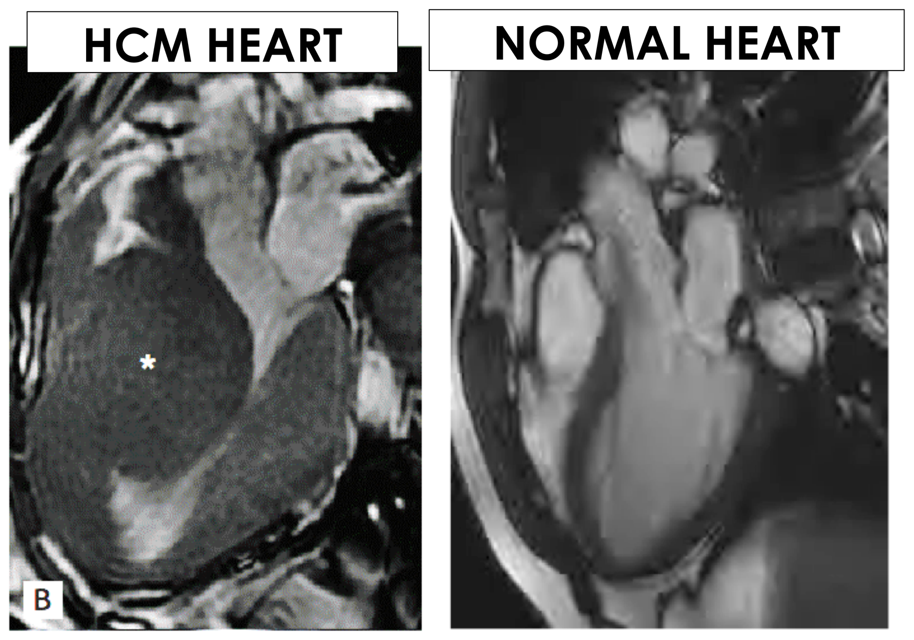
Towards Automated Biomechanical Analysis of Patients with Hypertrophic Cardiomyopathy

Renee Miller[1], Eric Kerfoot[1], Charlene Mauger[2], Alistair Young[1,2], David Nordsletten[1,3]

1. Department of Biomedical Engineering and Imaging Sciences, King's College London, London, UK, 2. Department of Anatomy and Medical Imaging, University of Auckland, Auckland, NZ, 3. Department of Biomedical Engineering, University of Michigan, Ann Arbor, USA

Introduction

Hypertrophic cardiomyopathy (HCM), a genetic disease characterised by an **abnormal thickening** of the ventricular myocardium, affects up to 1 in 200 people. If thickening occurs on the septal wall, left ventricular outflow tract obstruction (LVOTO) can occur which can be life threatening. A typical therapy for severe LVOTO involves either myectomy or alcohol septal ablation. However, better tools and further understanding are needed to classify the severity of HCM and develop an appropriate therapy plan.



