("geometrically interesting" points, points which define anatomical landmarks, or all points for the global stage)
2. Each landmark $u_s \in D$ on the source surface is mapped to landmark $u_t \in M$ on the target surface.
   - D_s deformed under h^k to yield new point set $h^k(D_s)$, each point $h^k(u_s)$ mapped to points $u_t \in M$ through closest point projection
   - Neighborhood defined around u_t, find point in neighborhood which minimizes $v^* = argmin(\|A_s(u_s) - A_T(v)\|)$

3. Corresponding points define displacements: $d^k = M_T(v^*) - M_S(u)$
4. Find differential displacement with small $\delta > 0$: δd^k
5. Deform surface points by corresponding differential displacement: $h^{k+1}(u) = h^k + \delta d^k(u)$

Luijk et al. investigate whether a certain region of the parotid gland that contains stem cells is more critical to avoid in radiotherapy. They perform a c-Kit assay on human and rat parotid glands *ex vivo* to determine the locations of the stem cell dense regions. They irradiate subsections of the parotid gland in rats and tracked their saliva production before and after radiation. They also analyze the predictive power of the dose to different sub-volumes of the parotid gland in humans on saliva production before and 1 year after radiation in 74 human patients with head/neck tumors by 10-fold cross-validation analysis.

Results

Baloch et al. validate their method by registration of outer ear surfaces. They collect ear scans from 17 patients, select one at random to represent the target patient, and register the other 16 patients to this target twice, with the proposed method and a rigid registration method developed previously by the same authors in [3]. The authors present error maps for qualitative comparison of these two registration methods, in which one can see that there is less error using the proposed method.

They also validate the anatomical correspondence of the registered surface to the target surface. They ask an "expert" to label the anatomy on all 17 surfaces, then register them and determine the overlap in anatomical areas as:

$$\frac{(Area_{label} \cap Area_{GT})}{(Area_{label} \cup Area_{GT})}$$

$Area_{GT}$ is the area of the segmented source surface after registration and $Area_{label}$ is the area of the labeled region on the target. The average value of this measurement is .94, indicating a large amount of overlap. Finally, they analyze the accuracy of the entire surface descriptor using a series of registrations in which different components of the descriptor are excluded. From the figures provided, the registrations performed with the complete surface descriptor (anatomical information and both components of geometric information) appear to have very little error compared with registrations that only use part of the descriptor.

Luijk et al. find that there is a stem-cell dense region of the parotid gland in rats and humans located near the ducts. They find that irradiation of the stem cell containing region of the parotid gland in rats leads to more of a decrease in saliva production after radiation and decreased regeneration of the parotid gland (less improvement in saliva production over time) compared to irradiation of the whole parotid. They also find that, in humans, radiation dose to this stem cell containing region of the parotid is more predictive of decrease in salivary function after treatment than radiation does to the entire parotid.

<u>Analysis</u>

The paper by Baloch et al. proposes a method with fairly detailed mathematical steps that appears to solve some of the problems involved with registration of complex organic surfaces. The idea of incorporating multiple types of surface landmarks and assessing these at different scales to iteratively deform the surface seems like a good one, and from the figures provided, the registrations performed with this method appear to be less error-prone than the registrations performed with a rigid method. There are many figures where one can qualitatively assume, from relative amounts of different colors on the surfaces representing different amounts of error, that this registration method is accurate on its own.

However, this paper has many limitations, especially in its analysis of the results. First, the method used for quantitative analysis of the labeling is not explained clearly. The authors had an "expert" (who they do not state the qualifications of) label different areas of the ear anatomy on all 17 ear surfaces, registered 16 of them to the one designated as the target, and then calculated how much the area of the registered source overlapped with the area of the target for each part of the anatomy. However, the actual description of this method was not clear enough that we could easily reproduce it. Also, the authors only state the average of their metric, with no information about variance or accuracy for different parts of the ear anatomy.

Aside from one average of an error measurement, the authors present no *quantitative* data showing the accuracy or efficiency of their method, on its own or in comparison with other methods. There is no information at all about the efficiency/speed of this method, which would be useful since this method appears to be more computationally involved than other deformable registration methods. The only comparison presented is with a rigid registration method developed by the same authors, which appears to show a qualitative improvement in registration accuracy [3]. Since the authors claimed in their introduction that popular deformable registration methods have limitations that are resolved by their method, some data showing improvement over the methods criticized by the authors would be useful in justifying the merit of their registration method. To their credit, the authors make no claim that their registration method is better than others, only that their feature vector is more distinguishing and that the incorporation of anatomical priors allows for anatomical correspondence. These statements may be theoretically true, but the authors do not prove that this leads to a "better" method. Quantitative data showing an improvement in accuracy or an improvement in efficiency over other *deformable* registration methods would greatly strengthen the paper.

The generalizability of the method presented is questionable. The method relies on previously defined anatomical regions of the ear, which may not exist for all anatomical surfaces. The authors state how to exclude the anatomical stage of the deformation in their algorithm if one does not have this information, but do not include statistics on how this affects the overall accuracy of the registration. In addition, the authors only test the method on registration of very small surfaces: there is no suggestion of how surface size/complexity would affect the usefulness

of this method. It is possible that this method would not be feasible for larger surfaces because of the number of complex calculations required for each point on the surfaces.

Luijk et.al present a very different type of experiment. Their paper shows evidence that an increased radiation does to the stem-cell containing region of the parotid gland in rats causes a decrease in saliva production and reduced regeneration of saliva production. They partially validate this hypothesis in 74 human patients by analyzing the correlation between the saliva production 1 year after radiotherapy and the dose to the whole parotid and just the stem-cell containing region. Their predictive model is relatively good, with a r = .65 correlation between predicted and actual change in saliva production. However, the r-value for the predictive power of the whole-parotid dose is .60, which is not much lower. The authors did not investigate whether other regions in the human parotid are more or less predictive of adverse effects. Although this may indicate that the dose to the stem-cell region is not actually significantly better at predicting adverse effects, the evidence presented in this paper is compelling and warrants further investigation in a larger data set to develop an improved predictive model. Members of our group are currently working on this problem using manual segmentation of the parotid to analyze the region-dependent dose-toxicity, to either support or counter the results in this paper. Our project hopes to provide our group the framework needed to automatically detect certain regions of the head and neck that are more or less predictive of adverse effects, without the need for manual segmentation of these regions.

References

1. Baloch, S., Zouhar, A., & Fang, T. (2011). Deformable Registration of Organic Shapes via Surface Intrinsic Integrals: Application to Outer Ear Surfaces. *Medical Computer Vision. Recognition Techniques and Applications in Medical Imaging Lecture Notes in Computer Science,* 11-20. doi:10.1007/978-3-642-18421-5_2
2. Luijk, P. V., Pringle, S., Deasy, J. O., Moiseenko, V. V., Faber, H., Hovan, A., ... Coppes, R. P. (2015). Sparing the region of the salivary gland containing stem cells preserves saliva production after radiotherapy for head and neck cancer. *Science Translational Medicine, 7*(305). doi:10.1126/scitranslmed.aac4441
3. Zouhar, A., Fang, T., Unal, G., Slabaugh, G., Xie, H., & Mcbagonluri, F. (2006). Anatomically-Aware, Automatic, and Fast Registration of 3D Ear Impression Models. *Third International Symposium on 3D Data Processing, Visualization, and Transmission (3DPVT'06).* doi:10.1109/3dpvt.2006.29