ANATOMICAL VARIABILITY OF ORGANS VIA PRINCIPAL FACTOR ANALYSIS FROM THE CONSTRUCTION OF AN ABDOMINAL PROBABILISTIC ATLAS

Mauricio Reyes[1], Miguel A. Gonzalez Ballester[2], Zhixi Li[3], Nina Kozic[1], See Chin[3], Ronald M. Summers[3], Marius George Linguraru[3]

[1]ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland
[2]Alma IT Systems, Barcelona, Spain
[3]Radiology and Imaging Sciences, Clinical Center, National Institutes of Health, Bethesda, MD, USA
lingurarum@mail.nih.gov

ABSTRACT

Extensive recent work has taken place on the construction of probabilistic atlases of anatomical organ. We propose a probabilistic atlas of ten major abdominal organs which retains structural variability by using a size-preserving affine registration, and normalizes the physical organ locations to an anatomical landmark. Restricting the degrees of freedom in the transformation, the bias from the reference data is minimized, in terms of organ shape, size and position. Additionally, we present a scheme for the study of anatomical variability within the abdomen, including the clusterization of the modes of variation. The analysis of deformation fields showed a strong correlation with anatomical landmarks and known mechanical deformations in the abdomen. The atlas and its dependencies will be freely and readily accessible for the scientific and medical community, as a potentially important research tool for abdominal diagnosis, modeling and soft tissue interventions.

INDEX TERMS: *probabilistic atlas, principal factor analysis, registration, clusterization, anatomical variability.*

1. INTRODUCTION

We are working on the development of an abdominal probabilistic atlas, which will be freely available for statistical and structural analysis and as a teaching tool in the scientific and medical community. The atlas allows the study of shape and location variability for segmentation, registration, diagnosis, biomechanical analysis and soft tissue modeling. Moreover, a multi-organ approach provides comprehensive information on inter-organ spatial relationship and interaction for pre-operative planning and guidance, and toward full-body medical diagnosis.

Recently, much work has taken place on the construction of probabilistic atlases of anatomical organs, especially the brain [4] and the heart [3] and their application in registration and segmentation. Particularly, the construction of an unbiased atlas was presented in [2], to build the average shape of brain structures. These techniques are leading the way into more comprehensively studies of groups of organs, such as the abdomen; to date, a four-organ probabilistic abdominal atlas has been constructed [5].

We propose an atlas of ten major abdominal organs (liver, spleen, 2 kidneys, 2 adrenal glands, gallbladder, pancreas, stomach and aorta), which retains structural variability by using a size-preserving affine registration, and normalizes the organ locations to an anatomical landmark (xiphoid). The spatial relationship between organs is preserved and organs are modeled in the anatomical (not image) space. Restricting the degrees of freedom in the transformation, the bias from the reference data is minimized, in terms of organ shape. Preserving the size of organs and normalizing their position to that of the xiphoid, there is no bias toward the reference size and location. The modifications in the proposed atlas construction method are new and well-suited for clinical applications, as exemplified by results on clinical data.

Independently, the analysis of shape variability of anatomy is of key importance in clinical studies; abnormality in shape is often related to disorders. Most existing statistical shape analysis methods rely on Principal Component Analysis (PCA) to build a compact model of principal modes of variation from a training set [2]. The deformation modes described by PCA can be sometimes difficult to interpret or correlate with intuitive shape descriptions employed by clinical partners, and are normally combinations of several localized shears, twists and rotations. In previous work, another decomposition technique called Principal Factor Analysis (PFA) was used for morphological analysis in MRI data [6]. The results showed the added value of PFA as a simpler analysis of shape variability by intuitively distinguishable factors.

The homogeneity of the deformation field across the surface for each mode of deformation offers a degree of interpretability of shape variability decomposition. Hence,

this paper introduces a technique to cluster a vector field describing a mode of deformation across a surface. Our method assesses the interpretability of the decompositions by PFA (and can be applied to other factor analysis techniques) in conjunction with anatomical variability.

Thus, complementary to the construction of an abdominal probabilistic atlas, we also present a scheme for the study of anatomical variability within the abdomen, including the clusterization of the modes of variation. Results suggest that different modes of decomposition offer complementary information on anatomy. As exemplified in the paper, the study of anatomical variability shows a strong correlation with clinical observations regarding the analyzed organs.