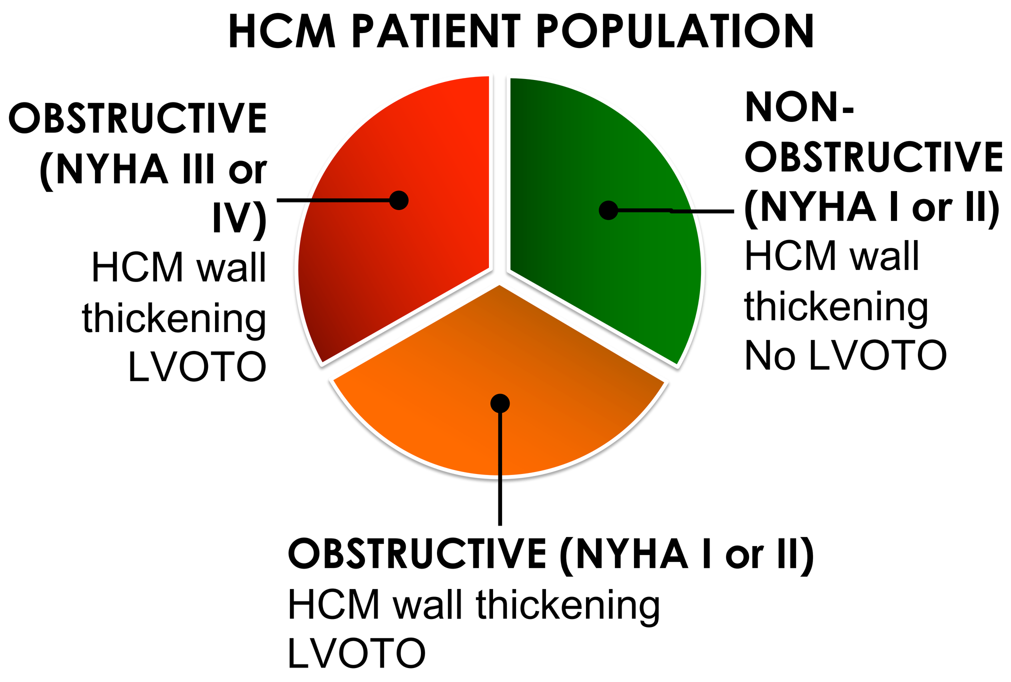


Fig 1. a) Example of HCM versus healthy heart, b) HCM classifications

With **magnetic resonance imaging** capabilities, **computational models** provide a unique tool with which to study the mechanics of HCM hearts, potentially uncovering new markers with which clinicians can use to stratify patients into risk groups and plan therapy.

Images to Models

Image Segmentation:

A **Residual U-Net (5 levels, 5000 iterations)** was trained on **1264 long axis and 9095 short axis images** manually labeled with the **left ventricular (LV) blood pool**, **LV myocardium** and **right ventricular (RV) blood pool**[1]. Data came from healthy volunteers, patients with HCM as well as patients with dilated cardiomyopathy. Images were acquired on both Siemens and Philips Scanners.

The data was **augmented** by adding:

- Contrast normalization
- Random flip/transpose
- Dropout in k-space (introducing artificial noise)
- Free-form deformation (introducing shape variation)
- Random translation/rotation/zoom

Images to Models

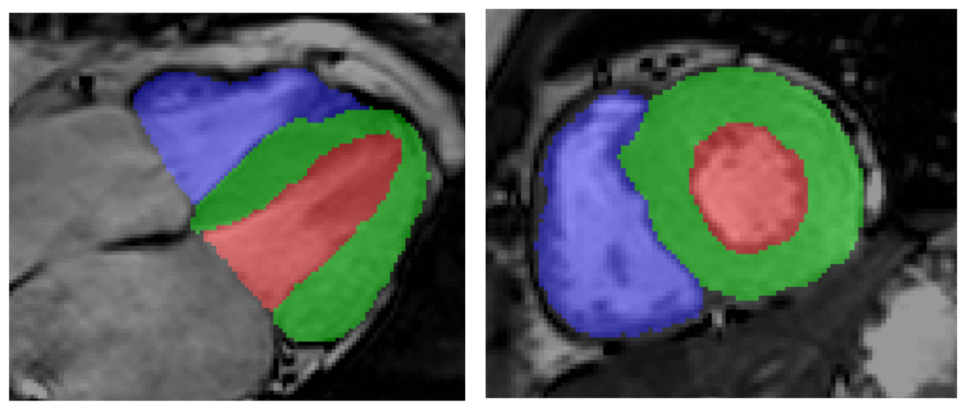


Fig 2. Example labels from the trained neural network on an HCM case

Model Fitting:

1. Register LA/SA masks and align SA masks (registration error used as weights in Step 4)
2. Masks (Fig 2) → 2D Contours
3. 2D Contours → 3D Data Points
4. Fit template surface mesh to 3D data points[2]
   - **a. Stiff fit**: Linear least squares fit
   - **b. Soft fit**: Quadratic fit with explicit diffeomorphic constraints

