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Common Shape Model and Inter-individual Variations of the Heart using Medial Representation

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Abstract

A lot of heart diseases result in or from morphologic variations; analysis of shape variability is therefore important for diagnostic classification and understanding of biological processes. The problem of analyzing shapes of complex objects like the heart is widely discussed in the image processing and analysis community, and different approaches have been published. The goal of the work presented here was to investigate the suitability of a medial based approach to fulfill the task of representing and analyzing individual heart shape and inter-individual variations. In a pilot study we analyzed 16 individual human hearts, their common shape, and their main inter-individual variations for a fixed time phase.

Electrocardiogram triggered MRIs of 16 subjects were segmented semi-automatically to derive an object ensemble containing the seven major structures: the left and right ventricle, the left and right atria, the pericardium, the radix of the aorta and the pulmonary trunk for each individual heart. These objects were modeled using a medial based representation providing inter-individual shape correspondence via an object intrinsic coordinate system. Based on this concept of correspondence, a common shape model was generated for both the single object and the object ensemble. The inter-individual variations were analyzed using an extended PCA method showing that almost 80% of variations are covered within the first 5 modes.

The results give promise that the method will have great value in quantifying inter-individual shape changes both for healthy and for clinically relevant populations, will allow education in anatomy to communicate variabilities, and furthermore may serve as a potential basis for

segmentation, classification, and diagnosis. This potential has to be validated with a statistically relevant population in the future.

Keywords

Heart Modeling, Cardiac Image Analysis, Statistical Shape Analysis, Medial Representation, Multiple Objects

1. Introduction

Analysis of shape has begun to emerge as a useful area of medical image computing because it has the potential to improve the accuracy of medical diagnosis, the correctness of image segmentation, and the understanding of processes behind growth and disease. Therefore, over the last years, a variety of object representations have been suggested for 3D shape analysis. Shape representation via deformable models, first introduced by Terzopoulous et al. [1] and developed first for statistics by Cootes & Taylor [2], has the special advantage of expressing the expected geometric conformation of objects in a way easily applicable to segmentation. One of the first approaches was the use of templates like circles to model the human eye [3]. Another approach uses volume vector fields to represent objects given as labeled voxels. This approach was developed by Miller and his students Christensen and Joshi [4] and applied, for example, by Csernansky [5] and by Evans [6] to neuro-anatomical objects. Active Contour Methods (or 'snakes'), based on energy minimizing curves, were introduced by Kass et al. [7]. A comprehensive survey of deformable models like these that record only local geometry is given in [8].

Since the local measures of shape in active contours seemed inadequate to describe shape and in particular did not adequately support a statistical framework and since the volume-based methods, with their dense vector fields, produced inefficiencies in segmentation and in statistics, Cootes et al. chose a global representation of relatively sparsely sampled boundary points to produce Active Shape Models (ASM) [2], which are now widely used for different applications. The use of Fourier descriptors [9] provides an alternative global representation,

in which each coefficient in the representation is global to the object. A similar idea of shape description by a few global parameters is the use of superquadrics [10]. Unlike the other boundary representations, active shapes were also capable of handling multiple objects, at least globally. A further approach followed, the Active Appearance Models (AAM) [11], in which correlations between image intensity statistics and shape information were recognized.

In the field of modeling and analyzing the complex shape of the human heart, methods among the above for surface and volume based representation were applied. The major contributions of shape modeling are to motion - during the cardiac cycle - of the left ventricle, e.g., using superquadrics or spherical harmonics [12-14]. In an early example of incorporating shape statistics, Cootes et al. used ASM for modeling the left ventricle [2]. A more recent successful application of using 3-D AAM of the right ventricle is given by Mitchell et al. [15, 16] especially focusing on segmentation. Other methods include physical information for modeling the shape of the ventricle [17-19]. A detailed review of existing cardiac shape modeling approaches is provided in [20]. Except for some approaches [19, 21-23], all focus on the left ventricle, which is, of course, physiologically the most interesting part of the heart and the easiest object to extract from MRI. Not much work has been done so far on analyzing the shape of the whole organ, though such analysis is a prerequisite for studying the general morphology and biology of this organ.

