Measurement and quantification of sheep cardiac myocyte and sheetlet orientation from high-field 80 × 80 × 160 µm contrast-enhanced T1W MRI.

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Target audience: MR scientists, clinicians and physiologists interested in high-spatial resolution MR (HR-MRI) and cardiac structure imaging.

Purpose: Imaging of cardiac structure is essential for understanding cardiac electrical and mechanical dysfunction in large animal models of heart disease. These models allow the replication of in vivo clinical imaging alongside high-spatial resolution imaging of explanted organs. Specifically in cardiac disease studies there is a need to know the heart geometry, myocardial myocyte orientation, and myolaminar/sheetlet structure. This is important because myocyte and myolaminar orientation influence electromechanics and are therefore essential for electromechanical computational modelling[1]. It has been demonstrated in rat that high-field high-resolution ex vivo MRI, followed by image quantification can provide this structural information. We describe the hardware requirements and provide the first demonstration of this approach in a sheep heart (~ size of a human heart).

Methods: Sample preparation: A 40 kg female sheep was anaesthetized and underwent a detailed CMR exam, followed by sternal thoracotomy, and euthanasia. The heart was rapidly removed and flushed with cold cardioplegic solution then perfusion fixed for 1.5 hr with 1 L 4% formalin in PBS containing 2 ml Dotarem (gadoterate meglumine, Guerbet, France). Imaging was carried out with the heart removed from formalin and immersed in Fomblin oil. Coil Design: For imaging large animal hearts a volume coil with an inner diameter providing enough space to accommodate the sample and perfusion apparatus is desired, while maintaining homogenous signal intensity and sufficient signal to noise ratio at reception. A prototype coil was developed (by Bruker BioSpin MRI, Ettlingen Germany) through simulation of the B_1 field generated by a 7 elements equally spaced overlapping loop design (100 mm width, 175 mm length) in FDTD (CST Microwave Studio, Darmstadt, Germany). All experiments were performed in a 9.4T magnet with an open bore access of 30cm using this prototype 7 elements transmit/receive array coil. A 3D T_1w FLASH sequence was applied to image the whole heart volume for 29 averages and TE=18ms; TR=50ms; alpha=30°; matrix-size=1380×850×512; voxel-dimensions=80×80×160µm; acquisition-time=97hr; partial-Fourier=1.8. Data treatment: Semi-automated segmentation of the cardiac geometry was carried out using Seg3D (SCI Institute, University of Utah). A structure tensor analysis was then carried out on these images as previously described[2]. The resultant smoothed structure tensor data set had 172×106×64 tensors and voxel dimensions 640×640×1280µm, and was used for myocyte orientation measurement and tracking. Eigenanalysis was used to extract the principal directions from the structure tensor (ST) at each discrete point. The eigenvector corresponding to the largest magnitude eigenvalue (e1) was taken as the laminae normal direction and the eigenvector corresponding to the smallest magnitude eigenvalue was taken as the myocyte direction (e3), following from the orthotropic organization of the myocardium[2]. Myocyte orientation tracking was carried out using Diffusion Toolkit (Centre for Biomedical Imaging, Massachusetts General Hospital, Boston, MA)

Results: A whole heart volume rendering is shown in Fig. 1A which demonstrates the epicardial anatomical detail obtained at 0.08-0.16 mm resolution. Cropping to the apical-posterior ventricles (Fig. 1B,TOP) shows the detail of myocardial sheetlet structure, which was quantified by structure tensor analysis. The left ventricle (LV) myocyte helix angle (α^H) and myocyte orientation tracking show the helical transmural profile as previously described from diffusion MRI (Fig. 1C&D, TOP). A transmural lateral LV region of interest (ROI) is quantified, and the sheetlets are clearly discernable and myocyte helix angle (α^H) and myocyte orientation tracking have a helical transmural profile (Fig. 1B-D, BOTTOM).

