AN INTEGRATED FRAMEWORK FOR ANALYZING THREE-DIMENSIONAL SHAPE DIFFERENCES: EVALUATING PROSTATE MORPHOMETRY

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ABSTRACT
Three-dimensional (3D) morphometric features of anatomical objects may provide important information regarding disease outcome. In this paper we develop an integrated framework to quantitatively extract and analyze 3D surface morphology of anatomical organs. We consider two datasets: (a) synthetic dataset comprising 640 super quadratic ellipsoids, and (b) clinical dataset comprising 36 prostate MRI studies. Volumetric interpolation and shape model construction were employed to find a concise 3D representation of objects. For the clinical data, a total of 630 pairwise registrations and shape distance computations were performed between each of 36 prostate studies. Graph embedding was used to visualize subtle differences in 3D morphology by non-linearly projecting the shape parameters onto a reduced dimensional manifold. The medial axis shape model used to represent the shape of super quadratic ellipsoids was found to have a large Pearson’s correlation coefficient $R^2 = 0.805$ with known shape parameters. For the prostate gland datasets, spherical glands were found to aggregate at one end of the manifold and elliptical glands were found to aggregate at the other extrema of the manifold. Our results suggest our framework might discriminate between objects with subtle morphometric differences.

Index Terms— Prostate Cancer, Shape Analysis, Medial Axis, Manifold Learning, Morphometry

1. INTRODUCTION
For many diseases, changes in morphology may provide important information regarding disease outcome [1, 2]. Difficulties in quantifying differences in morphology of anatomical organs have limited the universal use of these features for distinguishing between patients with different disease outcome. We present a quantitative framework to extract and visualize subtle morphometric differences. The overarching objective of our work is to use these morphometric differences to build a prognostic predictor for disease outcome.

Previous work in computer assisted quantification of anatomical morphology has focused primarily on the brain. Medial axis representations have been used to analyze 3D hippocampal shape variation using nonlinear analysis to obtain shape parameters [3]. Two methods for finding shape parameters of the corpus callosum, localized component analysis and sparse principle component analysis, use dimensionality reduction techniques to find independent local shape parameters [4, 5]. For ease of interpretation, shape models must comprise local uncorrelated features. Additionally, many anatomical organs have few or no internal features that can be detected. Hence for certain anatomical organs surface morphology alone must be capable of determining shape parameters. The medial axis model [6] is a surface based shape representation with localized parameters that allows for quantitatively measuring shape differences between objects within a population. A similarity measure must be formulated to compare the shape parameters in the population. A point based metric is the simplest method to ensure that a comparison between similar parameters is enforced. Given a set of pairwise distance measures between objects within a population a dimensionality reduction scheme can be used to visualize differences in the population. Graph embedding is a non-linear dimensionality reduction method that preserves local topology between shapes from the high to the low dimensional manifold [7].

We present an integrated computational framework for quantitatively assessing subtle morphometric differences between 3D shapes. We apply this framework to quantitate subtle 3D shape differences between two datasets: (1) a synthetically generated dataset comprising 640 super quadratic ellipsoids, and (2) clinical dataset corresponding to 36 prostates MRI studies acquired from patients with confirmed prostate cancer (CaP). To the best of our knowledge we are not aware of any methods that quantitatively and accurately describe morphometric features of the prostate. Our framework involves modules for (a) segmentation using an active shape model, (b) volumetric registration using mutual information, (c) shape-based interpolation, (d) shape representation using the medial axis, and (e) similarity computation in the medial axis shape space. Graph embedding is applied to project the shape differences encoded in the affinity matrix onto a lower dimensional shape manifold; object proximity on the shape manifold reflecting shape similarities.

2. METHODOLOGY

2.1. System Overview
We define a 2D intensity image scene as $C = (C, f)$, where $C$ represents a set of spatial locations (pixels in 2D or voxels in 3D), and $f(c)$ is the image intensity function associated with every $c \in C$. Each of the $M$ image sets contains $N$ 2D image slices. An image set is defined as $S^m = \{C^{m,i} | i \in \{1, \ldots, N\}, m \in \{1, \ldots, M\}$.

