

Computational Mesh as a Descriptor of Left Ventricular Shape for Clinical Diagnosis

Pablo Lamata^{1,2}, Merzaka Lazdam³, Anna Ashcroft³, Adam J Lewandowski³, Paul Leeson³, Nic Smith¹

¹Dept. Biomedical Engineering, King's College of London, London, UK

²Dept. Computer Science, University of Oxford, Oxford, UK

³Oxford Cardiovascular Clinical Research Facility, Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, Oxford, UK

Abstract

Shape and size of the left ventricle are cardiac biomarkers used in clinical routine practice. They are typically assessed by partial metrics including volume, length, diameter or wall thickness. The aim of this work is to illustrate the potential of an alternative shape analysis methodology based on a comprehensive description of the anatomy using a computational atlas. 40 cardiovascular magnetic resonance scans of young women defined the cohort data set. A stack of 7 to 8 slices from end diastolic frames of dynamic MRI studies were analysed by manual segmentation and automatic personalization of high order computational meshes. The most significant modes of variation of shape of this population were identified by principal component analysis. Statistical significant differences in shape were found in women with higher cardiovascular risk profiles ($P < 0.05$, Hotelling T2 test). The analysis revealed differences in the position of the apex in the left to right direction, which had not been captured by standard clinical parameters. These results show computational statistical atlases may offer the potential to improve stratification of cardiac diseases.

1. Introduction

Characterization of the shape and size of the left ventricle (LV) is a relevant diagnostic procedure [1,2]. Cardiac remodelling manifests clinically as changes in size, shape and function of the heart (mainly LV) as a result from cardiac load or injury [3]. Main causes are acute myocardial infarction, factors that result in increased pressure or volume overload, chronic hypertension, congenital heart disease with intracardiac shunting, valvular heart disease, and heart failure.

Geometrical characteristics of the heart including diameter, wall thickness or blood pool volume are widely applied biomarkers for the staging and characterization of

cardiac diseases. More advanced metrics are the sphericity index, major to minor axis ratio, or local curvature [4]. These metrics are nevertheless a limited characterization of the variability that the 3D geometry of the heart can manifest, and, as such, are unable to capture regional changes in a comprehensive manner, or to represent the relative position of anatomical landmarks such as valve planes or the apex.

Cardiac anatomical shape can be represented by a computational mesh, a description of a geometrical domain by a set of variables or degrees of freedom. Using this approach, anatomical variations can be characterised by means of a computational atlas, a statistical representation of anatomical variability [5]. Despite their successful application for the automatic segmentation of ventricular anatomy [5,6], cardiac atlases have, to date, made a limited clinical impact, with only a small number of studies using atlases to compare populations of subjects [7,8]. The development and clinical application of cardiac atlases is an active research field, and the Cardiac Atlas Project [9] is one of the main international efforts in this field.

This work presents the methodology of shape analysis using computational meshes of high order interpolation. Three groups of women with different levels of preeclampsia are compared, and differences were found in subjects with higher cardiovascular risk profiles.

2. Material and methods

The anatomy of 40 cases is captured by Magnetic Resonance Imaging (MRI), manually segmented, codified by the degrees of freedom of a computational mesh, and statistically compared by relevant clinical groups.

2.1. Cohort and data acquisition

The study was based on analysis of cardiovascular magnetic resonance images acquired as part of a follow

up study of women, discharged from the Oxford Maternity Unit between 1998 and 2003. The three clinical groups were defined by their history of hypertension during pregnancy as either early onset preeclampsia before 34 weeks gestation (n=12, group 3), late-onset preeclampsia (n=15, group 2), or uncomplicated pregnancy (n=13, group 1). All studies were approved by the Oxfordshire Research Ethics Committee, and participants provided signed informed consent or assent in accordance with the Declaration of Helsinki.

