Generation of an accurate 3D computational model of the mouse heart from MR images

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Introduction: Due to the development of genetically engineered strains, the mouse model has become an important tool in cardiovascular disease research. Several techniques have been used to quantify global geometry and function in the mouse heart; however, to determine regional cardiac functional parameters such as internal wall stress, computational modeling is necessary. Finite element (FE) models of human or large animal hearts have already advanced the understanding of ventricular biomechanics and electrical activation in diseased states[1]. An important component of these models is the incorporation of accurate cardiac geometries since diseased hearts are typically abnormal in shape and size. Due to its high spatial and temporal resolution, MRI is commonly used to obtain reliable *in vivo* geometric data for modeling of human or large animal hearts and may be particularly useful in characterizing smaller hearts[1]. However, a straightforward approach to generate a 3D anatomical model of a mouse heart from MRI data has not been developed. We have created and validated a method that quickly and accurately reconstructs the left ventricle (LV) of the live mouse heart from high spatial resolution and temporally resolved high field MR images. The resulting 3D geometry is directly applicable to FE model simulations.

Methods: The MRI protocol was performed on a 7T General Electric horizontal-bore scanner equipped with a 12 cm bore gradient system capable of a 740 mT/m gradient strength and 250 mT/m/ms slew rate. A custom-built volume coil with an inner diameter of 3.0 cm was used for transmission and reception. During scanning, mice were anesthetized with 1.5 Vol-% isoflurane, and their ECGs (450-550 BPM) were monitored. For cine-MRI of the heart, an ECG triggered 2D fast gradient echo pulse sequence was used (α=20°, TE=1.2ms, TR=5ms, 4 avgs). Each slice was 1mm thick with a FOV of 25 mm^2 and a data matrix of 128^2 (in-plane resolution=195um^2). During each cine acquisition, 25-30 phases during the cardiac cycle were collected. In previous MR studies of the mouse heart, 7-9 short-axis slices through the heart were collected[2]. However, to optimize spatial coverage of the LV, 5 long-axis slices of the heart were acquired instead (Fig.1A). The slices were centered along the long axis of the LV and separated radially by 36°.

Data Analysis: For each slice, the end-diastolic frame was chosen as the image with the largest LV cavity area. For image segmentation, a Canny filter in MATLAB helped define the endocardial and epicardial LV boundaries (Fig.1B). The points of the endocardial and epicardial edges were imported into a finite element package, and 2D prolate spheroidal meshes were fit to the endocardial and epicardial datasets using a linear least squares minimization of the "radial" lambda coordinate (Fig.1C). The resulting meshes were converted to rectangular Cartesian coordinates and additional fitting was done in the x, y, and z-directions. Finally, the 2 meshes were coupled to yield a 3D mesh (Fig.1D). The LV wall and end-diastolic volumes were determined from the mesh. To calculate wall mass, the wall volume was multiplied by a myocardial density of 1.05 g/ml. By using data from every image of the cine acquisition, a time series of the LV geometry could be constructed for the entire cardiac cycle with a temporal resolution of 5 ms.

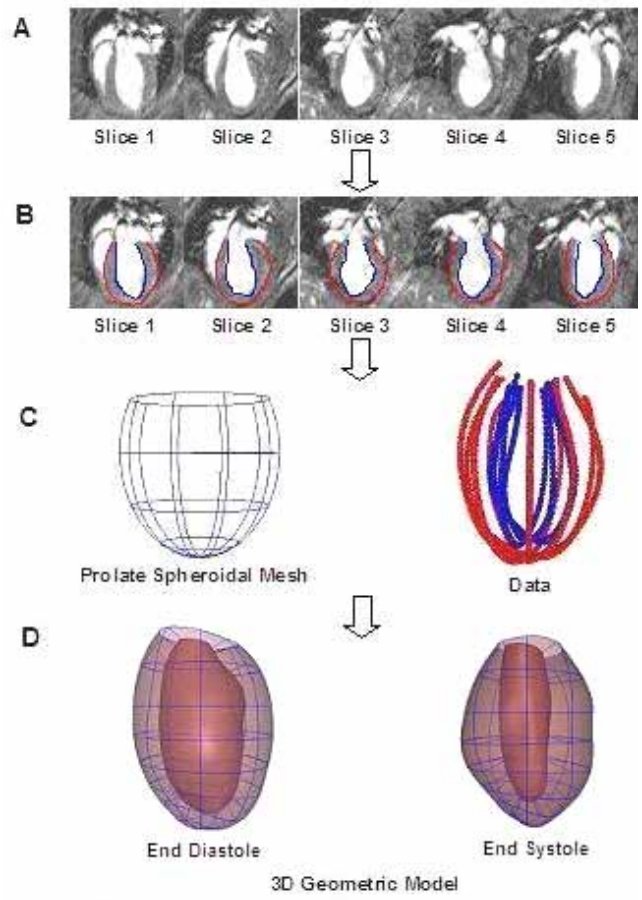

Figure 1: Development of a 3D anatomical model of a mouse LV from MRI data

Results: Anatomical models of a representative mouse LV are shown in Fig.1D with an end-diastolic volume of 36ul and end-systolic volume of 14ul. The root mean squared errors of the geometric fits were 0.030 mm (end-diastolic model) and 0.032mm (end-systolic model). To validate our 3D reconstruction method, mass measurements from the geometric models at end diastole were compared to direct necropsy measurements of the same mouse LVs (n = 10). Linear regression analysis showed a strong correlation between the necropsy and model-derived mass ($Mass_{NECROPSY} = 1.05 \times Mass_{MODEL}$ - 1.19mg, r = 0.99).

Discussion: We have developed a technique for creating 3D FE models of the mouse LV from high-resolution, temporally resolved high field MR data. With our image acquisition protocol, we collected detailed spatial data in both the short and long-axis directions. The resulting 3D MR/models allowed us to track LV geometry as a function of time throughout the cardiac cycle, and the results were validated with direct mass measurements. The geometries generated with our technique are applicable to a wide variety of computational experiments. The anatomical models are built in a finite element package that is capable of biomechanical and electrophysiological simulations. We are currently in the process of incorporating material properties and fiber angle data to our model. By coupling the completed LV model to a circulatory model, it will be possible to study regional mechanics and myocardial activation of a beating mouse heart *in silico*.

References:

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