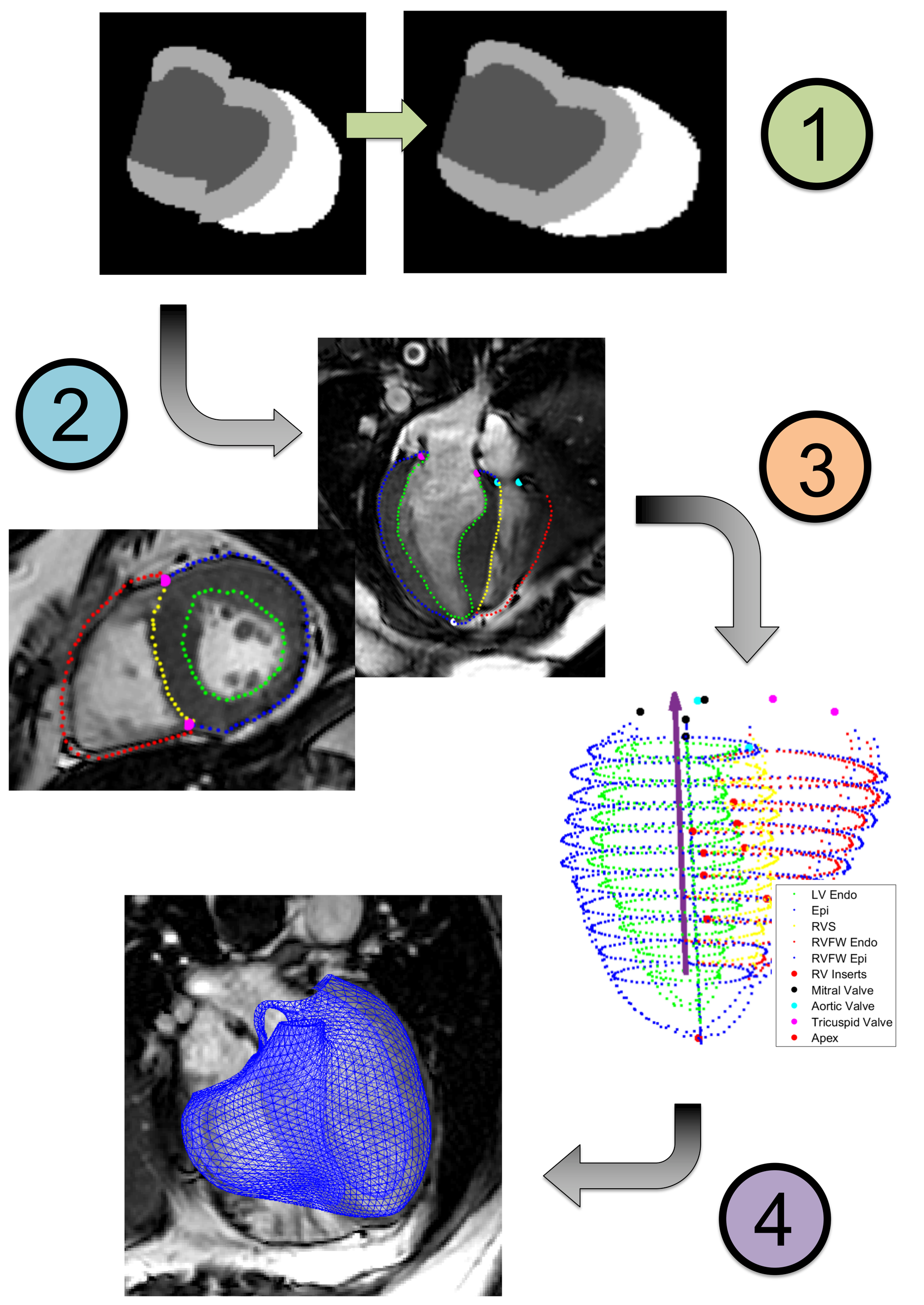


Fig 3. Illustration of pipeline from masks to models

Biomechanical Modelling

Simulations of the full cardiac cycle were performed, extending the methods in Asner et al.[3] to the biventricular case. Novel boundary conditions are introduced to model the influence of valve plane motion through the use of data-derived boundary energies, rather than Dirichlet conditions. In future work, passive and active parameters will be personalized by finding the best match between the geometric data from MR images and model results. A purely mechanical rather than electro-mechanical model is used.

Heart model based on energy potential minimization[3,4]

$$\Pi(\boldsymbol{u}, p, \boldsymbol{\lambda}_1, \ldots \boldsymbol{\lambda}_k) := \underbrace{\int_{\Omega_0} W(\boldsymbol{u}, p, \boldsymbol{\lambda}_k) d\boldsymbol{X}}_{\text{Internal Energy}} - \underbrace{\sum_k \Pi_k^{ext}(\boldsymbol{u}, \boldsymbol{\lambda}_k)}_{\text{External Energy}}$$

...

Lagrange Multipliers

Pressure

Displacement

Internal Energy

Reduced Holzapfel-Ogden passive constitutive law:

$$W_P = \frac{a}{2b} e^{[b(I_C - 3)]} - 1 + \frac{a_f}{2b_f} e^{[b(I_C-3)^2]} - 1$$

with patient-specific isotropic and fiber stiffness

Length-dependent active law: (a, a_f)

$$W_\alpha = \alpha(t)\phi(C_f)(I_{C_f} - 1)$$

with patient-specific active tension scaling

External Energy

Matching 0th order moments[3] over all valve planes:

$$\Pi_v^{ext}(\boldsymbol{u}, \{\boldsymbol{\lambda}_v^k\}) := \sum_m \boldsymbol{\lambda}_v^m \cdot M_0[\boldsymbol{u} - \boldsymbol{u}_d]$$

$$M_0[\boldsymbol{u}_d] = \int_{\Gamma_0^b} \boldsymbol{u}_d \, d\boldsymbol{X},$$

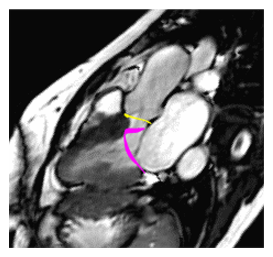


Fig 4. Mitral and aortic valve planes overlain on the 3-chamber long axis image

Simulation driven by LV/RV volumes[3]:

$$\Pi_\ell^{ext}(\boldsymbol{u}, \lambda_\ell^{lv}, \lambda_\ell^{rv}) := \lambda_\ell^{lv}(V_{lv}(\boldsymbol{u}) - V_{lv,d}) + \lambda_\ell^{rv}(V_{rv}(\boldsymbol{u}) - V_{rv,d})$$