Images were acquired by a 1.5-T Siemens Sonata scanner. Optimized left ventricular horizontal long-axis cine sequences were obtained with standardized basal slice alignment with a 7-mm slice thickness and 3-mm interslice gap. Imaging was retrospectively ECG-gated with a precordial 3-lead ECG and acquired during end-expiration breath holding. Image acquisition parameters for the steady-state free precession images were: echo time 1.1ms; repetition time 2.6ms; and flip angle 60°.

2.2. Ventricular shape description by mesh fitting

End diastolic frame from each cine sequence was segmented using Argus (Siemens Medical Solutions, Germany). LV short-axis epicardial and endocardial borders were manually contoured from the whole stack of 7 to 8 slices. Location of the right ventricle (RV) was also manually drawn by a small circle at the most basal slice.

High order interpolation meshes were fitted to the segmented anatomy using an image registration and variational mesh warping technique [10]. As a result, each anatomical case is described with a total of 3456 nodal variables (or degrees of freedom). The location of the right ventricle was used to align the ellipsoidal shapes of the left ventricle, breaking the symmetry of revolution in the circumferential direction.

An example of this process is shown in Figure 1.

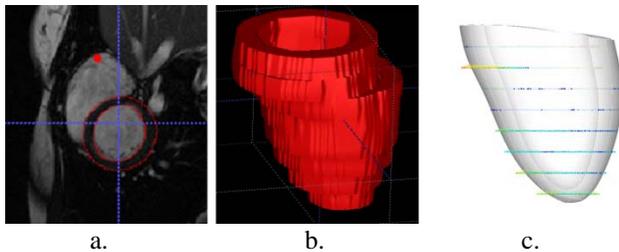


Figure 1: Shape description of the LV by computational meshes. a. Manual segmentation - note the small circle indicating the location of the RV. b. Isosurface of the manual binary mask of the LV from 8 slices. c. Resulting mesh (white semi-transparent) fitted to 8 slices of points, which are coloured by the distance between the contours defined in a. to the mesh (coded from 0mm-blue to 5mm-red).

2.3. Shape comparison

Principal component analysis (PCA) was undertaken to identify the main modes of variation of the ventricular shape. This approach enabled the concentration of the variability of shape, and the reduction of the parametric space for comparisons from 3456 to a small number of dimensions (typically 2 to 5).

Shape statistical comparisons were first done between each shape coordinate by Student's T-test. Since shape is in fact described by a vector of several coordinates (most significant ones are the first ones), shape coordinates are aggregated in a second statistical test, comparing not two distributions of scalar values, but two distributions of vectors by a Hotelling T2 test that evaluates whether two populations of vectors have the same average value. Grouped shape coefficients are compared in a gradual fashion, starting by grouping the two most significant modes of anatomical variation (student's T-test).

3. Results

Meshes were automatically fitted to the 40 cases, reaching an average residual error of 1.56mm. The first modes of variation of shape are illustrated in Figure 2.

The average shape of the control group was quite similar to the other two, as seen in Figure 4, and the individual axes of variability were not statistically different in each pair of comparisons (Student T test, results not reported). Coordinates 1, 2, 7, 10 and 14 were close to the 0.05 threshold in this comparison.

Statistical significance, with level 0.05, is found by grouping the two first shape coordinates in the comparison between groups 1 and 2. A visual inspection of the parameter space of these two coordinates is shown in Figure 5. No other significance is found in any other comparison (see Table 1) but with the addition of coordinate 14 (this small improvement is interpreted as a random effect since the 14th mode of shape variation represents nominal changes). It is checked that the statistical test is correctly applied by confirming that the covariance matrices are not significantly different (P=0.31), so the homoskedasticity was demonstrated.

Coordinates	1 vs 2	1 vs 3	1 vs. 2&3	1&2 vs. 3
1, 2	0.0425	0.3031	0.0906	0.8005
1, 2, 7	0.0596	0.3338	0.0955	0.8975
1, 2, 10	0.0668	0.0520	0.0655	0.1230
1, 2, 14	0.0139	0.4038	0.0746	0.8089

Table 1: P-values of the most relevant designs of grouped coordinates in a Hotelling T2 test. Significant values are highlighted in bold.