2. METHODS

For the generation of the atlas and analysis of anatomical variability, 10 abdominal CT scans of patients with no abnormalities in the ten studied organs were used: 5 male and 5 female (mean age of 59.9 years: 60.6 for male and 59.2 for female). Data were collected with a LightSpeed Ultra scanner (GE Healthcare) and image resolution ranged from 0.54 x 0.54 x 1.0 mm^3 to 0.77 x 0.77 x 1.00 mm^3. The liver, spleen, left kidney, right kidney, left adrenal gland, right adrenal gland, gallblader, pancreas, stomach and aorta were manually segmented in the CT scans.

The methods can be divided into two major steps: atlas construction and analysis of anatomical variability. It was implemented using Visual C++ 8.0 (Microsoft) and ITK 3.4.

2.1 Atlas Construction

For the construction of the atlas, a random image from the database is set as reference J, and all other subject data, addressed as images I, are registered to the reference. For all subjects, masks of the manually segmented organs were generated. Then each organ was registered individually to its corresponding mask in the reference set.

Previously, non-linear registration was used for the generation of an abdominal atlas [5]. In order to retain a higher level of organ variability in the atlas, we propose to restrict the degrees of freedom of the registration algorithm, as well as the size and relative position of each studied organ in the abdomen. Organ coordinates in each subject were normalized relative to the position of the xiphoid. Hence, we employed a modified affine registration method based on normalized mutual information M [9], where $p(I,J)$ is the joint probability distribution of images I and J, and $p(I)$ and $p(J)$ their marginal distributions, as in Equation (1). No scaling was permitted during the affine deformation and the physical coordinates of organs (image independent) were used, normalized by the xiphoid. Finally, organs were translated in the atlas to the location of the average normalized centroid.

$$M(I \mid J) = \frac{p(I) + p(J)}{p(I,J)}. \quad (1)$$

For the analysis of anatomical variability, a more flexible intra-subject registration is required to compensate for the residual deformation not covered by the affine registration used in the construction of the atlas. We employed the non-linear registration algorithm based on B-splines [8].

2.2 Anatomical Variability by Principal factor Analysis

Unlike PCA, which is a projection model, PFA can be considered as a generative model in factor analysis. Generative models estimate the density function that is assumed to have generated the data, under constraints that restricts the set of possible models to those with a low intrinsic dimensionality. Whereas PFA models covariance between variables, PCA models the total variance in the data and as such it determines the factors that account for the total (unique and common) variance in the set of variables. Contrarily, PFA determines the least number of factors that can account for the common variance (correlation). For more details and illustrative examples on PCA and PFA, please refer to [6].

2.3 Clustering

The result from the generation of the statistical models using PFA is a point distribution model (PDM). The PDM is able to describe the shape variability of the structure as a surface or point cloud embedded in the 3D space. Let $P = \{p_1, p_2, \ldots, p_M\}$, $M \in \mathrm{N}^*$, be a set of points that generate a surface in a domain $D \in \mathrm{R}^3$. For each $p_i \in P$, $i = 1, \ldots, M$, a vector V_i is computed as

$$V_i = v_i^+ - v_i^-, \quad \text{with} \quad v_i^+ = \bar{m} + \alpha_j \Phi_j \quad \text{and} \quad v_i^- = \bar{m} - \alpha_j \Phi_j. \quad (2)$$

v_i^+ and v_i^- denote the PDM model generated from PFA, where $\bar{m}$ corresponds to the mean shape and α_j is a scaling value for the j^{th} principal mode of the eigen-matrix ϕ_j.

The clusterization across the surface, was initially inspired by the work presented in [7], which was conducted for vector field segmentation of moving objects in 2D image sequences. We extend this work to unstructured 3D displacement vector fields across a surface. The clusterization process can be seen as a minimization problem of the following functional over a region or domain $\Omega \subseteq D$

$$C = \arg\min_{\Omega} J(M(\Omega)), \quad (3)$$

where J is an energy with two components: a first component takes into account the colinearity between vectors within the domain Ω and the predominant vector direction V_Ω in Ω, weighted by the vector length in order to give more weight to regions having a stronger deformation; the second term acts as a maximal area constraint.

$$J(M(\Omega)) = \int_{\Omega} \left(\frac{|V_\Omega \times V(m)|}{|V(m)|} \right)^2 \frac{L_{\max}}{|V(m)|} dm + \gamma \int_{D \setminus \Omega} dm, \qquad (4)$$

where γ is a real value and $L_{max} = max_D\{|V(m)|\}$. The dominant vector direction V_Ω is found as the highest eigenvalue of the following matrix [7]

$$M(\Omega) = \int_{\Omega} V(m) V^t(m) dm, \qquad (5)$$

The minimization of Equation (3) is done by a hierarchical scheme, where each pattern is first considered as a cluster and then iteratively visited and agglomerated according to the energy measure J, until all points on the surface have been analyzed.