Although all these methods succeed in representing the individual shape of one object, they differ concerning the effort needed to spatially relate inter-individual shapes to analyze variations over specific populations. Manual landmark setting, for example, as used in active

shape models is one idea to overcome the correspondence problem. These can either be anatomical landmarks or landmarks obtained via metric matching [18] or via parameterization such as that used for brain ventricles [24]. Over the last years the non-rigid semiautomatic landmark setting became popular using the iterative closest point algorithm from Besl et al. [25, 26] or in using harmonic maps [27, 28]. Other methods are based on surface matching [29] or on morphometry with point and line extraction of features [30]. In a more recent paper from Frangi et al. volumetric B-spline deformation is proposed for automatic landmark generation [22]. A similar approach has just been applied to a four chamber model [23].

As the object in one case is deformed into another via automatically chosen landmarks, the correspondence between landmarks may have errors, and these errors in correspondence may change the shape statistics under study. For example, the method of automatic landmarking in 3D proposed by Frangi et al. is a reasonable approach to overcome the time consuming process of finding correspondence, which is established via a volumetric non-rigid registration technique using multi-resolution B-spline deformations. However, the method is based on a set of prior classes of shapes (atlas), derived from manual segmentation, where the landmarks are extracted and copied to the individual patients. This copying is subject to error in landmark correspondence.

Focusing on the complex anatomy of the heart, including the atria, the pericardium and major vessels, most of these approaches will have major problems in allowing a representation and analysis of the whole interacting organ and its constituents at different scale levels. Fourier descriptors would not allow the construction of open boundaries, whereas the 'snakes' are not

optimal for locating objects which have a known shape. The very popular methods of Cootes et al. need landmarks to work, which are not as easy to find for the heart as for the brain. Including mechanics as shown in a hybrid model by Wang et al. [18] using physical and statistical shape models may be a possible solution, leading to a more complex model. However, we need an intuitive method providing correspondence between different subjects working for a complex multi-object.

Therefore we used a medial based approach (m-reps) proposed by Pizer et al. [31, 32] promising both, a straightforward method to establish correspondence without altering the individual shape on one hand a hierarchical and multiscale representation scheme on the other hand. Several single objects have already been successfully modeled and analyzed with this method [33]. However, this method has not previously been applied yet to a mechanically interacting and complex object ensemble, like the heart.

Objective

The presented work aimed to investigate the suitability of the medial representation approach to model and analyze shape and shape variations of a population of individual human hearts. The task can be divided in answering the following questions:

Multi-figure M-rep Modeling

Are m-reps an adequate method to represent the shape of a multi-object like the heart?

Is it possible to correlate a whole population of individual hearts using the medial based approach to establish correspondence?

Analysis and Validation

Does such a correlated population model allow reasonable statistical analysis of shape and shape variation?

Are the results of this shape analysis empirically valid?

Clinical Relevance

Is it possible to use this method for clinically relevant applications?

2. Methods

2.1 Data Sets and Pre-processing

For our pilot study we used MRI scans of 16 subjects, two healthy volunteers and 14 arrhythmia patients, which were accounted to be morphologically healthy. Atrial and ventricular geometry was acquired in CINE mode during breath-hold (expiration) using short-axis scans with 4 mm slice thickness for the atria and 6 to 8 mm thickness for the ventricle. In a first step we generated isotropic data sets to guarantee anatomically correct dimensions. Controlled semi-automated segmentation provided labeled data sets for each subject. In the segmentation of the left ventricle, the papillary muscles are considered to be part of the blood pool as is usual in functional cardiac analysis. These binary images are blurred slightly to smooth boundaries for edge detection during the image match optimization process.

