High resolution diffusion tensor imaging of adult and neonatal mouse hearts

G. J. Strijkers[1], P. R. Seevinck[1], A. M. Heemskerk[1], A. Vilanova[2], W. M. Blankesteijn[3], E. Heijman[1], K. Nicolay[1]

[1]Biomedical NMR, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands, [2]Biomedical Image Analysis, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands, [3]Department of Pharmacology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, Netherlands

Introduction

The mouse offers a unique platform to study the functional development of the healthy and diseased heart. The cardiac muscle architecture lies at the basis of the mechanical and electrical properties of the heart and dynamic alterations in fiber structure are known to accompany healing and remodeling, *e.g.* following myocardial infarction. Diffusion tensor imaging (DTI) is the only non-invasive technique that enables accurate determination of the cardiac myofiber structure. Previously, DTI has been applied to investigate the cardiac myofiber structure in a number of animal models, such as goat [1], rat [2] and adult mouse [3].

The aim of this work was to develop a high-resolution 3-dimensional DTI method to determine the cardiac muscle architecture of *ex vivo* adult and neonatal mouse hearts, which will enable the study of mouse myocardial development in health and disease.

Materials & Methods

Hearts: Three 3 months old adult mice (C57BL/6) were anesthetized and perfusion fixed with 3.5% formaldehyde, after which the hearts were surgically isolated. The size of the hearts was approximately 7×7×9 mm^3. One neonatal mouse was decapitated 24 hours after birth. The heart was perfusion fixed after which it was surgically removed. The size of this heart was approximately 1.5×1.5×2.5 mm^3.

MRI: DTI experiments were performed on a 6.3 T MR scanner with a Varian imaging console and Magnex shielded gradients. The hearts were contained in a plastic tube filled with Fomblin (Ausimont, NJ) for susceptibility matching, and placed in a one turn solenoid sheet RF coil with a diameter of 10 mm and a length of 15 mm. DTI experiments were done using a 3-dimensional fast-spin-echo sequence with twin navigators to correct for phase errors between even and odd echoes [4]. 3D volume images of the adult hearts were acquired with the following parameters: TE=10 ms, TR=1.4 s, ETL=4, NSA=4, FOV=12.8×12.8×12.8 mm^3, matrix=128×64×64 (readout×phase×phase) zero-filled to 128×128×128, resulting in a voxel size of 100×100×100 μm^3. The neonatal heart was imaged with the following parameters: TE=12 ms, TR=1.6 s, ETL=2, NSA=6, FOV=10×10×10 mm^3, matrix=128×64×64 zero-filled to 128×128×128, resulting in a voxel size of 78×78×78 μm^3. For both adult and neonatal hearts, diffusion weighting was introduced by pulsed field gradients around the first 180° pulse with δ=10 ms, Δ=20 ms, and G_{diff}=0 or 90 mT/m, resulting in b-value=0 or 996 s/mm^2. Diffusion weighting was applied in 6 non-collinear directions. Total acquisition time for the adult hearts was 11.1 hours, while amounting to about 38.2 hours for the neonatal heart.

Data analysis: Diffusion tensor, eigen-vectors and eigen-values were calculated using Mathematica (Wolfram). Fiber orientations were visualized as a vector field, for the projection of the local fiber orientations on the short-axis plane, and in color-coding, for the out-of-plane component. Myofiber orientations were quantified by the helix and transverse angles. Fiber tracking was performed using a tool developed by Vilanova et al. [5].

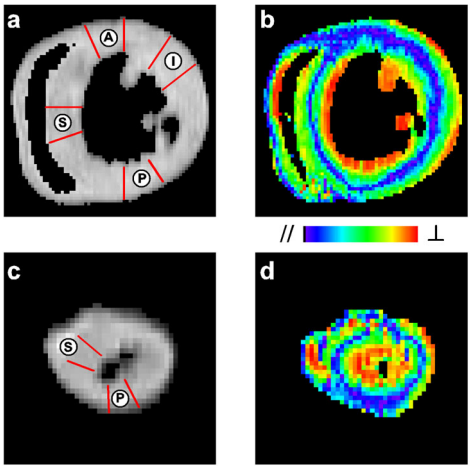

Figure 1: (a) Short axis equatorial slice of adult mouse heart. (b) Out-of-plane components of principal eigenvectors. (c) Short axis equatorial slice of neonatal mouse heart. (d) Out-of-plane components of principal eigenvectors. Color-coding: blue=in-plane (//), red=out-of-plane (⊥).

Results & Discussion

The fast-spin-echo sequence with twin navigation correction resulted in images without visible artefacts, as can be seen in figure 1a and 1c for short axes slices near the equator. The average ADC and FA were (0.83±0.02)×10^{-3} mm^2/s and 0.37±0.02, respectively. The right hand side of figure 1 shows the typical out-of-plane fiber orientations for one of the adult hearts (b) and the neonatal heart (d). Both hearts display a characteristic blue ring of midwall fibers that run predominantly in the circumferential direction. More axially oriented fibers are found near the epicardium, the endocardium, and in the papillary muscles. Figures 2a and 2b show the transmural course of the helix angles at the septum (S) and intrapapillary muscle site (I). The position is normalized from endocard (0) to epicard (1). For the adult heart, the transmural course of the helix angle typically ranged from +70° to -70° at the posterior site (P), from +60° to -60° at the anterior site (A), from +70° to -60° at the septal (S), and +50° to -70° at the intrapapillary muscle site (I). The inter subject standard deviation for the helix angles was 9°. For the neonatal heart helix angles are presented in figure 2c and 2d. A similar smooth transition of helix angles from 60° to –60° was observed through the cardiac wall. The helix angles are in agreement with previously reported values for the goat and the rat [1,2].

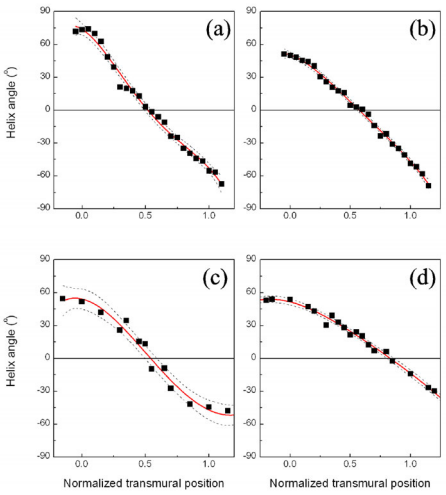

Figure 2: Helix angles of adult (a,b) and neonatal (c,d) mouse hearts at septum (S) and intrapapillary (I) muscle sites (see Fig. 1). The solid line is the average helix angle course with 95% confidence bands (dashed lines).

Conclusions

In conclusion we have presented a high-resolution 3-dimensional DTI method, which enables the determination of the cardiac myofiber orientations in neonatal and adult mouse hearts, opening the possibility to study myofiber development of healthy and diseased hearts in the mouse.

References

[1] Geerts et al., Am. J. Physiol. Heart Circ. Physiol. 283, H139 (2002).
[2] Chen et al., Am. J. Physiol. Heart Circ. Physiol. 285, H946 (2003).
[3] Jiang et al., Magn. Reson. Med. 52, 453 (2004).
[4] S. Mori et al., Magn. Reson. Med. 40, 511 (1998).
[5] Vilanova et al., in proceedings VisSym '04 Joint Eurographics, 173 IEEE (2004).