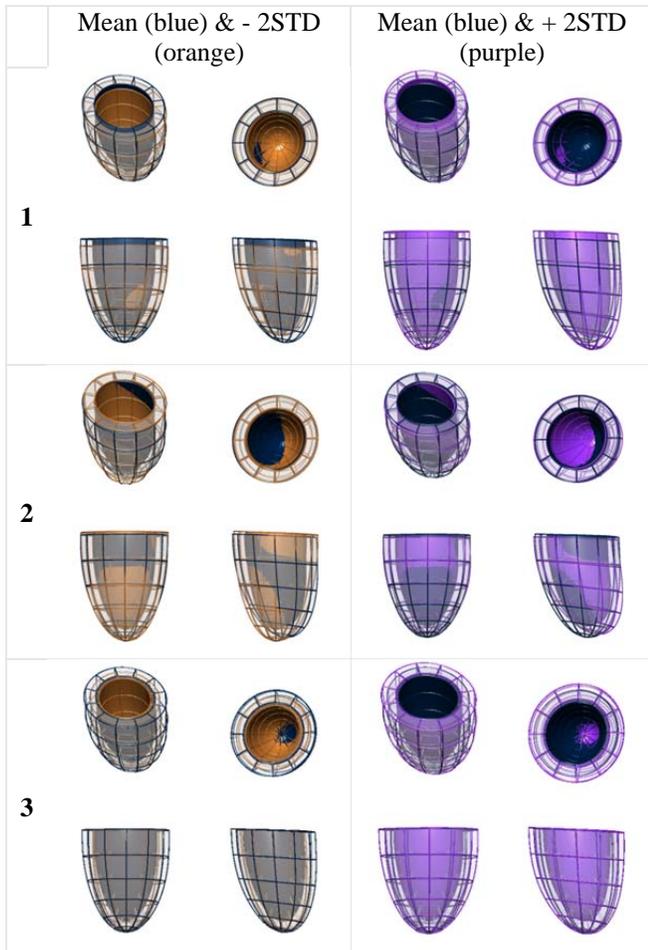


Figure 2. First three modes of variation of the PCA of the shape of 40 left ventricles.. Mode 1 mainly captures changes in length, mode 2 changes in relative position of the apex with respect to the base, and mode 3 changes in diameter. They are responsible for 29%, 21%, and 17% of the variance respectively.

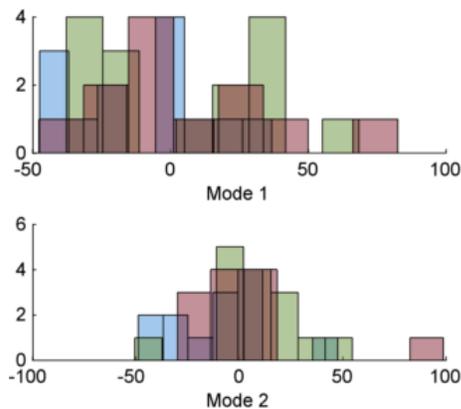


Figure 3. Distribution of the first two shape coordinates of all 40 cases analysed. Note that the coordinates of the first mode are distributed like the addition of two Gaussians for the three groups.