2.2 M-Rep Correspondence

The concept and application of m-reps have already been described in detail [31, 32]. The key idea of establishing geometric correspondence for a population of individual objects with shape variations is the use of the same discrete n x m grid of atoms whose hubs form a medial sheet. An atom, consisting of two equal length spokes, attached at a hub and forming a track

of interior points in the object, is represented computationally by a tuple of parameters describing the hub and spokes and thus the local shape in terms of all of local position, local orientation, and local size. Thus a grid of atoms represents the interior morphology of the object and implies the outer boundary (Fig. 1). Once an adequate atom grid has been found for an object, it can be matched to the whole population in an iterative optimization process (see 2.3). This optimization process is designed to maintain spatial correspondences, because the relative positions, orientations, and sizes of neighboring atoms are easily accessible and thus maintainable, subject to the deformations necessary to fit the segmented object being fitted.

The result of this optimization process is grids with different individual shapes, representing inter-individual variations where a certain position within the grid corresponds to the correlating point in all the other grids (see Fig. 1). This holds under the assumption of no self-intersection, a smooth unfolded boundary and topologically invariant atom grids [34].

2.3 M-rep Generation

Starting with an adequate atom grid, the individual atom parameters are modified successively using the conjugate gradient descent method [35] in the following coarse to fine cascade: optimization of figures, optimization of atoms, and finally optimization of boundaries to achieve an optimal fitting model [32, 36]. At each stage the objective function F being optimized combines maintenance of the m-rep geometry by a measure G called "geometric typicality" and an "image match" measure L of Gaussian derivatives across the boundary

implied by the m-rep to the contrasts in the binary image defining the object. The weight α of G relative to L is set by experience. The implied boundary is calculated via a subdivision surface method [37].

Figural stage

In this first stage a global positioning (rotation, translation, magnification) of the whole atom grid is performed to achieve maximum image match.

Atom stage

In this stage the atoms are successively moved one by one within a certain range to optimize F. These optimizations are applied in random order, and the random passes through atoms are iterated until convergence is achieved.

In this stage the geometric typicality consists of two terms, one, P, concerning the relation of the atom to its value at the previous level of scale and the other, N, concerning its relationship to the neighboring atoms. Maximizing the latter term keeps medial atoms in the same relationship to their neighbors. The two terms are averaged in a weighted fashion, with the neighbor term weighed by a factor β (neighbor penalty weight) [36] chosen by experience. These relationships are given by the following equations.

$$F(M,I) = L(M,I) + a.G(M) \qquad \text{Eq.1}$$

$$G(M) = (1-b)P(M) + b.N(M) \qquad \text{Eq.2}$$

(with M=m-rep model, I=image, F=objective function, L=image match based on image information, G=geometric typicality, P=previous scale level, N=neighbor atom and α=geometry weight and β=neighbor penalty weight)

Boundary stage

This stage refines the yet approximate boundary by keeping the geometry of the grid but displacing the finely tiled boundary at its vertices along the medially implied normals. Here the objective function sums the image match with a weighted geometric typicality produced from a term rewarding small displacements.

2.4 Application to Data

The different tasks to generate m-rep models for a given grid are implemented in the software framework developed by the Medical Image and Display Group at the University of North Carolina, called "Pablo", described in user-oriented terms in [38]. Fig. 1 shows the idea of correspondence. The same atom grid, a 4x5 grid describes two individual right ventricles with spatial corresponding atoms. In a first 'bottom up' strategy we found an adequate atom grid for each object of the whole population, and in a following 'top down' strategy, using the prior model we attempted to find the best match of the model to the data image. Fig. 2 gives a 2D impression of generating the m-rep model and the image match for the right ventricle using the consecutive stages of figural stage (b), atom stage (c) and boundary stage (d). In this way we constructed the single m-rep models for the major objects of the whole population,

which enables the generation of an overall common shape model and the analysis of shape variations by comparing individuals atom by atom. The resulting m-rep models for each subject represent the individual shape, on the one hand, and provide an object intrinsic coordinate system, on the other hand, in which each coordinate corresponds to the identical coordinates in all other objects within the topological invariant population. These models give a compact representation of allowable variations, however they are specific enough not to allow arbitrary variations different from those in the training set.

Using a geometry weight $\alpha = 0.9$ and a neighbor penalty weight $\beta = 0.35$, we defined a target fitting criteria of an image match of more than 80% in the atom stage and more than 90% in the boundary stage for the m-reps of the four chambers and the pericardium. A flow diagram of the whole processing is given in Fig. 3.