The number of clusters is not pre-set in our application. Through functional minimization and the tradeoff between sparseness of the deformations and clusters size, the algorithm provides a clusterization of the 2D surface embedded in the 3D space (we emphasize again the tailoring of this approach compared to [7]) with no preconditioning on the expected number of clusters. Our method was designed to assess the interpretability of the decompositions by PFA in conjunction with anatomical variability.

3. RESULTS

Given the relative rigidity of the kidneys, a rigid transformation was sufficient to compute the atlas probabilities of the left and right kidneys. For the other eight abdominal organs, modified affine registrations were used, as described in Section 2. The probabilistic atlas constructed using the 10 subject dataset is shown in Figure 1.

The results of the anatomical variability analysis focus on the identification and interpretation of deformation modes to better understand the modeling and biomechanical characteristics of abdominal organs. In Figures 2 and 3 we show sets of clusters for the first three modes of variation from PFA for three organs: the spleen, right kidney, and pancreas. Each image is a set of points in space with random colors representing each cluster. The number of clusters reflects the degree of homogeneity of the deformation fields per principal mode.

As expected, the clusters of deformations are related to the anatomical and mechanical constraints in the abdomen. The clusters of modes of deformation might be explained by abdominal ligaments that join the spleen, liver and, stomach, or the presence of large blood vessels and contact with neighboring organs. For example, in Figure 2, the clusters of the PFA first mode of the spleen separate at the entry of the splenic vein, and the second mode clusters reflect the positions of the gastric, colic and kidney impressions and the biomechanical deformation associated with them. Similarly, the analysis of the kidney modes of variation in Figure 3(a) emphasizes the superior pole located against the liver, and the inferior pole with the abdominal muscles impression, with an anterior-posterior separation at the location of the renal pelvis and blood vessels. In Figure 3(b) there is a clear correlation between the clusters of the first mode and the anatomical boundaries between the head, body and tail of the pancreas; the head is the best-anchored part of the organ and the tail the most mobile.

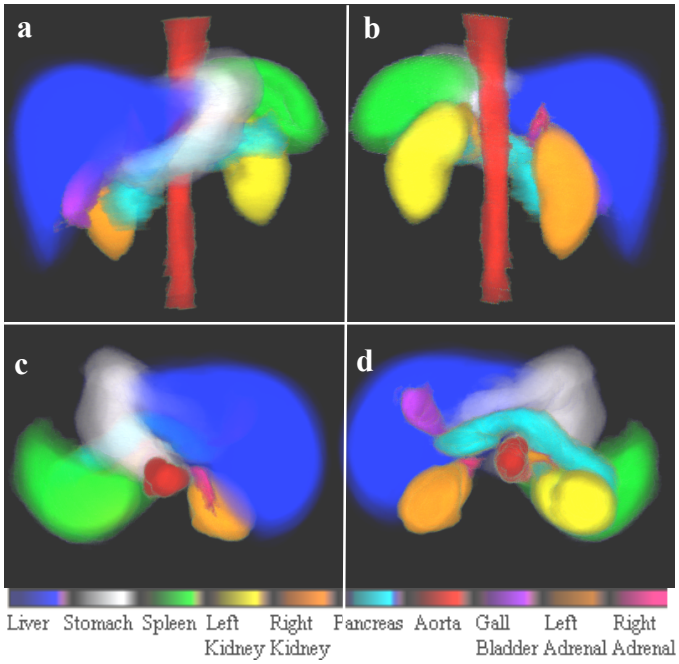

Figure 1: 3D 10-organ probabilistic abdominal atlas. We show (a) frontal, (b) back, (c) top and (d) bottom views of the atlas, along with an organ colormap. Dark shades correspond to low probabilities and bright colors to high probabilities.

The anatomical variability analysis is correlated with key anatomical landmarks of the studied organs, which can be input as physical and biomechanical constraints in the analysis of the abdomen. The examples shown in this paper include a more rigid abdominal organ, the kidney, a soft organ, the spleen, and the pancreas, an organ with a fixed head and a movable tail. The analysis of the remaining seven studied abdominal organs was also performed, but not presented in this paper due to the limited space.

Mode 1 Mode 2 Mode 3

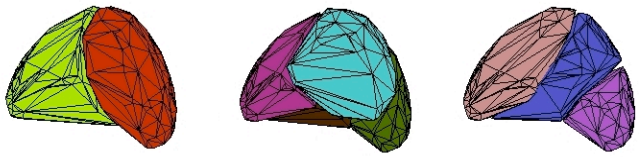

Figure 2: Clusterization results for the first three modes of anatomical variability of the spleen using PFA. Clusters colors are random.