For every $S^m$ an active shape model (ASM) automatically segments the object boundary on each 2D slice. Volumetric interpolation on 2D segmentations define a 3D surface. The images are registered to a common coordinate frame, and a volumetric shape model is constructed and used to calculate distance between shapes. Figure 1 presents a flowchart of this methodology.
2.2. Active Shape Model Segmentation

Each image slice was first segmented using a 2D ASM [8]. Expert labeled anatomical landmarks were used to train the ASM. \( \forall C^m, \; m \in \{1, \ldots, M\}, i \in \{1, \ldots, N\} \), the ASM finds a set of pixels \( X^m_i \subset C \) corresponding to the object edge. To segment a new image, landmarks on the object border were located by extracting a set of statistical texture features and matching the texture of the new image to a learned texture model of the object border [9]. For a given image set \( S^m \), we define the object surface as \( \mathcal{O}^m = \{X^m_i \mid i \in \{1, \ldots, N\}\} \).

2.3. Affine Registration using Mutual Information

Registration between object pairs is performed so two image sets \( S^a \) and \( S^b \) are in a common coordinate frame. Mutual Information (MI) is maximized over an affine transformation space \( T \) [10]. \( T(S) \) represents the image set \( S \) transformed by the affine mapping \( T \). We define the optimal transformation of two sets as,

\[
T^m = \underset{T}{\operatorname{argmax}} \ MI\{T(S^a), S^b\}. \tag{1}
\]

2.4. Shape-Based Interpolation

The dimensions of the each voxel in a given image set \( S^m \) may not necessarily be isotropic. Shape interpolation is applied to all image sets to obtain voxel isotropy in 3D. An edge-based interpolation method is employed [11]. The interpolated image slices are represented as \( \hat{S}^m \). Given an affine transformation \( T^m \), we define our registered, interpolated set of image edges as \( \hat{S}^m = T^m(\hat{O}^m) \).

2.5. Medial Axis Shape Model Parameterization

For each object a medial axis [6] \( \hat{O}^m \) is calculated that attempts to approximate \( \hat{O}^m \). The medial axis model is a set of medial axis points, \( \{M^m|m \in \{1, \ldots, M\}\} \), and surface vectors, \( \{\hat{Y}^m|m \in \{1, \ldots, M\}\} \) where \( M \) is the total number of image sets. We define each point on the medial axis as a medial atom \( \{t^m_p \subset \mathcal{M}^m|l \in \{1, \ldots, P\}\} \) and one surface vector is as \( \{\hat{v}^m_k,p \subset \hat{Y}^m|p \in \{1, \ldots, P\}, k \in \{1, \ldots, K\}\} \) given that \( P \) is the number of medial atoms and \( K \) is the number of surface vectors for each medial atom. For the datasets presented \( K \) was discovered empirically to be 2. \( \mathcal{M}^m \) is defined as the local minimum of the Euclidean distant map of the object, \( d_{\text{map}}(\hat{O}^m) \) [12].

\[
\mathcal{M}^m = \min_{\hat{O}^m}\langle\nabla d_{\text{map}}(\hat{O}^m)\rangle \tag{2}
\]

Evaluating the distance map at the medial axis gives the distance to the closest points on the surface, \( d_{\text{map}}(\mathcal{M}^m) = R^m \). To find \( \hat{Y}^m \) we define a maximally inscribing sphere centered at \( t^m_p \) as \( B(t^m_p) \). A set of surface vectors, \( \{\hat{v}^m_k,p|k \in \{1, 2\}\} \), is then defined as two intersections between the object and a maximally inscribing sphere,

\[
t^m_p + r^m_p \hat{v}^m_k,p = \hat{O}^m \cap B(t^m_p). \tag{3}
\]