2.5 Principal Geodesic Analysis

Principal component analysis (PCA) has proven to be useful for understanding geometric variability in populations of parameterized objects [2, 11]. The statistical framework is well understood when the parameters of objects are elements of a Euclidean vector space. However shapes that are represented by m-reps operate in a figural space including local magnification and rotation and thus are not elements of a Euclidean space. Therefore the PCA was extended by Fletcher et al. [33, 39] to principal geodesic analysis (PGA), which is also valid in figural space.

As a first step PGA was applied to each single object using the results from the atom stage. Potential outliers were indicated by the statistics, causing atom movements out of the implied boundary in one of the first 5 main components within a range of two standard deviations. The fitting process was redone for those. Subjects that remain outside were eventually accounted to be true outliers. In a second step PGA statistics were applied to the whole object ensemble.

3. Results

3.1 Single object modeling

The numbers of atoms satisfying the required match criteria for the seven objects are within a range from 12 to 20 atoms. In detail the left ventricle is described with 15 atoms (5x3), the right ventricle with 20 (4x5), the left atrium with 16 (4x4), the right atrium with 12 (4x3) and the pericardium with 16 (4x4). The image match for the major vessels with 14 atoms for the aorta (2x7) and 18 atoms for the pulmonary trunk (2x9) is lower (77 % for the aorta and 75 % for the pulmonary trunk, both for the atom stage) than expected. The main component distribution of the more interesting right atrium over all subjects is given in Fig. 4. Two right atria (subject 4 and 15) lying almost beyond a normal Gaussian distribution are marked as filled circles. The following discussion will indicate why both of them - statistically indicated as diametrically opposed shapes - are indeed different in size (a) and elongation (b).

3.2 Multi-object modeling

The statistical distribution of the normalized main components of the complete object ensemble, taken as a whole, over the population is shown in Fig. 5. In the upper part the first three main components are plotted against each other, in (a) the 1st vs. the 2nd and in (b) the

2nd vs. the 3rd. In the lower part (c) the 2D distributions are plotted in 3D to show their spatial statistical position. For reasons of low image match on one side and no definite region limits on the other side, we excluded the vessels (aorta and pulmonary trunk) from PCA. The first 5 main components cover a shape space of 78% of variations, the first 11 components cover a shape space of 95% within the population (see Fig. 5, lower right part (d)). Fig. 6 demonstrates the derived mean m-rep model of the heart blended into the MRI images of subject 2 (boundary contours (a), and the solid shape (b)). The bottom of the figure shows the modified mean model by the first three main components, given by the distribution for subject 2 in Fig. 5. Fig. 7 demonstrates the variations of the shape variability due to the first 5 modes for ±2 standard deviations (σ) and the percentage weight with respect to their impact to the shape space. The major possible variations of the population are covered within a range of $\pm 2\sigma$ for each single mode.

3.3 Analysis and characterization of population specific shape variations

The analysis of the variations along the different modes revealed characteristic shape movements that cannot be demonstrated by still images but should be described qualitatively to give an impression of PGA based decomposition of interindividual variations into specific components.

The 1st mode especially describes the size differences of the hearts, as may be seen in Fig. 7, 1st mode. The 2nd mode describes a twisting and a volume shift between the atria and the

ventricle. The 3rd mode may be summarized as a rotation, a bending in the horizontal plane including a twisting. The 4th mode includes a twisting and a shift in the valve plane, and the 5th mode is a combination of a twisting an vertical bending.

The main characteristic variations consist of size difference, twisting, rotation or combinations for each of them with different values, but with decreasing impact to the total shape space for higher modes. The decomposition into specific characteristic changes of shape is promising to be a tool for comparison and classification of pathological alterations in future studies.

4. Discussion

This paper presents the application of the m-rep method including shape statistics to the organ heart. It is shown that this method is able to describe the shape of such a complex organ consisting of the following major objects: left and right ventricle, left and right atrium, pericardium, and initial parts of the two major vessels: aorta and pulmonary trunk.