where $V_{lv}(\cdot)$ and $V_{rv}(\cdot)$ measure model volume over CINE SA planes.

10 Criteria for Credible Models	
Define context clearly	A pipeline for rapidly generating patient-specific biomechanical models, which captures the shape heterogeneity in an HCM cohort, has been implemented
Use appropriate data	Short and long axis MR images were acquired from a clinical protocol
Evaluate within context	Neural network segmentations have been evaluated and compared against manual segmentations for 14 HCM cases to ensure adequate dice scores (Fig 5). Additionally, the geometric models and fitting process have been evaluated to ensure an accurate fit to contour data (Fig 6 and 7).
List limitations explicitly	The methods are limited by the image quality. A few cases have been obtained with poor image quality (low SNR), resulting in poor labelling by the neural network. In these cases, models cannot be fit accurately.
Use version control	The neural network for image labelling is on Github. Code for segmentation cleaning, contour extraction and model fitting is kept on a local development machine with backups.
Document adequately	Steps of the pipeline are documented in detail for ease of use.
Disseminate broadly	Portions of this work have been published already: https://link.springer.com/chapter/10.1007/978-3-030-12029-0_40 and https://ieeexplore.ieee.org/stamp/stamp.jsp?arnumber=8512394
Get independent reviews	Feedback has been obtained throughout the development process from both clinicians and scientists to develop accurate and useful patient-specific models.
Test competing implementations	Numerous iterations of the neural network (with differing data augmentation steps and training datasets) have been tested to create a neural network which is robust in accurately labelling images from diverse sources (e.g. different scanners and sequences).
Conform to standards	The segmentations from the neural network are validated against those either performed or checked by an expert clinician.