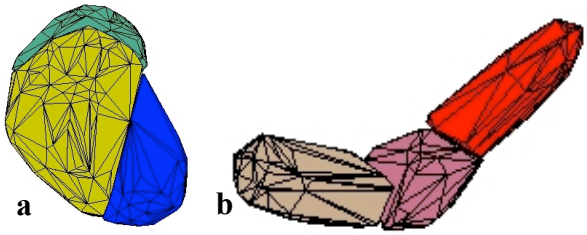

Figure 3: Clusterization results for the first mode of anatomical variability of (a) the right kidney and (b) the pancreas, using PFA. Clusters colors are random.

4. DISCUSSION

The paper introduces a probabilistic atlas of ten abdominal organs to assist researchers with the statistical and structural analysis of the abdomen. The atlas will provide a manually-segmented testing set of the ten organs (liver, spleen, kidneys, adrenal glands, gallbladder, pancreas, stomach and aorta) for the validation of algorithms. The applications of the atlas should provide new prospects for scientists and clinicians interested in abdominal anatomy and biomechanics, inter-subject variability, diagnosis and the evaluation of organ- and abdominal-based disorders.

A clusterization technique aimed to quantitatively study the interpretability characteristics of PDM/PFA was further presented. We contend that shape variability decomposition is easier to interpret using clusters of regular or homogeneous patterns of the shape deformation on the surface. The analysis of deformation fields showed a strong correlation with anatomical landmarks and known mechanical deformations in the abdomen. Clinical applications of the method include, the development of registration techniques based on uncertainty and sensitive to the organ shape and rigidity. The ability to characterize shape deformation in terms of its preferred direction and the region of interest where this deformation is predominant could greatly aid in the segmentation of soft tissue from incomplete data.

The results of the anatomical variability analysis are preliminary and focus on the identification and interpretation of deformation modes to better understand the modeling and biomechanical characteristics of abdominal organs and soft tissue in general. They will be expanded to the analysis of the abdomen deformation, beyond organ-based analysis. Nevertheless, the results in this paper give an overview of the wide range of potential analyses that can be extracted from the analysis of the abdominal atlas.

Future work will focus on the potential of the atlas to become an important reference and statistical tool for the analysis of normal and abnormal soft tissue. We will expand our analysis of anatomical variability from the organ level to the abdominal level. Upon the completion of the atlas and its dependencies, it will become freely and readily accessible for the scientific and medical community.

ACKNOWLEDGEMENT

This work was supported by the Intramural Research Program of the National Institutes of Health, Clinical Center.

REFERENCES

[1] Fodor, I.: A survey of dimension reduction techniques. Lawrence Livermore National Laboratory Technical Report no. UCRL-ID-148494 (2002)

[2] Joshi, S. Davis, B. Jomier, M. Gerig, G.: Unbiased diffeomorphic atlas construction for computational anatomy. NeuroImage, Vol. 23(1) (2004) S151-S160

[3] Lorenzo-Valdes, M. et al.: Segmentation of 4D cardiac MR images using a probabilistic atlas and the EM algorithm. Med Image Anal, Vol. 8(3) (2004) 255-65

[4] Mazziotta, J. et al.: A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). Philos Trans R Soc Lond B Biol Sci, Vol. 356(1412) (2001) 1293-322

[5] Park, H. Bland, P.H. Meyer, C.R.: Construction of an abdominal probabilistic atlas and its application in segmentation. IEEE Trans Med Imaging, Vol. 22(4) (2003) 483-92

[6] Reyes, M. Linguraru, M.G. Marias, K. Ayache, A. Nolte, L.P. González Ballester, M.A.: Statistical shape analysis via principal factor analysis. IEEE International Symposium on Biomedical Imaging (ISBI) (2007) 1216-1219

[7] Roy, T. et al.: Segmentation of a vector field: dominant parameter and shape optimization. Journal of Mathematical Imaging and Vision, Vol. 24(2) (2006) 259-76

[8] Rueckert, D. et al.: Non-rigid registration using free-form deformations: Application to breast MR images. IEEE Transactions on Medical Imaging, Vol. 18(8) (1999) 712-21

[9] Studholme, C. Hill, D.L.G. Hawkes, D.J.: An overlap invariant entropy measure of 3D medical image alignment. Pattern Recognition, Vol. 32(1) (1999) 71-86