The provided tagged MRI data, acquired in the clinical routine, were not equally spaced and required some pre-processing. The influence of motion due to respiration during the measurement could be corrected by removing corrupted slices or correcting positions. The manual segmentation process was done by a medical expert and a computer scientist and controlled vice versa to guarantee a maximum of objectivity.

Since the model currently consists of only 16 subjects the results are not valid in a statistical sense, but they allow a discussion of the questions formulated in the introduction.

4.1 Multi-figure M-rep Modeling

The m-rep method, already successfully applied to some non structured anatomical objects, e.g., the kidney and the hippocampus [36], works for the more complicated major components of the heart as well. The image match concerning the main chambers and the pericardium is

rather high. It reaches the target values, except for the left atrium. This is a result of including the ear part in a single m-rep. The latter widely differs anatomically from subject to subject. Therefore it should be modeled using a subfigure in a future step.

The high image match and the atom grid correspondence allow the comparison of single objects and furthermore the whole ensemble between the different subjects. This allows global and local analysis as well as common and individual analysis - which is not provided by any other method yet. Moreover this method requires neither landmark setting nor deformation as commonly used [11, 23].

4.2 Analysis and Validation

The empirical results of our pilot study confirm the correctness of establishing spatial correspondence based on atom-wise correlation of the medial sheets; they will be discussed in detail in the following.

The first two components for the right atrium had a wide distribution. Two objects appeared to be outliers when we also included the size difference in the statistics (see Fig. 4, a). In fact, these are both anatomically quite different structures of this population consisting of 13 male and 3 female subjects (mean age: 37 years, mean weight 85 kg). Subject 4 was the oldest man (57 years, weight: 85kg), whereas subject 15 was a young female (25 years, the lightest with: 45 kg). Applying statistics without size difference, both of them have still different elongation

(see Fig. 4, b) - the right atrium of subject 4 is shortened whereas the one of subject 15 is very elongated.

However, the statistics of the object ensemble (without the aorta and pulmonary trunk) taken as a whole lie inside a normal statistical Gaussian distribution for the main components (see Fig. 5). The common shape model of the heart is given in Fig. 6. The mentioned difference between subject 4 and 15 is also evident for the object ensemble. However, obviously almost 80% of the shape space is covered with the first 5 modes (Fig. 5, right hand side). An example of how the mean model and the individual weight of the main components fits to a specific subject (2) is shown in Fig. 6. The modified model fits best to the contours for the chambers given in the MR images.

4.3 Clinical relevance

Concerning this population we cannot yet give specific clinical results. However, first ideas of clinical applications with medial based methods seem to be obvious.

First of all, it is possible to model an organ like the heart, and based on the correspondence concept, a first characterization of the major shape variations is enabled. This allows either a single mode interpretation, or the interpretation of potential combined modes. The 1st main component especially describes the size differences of the hearts, as may be seen in Fig. 7, 1st mode. The 2nd mode describes a twisting and a volume shift between the atria and the ventricle, a possible different filling state for the same time. The 3rd mode may have a

connection to the different heart types, e.g., horizontal, normal, or vertical type, and the 4th mode may demonstrate anatomical variations of the annulus vibrosus. These biological interpretations and those of the other modes and/or possible and/or valid mode combinations, including global variations like twisting, elongation, dilation, rotation, bending or others may be postponed to a study with a large population (see Fig. 7, 1st, 2nd ,3rd , 4th, and 5th mode). Another future step will be the study of local variations by analyzing simple atoms or groups of them.

The 2nd mode describes a twisting and a volume shift between the atria and the ventricle. The 3rd mode may be summarized as a rotation, a bending in the horizontal plane including a twisting. The 4th mode includes a twisting and a shift in the valve plane, and the 5th mode is a combination of a twisting an vertical bending.

Although the image match in the atom stage is not 100%, the method is sensitive enough to detect very small variations as indicated for the right atrium, where a wide spread shape variation for this population of arrhythmia patients is given, in comparison to other organ objects. This leads to the idea that arrhythmia probably is related to some extent to morphology. These two intentions, among many of others, indicate the value to be followed in future studies with a clinical relevant population.