Results & Conclusions

Neural Network Dice Scores:

$$DSC = \frac{2|X \cap Y|}{|X| + |Y|}$$

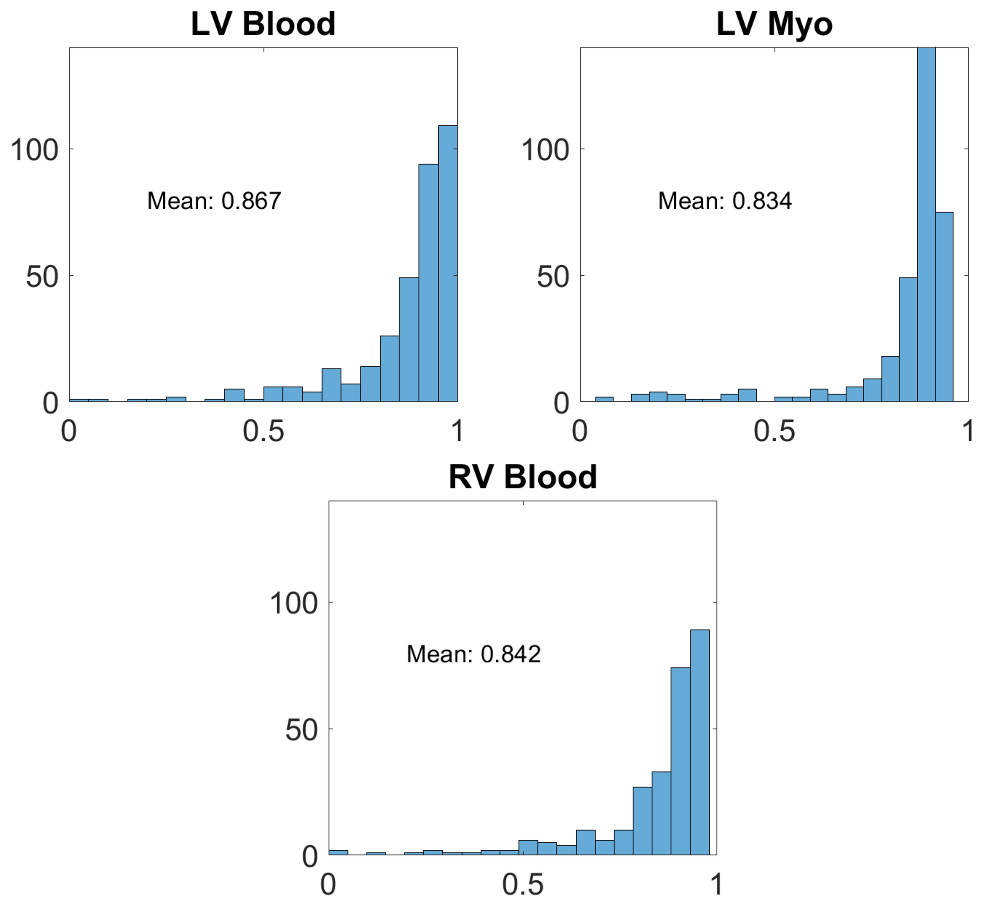


Fig 5. Dice scores calculated between neural network segmentations and manually drawn segmentations