2.6. Pairwise Distance Measure Between Shape Models

A point correspondence measurement was chosen as an appropriate similarity measure between shapes given the constraint of consistent sampling along \( \mathcal{M}^m \). Point matching which minimizes the distance between two sets of medial atoms, \( \mathcal{M}^a \) and \( \mathcal{M}^b \) was used to find correspondence between two medial axes. Once point correspondences were established, distance between two shapes was calculated,

\[
D(a, b) = \sum_{p=0}^{P} w_1||t^a_p - t^b_p|| + w_2||\hat{v}^a_{t^a_p} \cdot \hat{v}^b_{t^b_p}|| + w_3||\hat{v}^a_{t^a_p} \cdot \hat{v}^b_{t^b_p}|| \tag{4}
\]

The weights, \( w_1, w_2, \) and \( w_3, \) were set equal to 1 to give equal weighting to all features.

2.7. Graph Embedding for Visualization of Shape Space

Graph embedding [7] was used to non-linearly project the high dimensional object shapes into a low dimensional space. Given \( \mathcal{D} \) we can find the optimal embedding vector \( \chi \) over all objects such that relative distance between points is preserved [7]. We evaluated graph embedding for two different kernel functions (a) linear, \( W(a, b) = \mathcal{D}(a, b) \), and (b) exponential, \( W(a, b) = e^{\theta(a, b)/\kappa} \), where \( \kappa \) is set empirically. From \( W(a, b) \) the optimal embedding is found which satisfies the following equation,

\[
\mathcal{E}(\chi) = 2(M-1) \cdot \text{trace} \left[ \chi^T (\mathcal{D} - W) \chi \right] \tag{5}
\]

where \( \mathcal{D} \) is a diagonal matrix defined \( \forall j \in \{1, \ldots, M\} \) as \( \mathcal{D}(j, j) = \sum_k W(j, k) \). The 3D embedding space is defined by the eigenvectors corresponding to the 3 smallest eigenvalues of \( (\mathcal{D} - W)^T\chi = \lambda \chi \).
2.8. Evaluation of Registration and Shape Model Accuracy

Given two shapes, $O^a$ and $O^b$, registration accuracy was evaluated using the Dice similarity coefficient $\phi$ [13],

$$\phi(O^a, O^b) = \frac{2|O^a \cap O^b|}{|O^a| + |O^b|}$$  \hspace{1cm} (6)

The object volume of a shape model can be reconstructed by Delaunay triangulation of $\mathbb{S}^m$. Reconstructed volumes are then compared with the original prostate. Given the full image set, $S^m$, an object volume, $O^m$, and the reconstructed shape model volume, $\hat{O}^m$, we define the following area based metrics,

$$TP = \frac{|O^m \cap \hat{O}^m|}{|\hat{O}^m|} \hspace{1cm} TN = \frac{|S^m - (O^m \cup \hat{O}^m)|}{|\hat{O}^m|}$$

$$FP = \frac{|O^m - (O^m \cap \hat{O}^m)|}{|\hat{O}^m|} \hspace{1cm} FN = \frac{|\hat{O}^m - (O^m \cup \hat{O}^m)|}{|\hat{O}^m|}$$

We then calculate overlap, $(TP)/(TP + FP + FN)$, and predictive positive value (PPV), $(TP)/(TP + TN)$. Two edge based measures, Mean Average Distance (MAD), and Hausdorff distance are calculated as,

$$MAD = \frac{1}{N} \sum_{(d \in O^{m})} \min_{(e \in \hat{O}^{m})} ||d - e||$$

$$H(O^a, \hat{O}^a) = \max_{(e \in O^a)} \min_{(f \in \hat{O}^a)} ||e - f||$$

given $h(O, \hat{O}) = \max_{(e \in O)} \min_{(f \in \hat{O})} ||e - f||$.

