CONTRAST-ENHANCED µCT FOR EX-VIVO DIGITAL RECONSTRUCTION OF WHOLE HEART AND MITRAL VALVE IN AN AGED POPULATION

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Introduction

Mitral valve (MV) pathology is a growing cardiac epidemic, with mitral regurgitation alone leading to the degradation of physical function, quality of life and longevity for 24.5 million patients worldwide [1]. However, there is currently no large animal disease model of MV pathology that can test treatment devices, such as transcatheter MV replacement [2]. To address this, researchers use numerical predictive models, known as finite element analysis, to simulate a beating heart and predict cardiac deformation and fluid flow [3]. However, these models fail to account for morphological variation in the whole heart and MV due, in part, to a shortage of high-resolution 3D reconstructions of whole-aged human hearts. In this study, we present a methodology to use contrast-enhanced µCT to capture the geometry of aged cadaveric specimens ex-vivo and create a digital repository of aged human cardia. Using this repository, we can quantify the anatomic variation present in whole cardia and MV of an aged cohort and in future, develop finite element models that can relate morphological variation to changes in cardiac biomechanics and fluid flow.

Methods

Using ex-vivo iodine-enhanced µCT, we determine how whole heart and MV gross morphology present in the geriatric heart (n=3). All samples originate from cadavers donated to the RCSI Anatomical Gift Program. Donors aged from 89-100 years at time of death (two male, one female). Whole cardia were extracted, then immersed in 5% potassium triiodide (I_3K) for 14 days [4], washed, then inflated with 4% w/w warm agar solution [4] to emulate end diastolic position. External agar was removed, and cardia were imaged in a µCT scanner (Nikon Metrology, USA) at 65-85µm (220kv, 130µA, 0.5mm copper filter, 1.42 fps). The MV was then dissected, mounted with suture on a custom-made 3D-printed holder, and immersed in olive oil [5]. Explanted MVs were µCT imaged at 39-46µm (190kV, 130µA ,1 fps). All µCT data were then preprocessed using VGS StudioMax (VolumeGraphics v3.0) and imported into 3D Slicer (v5.03, http://www.slicer.org). 3D reconstruction of whole ventricles and MV was completed using a combination of semi-automatic and manual segmentation. MVs were then anatomically registered against whole cardia. All measurements were taken using 3D slicer digitally and no statistical analysis was conducted due to prohibitive sample sizes.

Results

Left ventricular (LV) segmentation (Figure 1) allowed for the measurement of LV volume and wall thickness (in triplicate) at both the apex and the lateral wall. LV wall thickness decreased relative to volume (volume D5<D9<D12), and apex ventricular wall thickness did not. µCT imaging of MV successfully facilitated high resolution (45-65µm) reconstruction of MV anatomy in end diastolic position (Figure 1). Morphological variation in MV annular area (area D5<D9<D12) was driven by variation in the anterior-posterior distance and was largest in specimen D12.

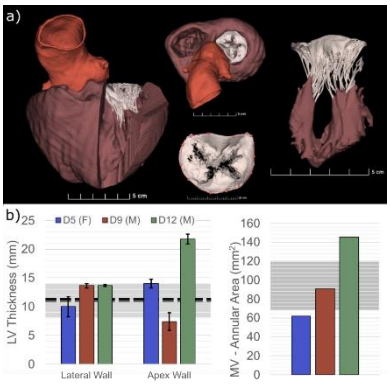

Figure 1: a)3D reconstruction of heart and MV morphology of one specimen imaged using contrast-enhanced µCT. b) Measurements of LV wall thickness (mean and standard deviation of triplicate measurements) at mid-lateral wall and base and MV annular area of three ex-vivo human specimens. Shaded area and dotted line represent the range and mean of values for LV thickness [6] and MV area [7] from literature.

Discussion

Left ventricular wall thickness and MV annular diameters were within the values reported from in vivo echocardiographic measurements of elderly patients (11.1±3.3mm) [6] and healthy adults (annular area 70-120mm) [7], respectively. However, there are differences between individuals in all measurements taken. High-resolution MV models represent the most detailed human MV 3D reconstructions to date and display complex chordal attachment and varying valve leaflet thickness. Validation of intrasubject and covariate (LV and MV) morphological variation will necessitate imaging further samples. Using FE analysis, these 3D models will be used to study the mechanical implications of morphological variations to improve our understanding of MV mechanics in an aged cohort.

References

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