Model Fitting Errors:

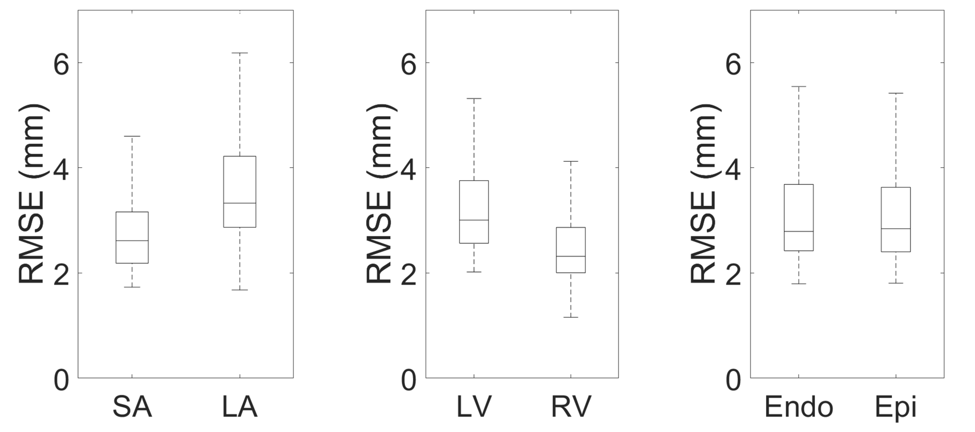


Fig 6. RMSE fitting errors (outliers not shown) between surface meshes and contour points. Due to the fact that registration errors were used as fitting weights, some outlying errors are high (> 10 mm) since they were given small weights in the fit.

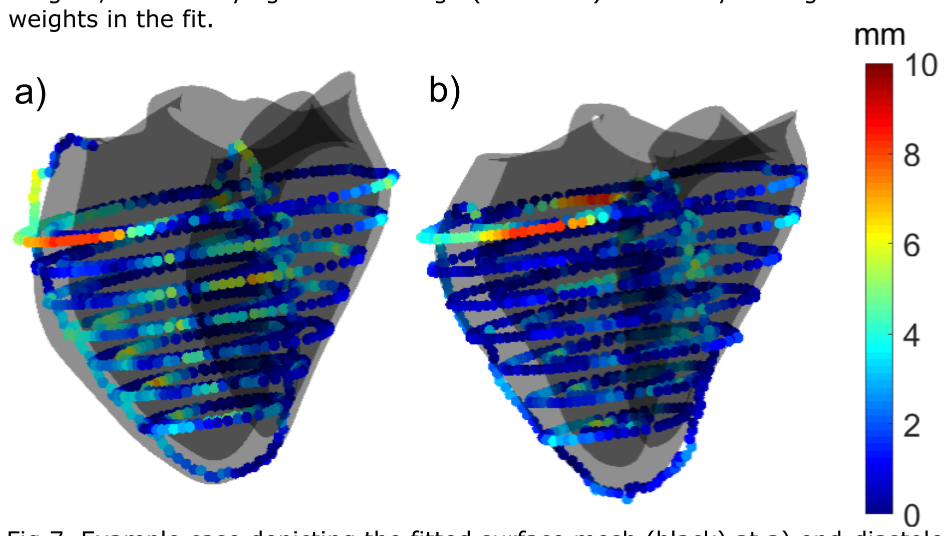


Fig 7. Example case depicting the fitted surface mesh (black) at a) end-diastole and b) end-systole for one case as well as contour points with color depicting error (distance from surface)

Biomechanical simulations are being carried out using the models fitted using this automated pipeline. The steps, including **automated segmentation and model fitting, enable for rapid generation of high-quality patient-specific biventricular models**.

References

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2. Mauger et al. (2018). An Iterative Diffeomorphic Algorithm for Registration of Subdivision Surfaces: Application to Congenital Heart Disease. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS, 2018-July*, 596–599.
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