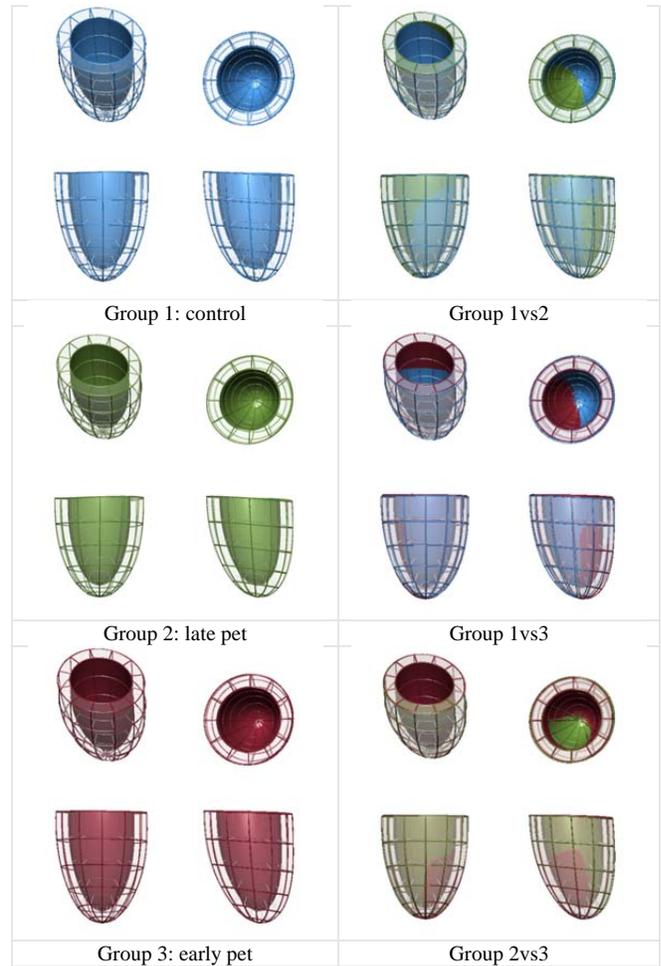


Figure 4. Average shape of each group, and comparison between them.

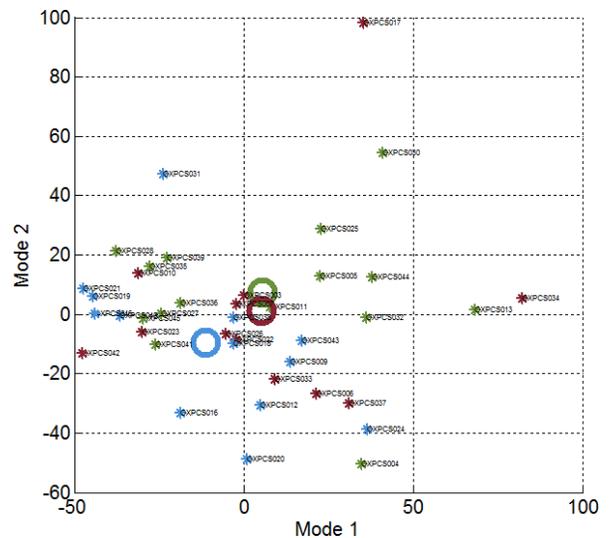


Figure 5. Distribution of the first two shape coordinates of all 40 cases analysed. The blue (group 1, control) is different from group 2 (green, late pet) – $P=0.0425$, but not from group 3 (red, early pet).

4. Discussion

Differences in shape between groups with different cardiovascular risk were found. The analysis revealed differences in the position of the apex in the left to right direction, which could not be captured by standard clinical parameters. These results show computational statistical atlases may offer potential to improve stratification of cardiac diseases.

High order interpolation computational meshes were used in this study to codify shape. These meshes are smooth and continuous, what brings a fundamental advantage: an implicit spatial regularization of shape that reduces acquisition artefacts or segmentation errors. These meshes are also compact, i.e. they require a much smaller number of nodal variables to codify shape compared to linear meshes. Another strength of our methodology is the capability to reconstruct the apex of the ventricle from a set of short axis slices.

Our shape analysis methodology has already been able to find shape differences between young adults of different gestational ages, where statistical significance was found in the individual comparison of the first six modes of variation in a cohort of 234 cases ($P < 0.01$) [8]. The differences in shape of the present study were thus much smaller, and could be partially attributed to the smaller sample size (40 cases). Results also revealed a mixture of two Gaussian distributions in the first coordinate value (see Figure 3), suggesting the existence of two sub-groups inside the clinical groups.