The results so far confirm the approach to be able to fulfill the requirements we stated in the introduction. Not much data concerning the complex 3D shape and variations of the heart can be found in literature to compare and validate our findings. Frangi et al. analyzed the left and

right ventricle of 14 subjects [22]. They used automatic landmark setting derived from atlases and they focus on the automatic method rather than on the clinical relevance. A similar approach was used by Lötjönen et al. on a four chamber model [23], but without quantitative validation. The intuitive method we used is working without landmarks and preserves shape, which a priori is not given for correspondence using point distribution models. The results so far confirm the correctness of this approach to establish correspondence.

Using m-reps turned out to be a powerful method to model the complex shape of the human heart and is very promising to be a valuable tool for clinical applications. We concede that the number of data as well as the data themselves are the crucial point for interpretation of the analysis, especially for the major principal components. Moreover, refinement using enhanced multi-figure objects, attaching, for example, the atria to the corresponding ventricle, and including interpenetration terms between objects, will certainly improve the shape modeling. But these are precisely capabilities allowed by m-reps that will be provided in future versions of the software.

5. Conclusion

The results of this study showed both the power of medial based representation to quantify inter-individual shape variations on the methodological side and in addition first interesting trends in understanding the common and individual shape of the human heart. Modeling the shape of anatomical objects with m-reps has proven to be an intuitive approach to inter-individual correspondence. The generation and optimization of individual models is working very robustly, once the topology of the medial plane is fixed. The correlation of the individual structures and sub-structures by means of the medial plane avoids the common problems of point- and surface-based methods in finding an appropriate distribution of matching pairs of points.

Using geodesic principal component analysis, common shape models could be generated capturing nearly 80% of the variations within the first 5 modes. The smooth decreasing of the impact of the following modes to the total shape space, covering 90% with 8 modes or 95% with 11 modes demonstrates that the resulting shape-space includes legal, real shapes. Skipping modes higher than 5 only results in a loss of details but do not produce illegal shapes.

Although the small number of subjects does not allow valid biomedical statements now, the results so far enable a first characterization of the major shape variations of the investigated

population. The widespread shape variation of the right atrium in this population of arrhythmia patients indicate the method's sensitivity to register very small variations.

Overall these first results promise the method to be a very helpful and valuable tool for clinical analysis and education and comparison of significant, complex shape differences between healthy and pathological populations supporting diagnosis, prognosis, and therapy in the future.

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Figs.

Fig. 1: Right ventricles from two different subjects (left, right) using the same atom grid of 4x5. The upper part shows the solid shaped model, the lower part shows the interior atom grid representing the medial sheet. The arrows indicate corresponding atoms on the different subjects (see text for details).

Fig. 2: Original MRI Image (a), and the results of m-rep generation of the right ventricle for the different stages: Figural Stage (b), Atom Stage (c), and Boundary stage (d).

Fig. 3: Flow diagram from raw data to common shape (CS) and main variation (MV).

Fig. 4: First (I) and second (II) main principal geodesic component of the right atrium including scaling (upper part, (a)); First (I) and second (II) main principal geodesic component of the right atrium using only similarity (lower part, (b)). Two interesting subjects (4 and 15) are marked as filled circles (see text for detailed description).

Fig. 5: The 2D principal component distribution of the complete object ensemble (without aorta and pulmonary trunk) over the population is given in the upper part, (a), (b), and the combined 3D distribution in the lower left part (c). In the lower right part (d) the percentage impact of the corresponding first 15 eigenvalues is shown together with the cumulative

influence. As in Fig. 4 subject 4 and 15 are marked as filled circles (see text for detailed description).

Fig. 6: 3D MRI Images of subject 2 and the following shape models of the heart: In the upper figure the mean model is placed into the images (the implied boundary on the three different axis (a) and the solid shape (b)). In the lower figure the shape generated using the main components, as given in Fig. 5 for subject 2 is shown (implied boundary (c) and solid shape (d)). The major vessels are not included in the model (see text for detailed description).

Fig. 7: Shape variability of the common shape model demonstrating the first five modes within ±2 standard deviations including their percentage impact to the shape space.