### 3. EXPERIMENTAL RESULTS

#### 3.1. Super Quadratic Ellipsoids

Over 600 superquadric ellipsoid shapes [14] were created by varying parameters, $\{p_j | j \in \{1 \ldots 6\}\}$. Exponential graph embedding was used to generate a manifold of the shape space (Figure 2). Visual inspection of the manifold and superquadric ellipsoids confirm the manifold accurately captures underlying subtle differences in morphological variation among the superquadric shapes. A surrogate for ground truth of known shape parameters was defined as the sum of the absolute difference between parameters,

$$\Delta p = \sum_{j=1}^{6} ||p^j - \hat{p}^j||,$$  \hspace{1cm} (7)

Pearson’s correlation coefficient between $\Delta p$ and geodesic distance on the manifold was $R^2=0.805$.

#### 3.2. Prostate Magnetic Resonance Imaging

Thirty-six *in vivo* 3 Tesla T2-w MRI sets of the prostate were collected from patients diagnosed with prostate cancer. We quantitatively evaluated registration accuracy and shape model reconstruction. Qualitative results suggest that the prostate shapes are arranged on the low dimensional manifold based on morphometry.

Registration accuracy was evaluated using the Dice similarity coefficient. For 630 pairwise registrations among the 36 different prostate shapes the similarity coefficient was $84.3 \pm 0.1 \%$. Given that only an affine registration algorithm was used so as to not compromise subtle study specific morphometric differences, this similarity coefficient is within the expected range.

Figure 3 shows a 2D prostate MRI slice with boundary results for segmentation, volume interpolation, and shape model. Shape interpolation does not alter the defined boundaries of the prostate while the shape model deviates from the segmented boundaries. Figure 4 shows 3D volume interpolation and shape model surfaces; the same types of disparities between prostate gland and shape model appear.

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Table 1 shows quantitatively the reconstruction error is $15 - 18\%$ of total volume. Fewer medial atoms results in loss of shape information, shown by higher error rates. We chose to use 400 medial atoms for high reconstruction accuracy and computational simplicity. Figure 5 shows the 3D manifold of the shape space found via exponential graph embedding. Prostate shapes that lie adjacent to each other on the manifold have similar surface morphometry. Prostate volumes (0-5) arranged on the top of the manifold are elliptical in shape while prostates near the bottom (6-9) appear to be spherical. The qualitative results support that our shape model and similarity metric capture differences between the glands. Figure 6 shows surface renderings of three prostates. The prostate shapes shown in Figure 6 (a),(b) are arranged close to each other on the manifold and have a well-defined interior convex surface, while the other prostate (c) is far away and has a relatively flat inferior surface. The prostates that are close together are more elliptical, having longer width than height, while the other prostate that is spherical in shape.

![Fig. 5. Three-Dimensional projection of a manifold found via exponential graph embedding with a weight constant of $\kappa = \max(D)$. Representative prostate glands corresponding to different locations with the manifold are shown. Lines connect each point to its three nearest neighbors, as defined by geodesic distance on the manifold.](image)

![Fig. 6. Surface rendering of 3 prostates, view from sagittal (bottom) and coronal (top) plane. (a) and (b) are relatively close on the low dimensional manifold while (c) is far away.](image)

4. CONCLUDING REMARKS

We have presented an integrated framework to quantitatively compare subtle morphometric differences between shapes by segmenting object boundaries, registering object volumes, extracting shape features and then projecting these features onto a reduced dimensional manifold. Registration accuracy was above 80% for over 600 registrations. Results show the medial axis shape model preserves most of the 3D shape of the prostate with 85-95% reconstruction accuracy. We validated the efficacy of the quantitative morphometric framework on synthetic data. For future work, finding accurate surrogate measures for ground truth of shape are important to validate differences in morphometric features. Our ultimate goal is correlating shape variations with known clinical outcome. This paper represents the preliminary steps in developing a framework to analyze morphology of the prostate in a robust and quantitative way.

5. REFERENCES