We acknowledge a number of limitations in our approach. The use of short axis cine MRI data cuts the anatomy at the ventricular base, although this issue can be mitigated with the incorporation of long axis slices [7]. The stack of cine MRI slices was not corrected for patient movement, and shifts in between slices can be present. The degrees of freedom of our choice of high order interpolation mesh were not homogeneous (we used cubic Hermite interpolation, with both nodal values and derivatives), what makes the relative importance of vector coordinates unbalanced for a PCA analysis [5]. Future work will address these limitations together with the need of more meaningful modes of variation of shape, a common problem of PCA that has been previously addressed in the study of deformation [11].

To conclude, the shape of the left ventricle can be effectively codified and compared by means of computational meshes with high order interpolation.

Acknowledgements

The EC's 7th FP (224495, 250429 and 269978); the UK EPSRC (EP/G007527/2, EP/H02025X/1) and Wellcome Trust (WT 088641/Z/09/Z); the Department of Health via the NIHR comprehensive Biomedical

Research Centre award. P. Lamata holds a Sir Henry Dale Fellowship jointly funded by the Wellcome Trust and the Royal Society (Grant Number 099973/Z/12/Z). Nic Smith acknowledges supports from the BHF Centre of Research Excellence at KCL. M. Lazdam holds an OHSRC BRC fellowship.

References

- [1] Kono T, Sabbah HN, Rosman H, Alam M, Jafri S, Goldstein S. Left ventricular shape is the primary determinant of functional mitral regurgitation in heart failure. *J Am Coll Cardiol* 1992;20(7):1594–8.
- [2] Douglas PS, Morrow R, Ioli A, Reichek N. Left ventricular shape, afterload and survival in idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 1989;13(2):311–5.
- [3] Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling—concepts and clinical implications: A consensus paper from an International Forum on Cardiac Remodeling. *J Am Coll Cardiol* 2000;35(3):569–82.
- [4] Mitchell GF, Lamas GA, Vaughan DE, Pfeffer MA. Left ventricular remodeling in the year after first anterior myocardial infarction: A quantitative analysis of contractile segment lengths and ventricular shape. *J Am Coll Cardiol* 1992;19(6):1136–44.
- [5] Young AA, Frangi AF. Computational cardiac atlases: From patient to population and back. *Exp Physiol* 2009;4(5):578–96.
- [6] Mitchell SC, Bosch JG, Lelieveldt BPF, Van der Geest RJ, Reiber JHC, Sonka M. 3-D active appearance models: Segmentation of cardiac MR and ultrasound images. *IEEE Trans Med Imaging* 2002;21(9):1167–78.
- [7] Medrano-Gracia P, Cowan BR, Bluemke DA, Finn JP, Lima JAC, Suinesiaputra A, et al. Large scale left ventricular shape atlas using automated model fitting to contours. *Lect. Notes Comput Sci* 2013; 7945:433–441.
- [8] Lewandowski AJ, Augustine D, Lamata P, Davis EF, Lazdam M, Francis J, et al. Preterm heart in adult life: cardiovascular magnetic resonance reveals distinct differences in left ventricular mass, geometry, and function. *Circulation* 2013;127(2):197–206.
- [9] Fonseca C, Backhaus M, Bluemke D, Britten R, Chung J, Cowan B, et al. The Cardiac Atlas Project—an imaging database for computational modeling and statistical atlases of the heart. *Bioinformatics* 2011 15;27(16):2288–95.
- [10] Lamata P, Niederer S, Nordsletten D, Barber DC, Roy I, Hose D, et al. An accurate, fast and robust method to generate patient-specific cubic Hermite meshes. *Med Image Anal* 2011;15:801–13.
- [11] Remme EW, Young AA, Augenstein KF, Cowan B, Hunter PJ. Extraction and quantification of left ventricular deformation modes. *IEEE Trans Biomed Eng* 2004;51(11):1923–31.

Address for correspondence:

Pablo Lamata. Dept. Biomedical Engineering, Imaging Sciences & Biomedical Engineering Division.
St Thomas' Hospital
Kings College London SE1 7EH