Discussion HR-MRI followed by ST has previously been used to measure myocardial laminar and myocyte orientations in rat hearts at 9.4T at 50µm resolution and was more accurate than diffusion-tensor MRI[2]. It was uncertain how well this methodology could be scaled up to image large hearts. We show that the same approach applied to the sheep heart at 9.4T with 80×80×160 µm resolution is adequate to allow quantification of transmural myolaminar and myocyte orientation. The current approach has a long acquisition-time but parallel imaging will be investigated to reduce this.

Conclusion: We present first high-spatial resolution ex vivo MRI of myocardial sheetlet structure from the sheep heart, obtained at 9.4T/30cm, using a novel 7 elements transmit/receive array coil. This image data allowed us to reconstruct the ventricular sheetlet and myocyte orientations. The methodology will be applied in wider studies correlating ex vivo myocardial structure to in vivo excitation and myocardial strain/shear distributions.

References: 1. Trayanova NA et al. Whole-heart modeling: applications to cardiac electrophysiology and electromechanics. Circ Res. 2011;108(1):113-28. 2. Gilbert S H et al, EMBC-Annual International Conference of the IEEE, 2012, 4063-4066.

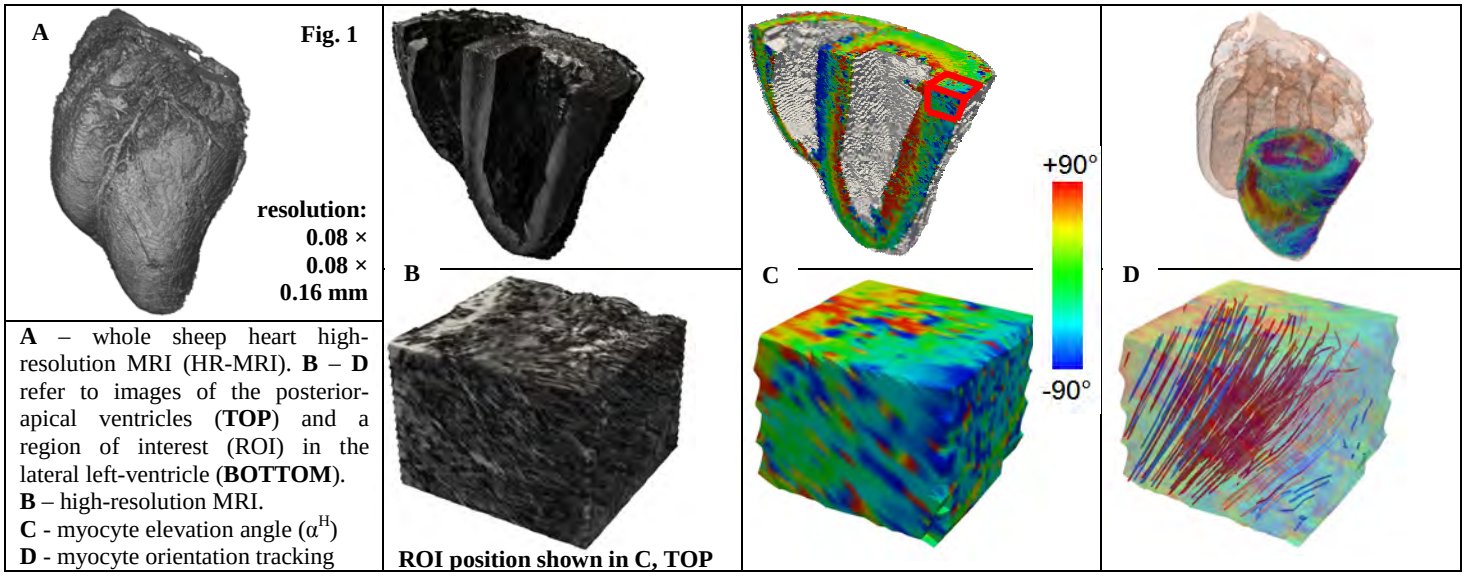

Fig. 1

A – whole sheep heart high-resolution MRI (HR-MRI). **B** – **D** refer to images of the posterior-apical ventricles (**TOP**) and a region of interest (ROI) in the lateral left-ventricle (**BOTTOM**).
B – high-resolution MRI.
C - myocyte elevation angle (α^H)
D - myocyte orientation tracking