Comparison of methods for the measurement of cardiac function in rats

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Introduction - Cardiac MRI is the gold standard for the assessment of animal models of heart failure. Accurate image analysis is necessary to estimate functional parameters of the heart. This is traditionally performed using manual methods, which are time consuming. However, semi-automatic methods have become commercially available which may offer reduced analysis time. There is little data available in the literature for the comparison of different methods [1-3] and in particular for rodents [4]. In this study we compared two different clinical cardiac analysis tools against manual segmentation to establish the intra-observer variability and preclinical applicability for rats pre- and post-myocardial infarction (MI).

Methods - The study was approved by the ethics committee of University College London and the Home Office (London, UK). Wistar rats (n = 6) were anesthetised and imaged using a 9.4T (400 MHz) Varian scanner (Varian Inc. Palo Alto, CA). Following a pre-MI scan, a thoracotomy was performed and the left anterior descending coronary artery was occluded for 30 minutes. Two hours after reperfusion, post-MI images were acquired using a double gated gradient echo sequence: flip angle 15°, TE 1.7ms and TR 7.5ms, 20 frames/cycle, FOV 40x40mm^2, matrix size 192x192, slice thickness 1 mm, 15-20 slices. The acquired datasets were converted to DICOM format using an in-house Matlab script (Mathworks, Natick, ME), randomised and analysed with three different methods; i) manual segmentation (ImageJ [5]), ii) semi-automatic segmentation using Segment (v1.699d) [3,6] and iii) semi-automatic segmentation using CMRTools [7]. Global functional parameters such as end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) were calculated to compare the different methods. The segmentation process was repeated for all datasets and the difference used to estimate intra-observer variability. For ease of comparison we have calculated relative difference, which is given as mean difference divided by their mean (first and second segmentation). Data from control and MI scans were grouped together for the analysis.

Results and Discussion - The average data analysis time was 22 ± 1 minutes for manual segmentation, 17 ± 2 and 32 ± 4 minutes for semi-automatic segmentation with Segment and CMRTools respectively. The longer analysis time associated with CMRTools is partly due to the use of thresholding for fine adjustment of the blood pool (see Figure 5) which was not always straightforward with our data, since flow compensation has not been implemented yet to minimise flow artefacts in the blood pool. Figure 1 shows the relative intra-observer variability for the three methods as the mean and standard deviation (SD) of the relative difference. Intra-observer variability (based on SD) was similar e.g. EF 3.6%, 2.2% and 3.1% for manual, Segment and CMRTools respectively. Figure 2 demonstrates the level of agreement between manual and semi-automatic segmentation. EDV and ESV were underestimated with Segment (offset 1.5 and 1.9%) and overestimated with CMRTools (offset -6.9 and -7.1%) in comparison to manual segmentation. This may be as CMRTools uses valve plane definitions in 3D-space to define the cut off for the most basal slices. Figures 3 and 4 show Bland and Altman plots for the EF. There was a systematic trend for the semi-automated methods to underestimate and overestimate EF below and above 50% respectively relative to manual segmentation. Further analysis showed that this was due to differences in the ESV, which is probably caused by through-plane partial volume effects. These differences are also responsible for the higher ESV intra-observer variability (1.2 - 4.9%) shown in Figure 1. Partial volume effects are larger for ESV due to the smaller blood volume and bias the MI data due to changes in the endocardium curvature in respect to pre-MI data.

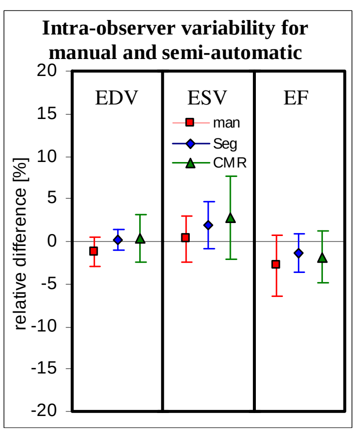

Figure 1: **Intra-observer variability**; man: manual, Seg: Segment, CMR: CMRTools

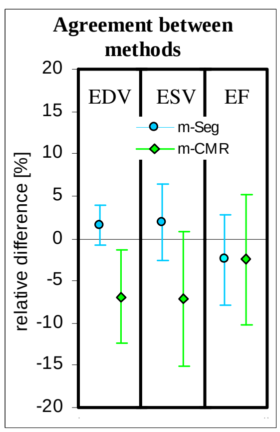

Figure 2: **Agreement between methods**; m-Seg: manual minus Segment, m-CMR: manual minus CMRTools

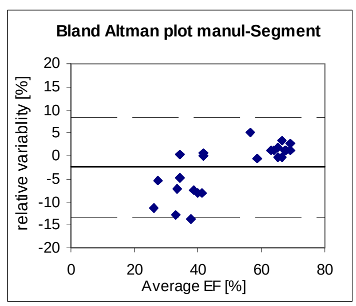

Figure 3: Bland and Altman plot for the EF: manual segmentation minus Segment

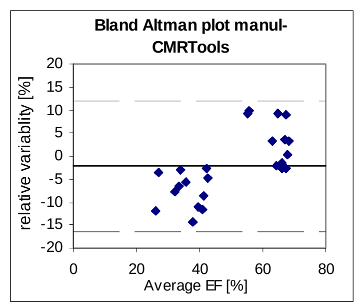

Figure 4: Bland and Altman plot for the EF: manual segmentation minus CMRTools

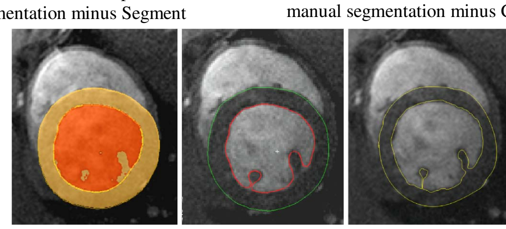

Figure 5: Example segmentations: left to right: CMRTools, Segment, manual

Conclusion - The semi-automated methods that we investigated offer faster analysis time, together with similar intra-observer variability and acceptable limits of agreement compared to a manual method for rodent CMR. Surprisingly, both semi-automated methods under- and overestimated the EF below and above 50% respectively to manual segmentation, which may affect analysis of small animal MI work, especially efficacy studies. In this study we found that the most efficient tool for cardiac MRI image segmentation of our data was Segment. However, further experiments are necessary to validate the methods with phantoms containing accurately known volumes.

References – [1] Sardanelli, F. et al. Segmentation of Cardiac Cine MR Images of Left and Right Ventricles: Interactive Semiautomated Methods and Manual Contouring by Two Readers With Different Education and Expericene. J Magn reson Imaging 27, 785-792 (2008); **[2]** Van Geuns, R. J. M. et al. Ventricular Analysis of Cine MR Images by Using Three-dimensional Information for Contour Detection. Radiology 240, 215-221 (2006); **[3]** Heiberg, E., et al. Time Resolved Three-dimensional Automated segmentation of the Left Ventricle. Proc. IEEE Computers in Cardiology 32, 599-602 (2005); **[4]** Heijman, E. et al. Evaluation of manual and automatic segmentation of the mouse heart form CINE MR images. J Magn Reson Imaging 27, 86-93 (2008); **[5]** http://rsb.info.nih.gov/ij; **[6]** http://segment.heiberg.se; **[7]** http://cmrtools.com