Myofiber developmental plasticity in fetal and adult pig hearts delineated with diffusion tensor MRI

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Introduction: Cardiac functions in pre- and post-natal stages are different because of the reduced workload of right ventricle (RV) relative to left ventricle (LV) after birth. We hypothesize that myocardial fiber structure in fetal hearts differs from that of the adult hearts as a response to the change in cardiac function. The objective of this study is to quantitatively evaluate myocardial fiber structure in fetal and adult pig hearts using diffusion tensor MRI (DTI).

Materials and Methods: Formalin fixed fetal pigs at mid-gestation (60 gestation day, n = 6), and pre-born (110 gestation day, n = 6) were purchased from Nebraska Scientific, Omaha, NE and hearts were excised upon delivery. Adult pig hearts (n = 6) were harvested from local slaughterhouse (Schubert's Packing, Millstadt, IL). All excised hearts were fixed in 10% formalin. DTI of fetal pig hearts were performed using a 3cm birdcage coil on an 11.74 T Varian INOVA MR system with 8-cm gradient insert. Adult pig hearts were scanned using a 12cm birdcage coil on a 4.7T Varian INOVA MR system equipped with a 21-cm gradient insert. A multi-slice diffusion-weighted spin-echo pulse sequence was used on both scanners. Imaging parameters were: TR, 2 s; TE, 33 ms; δ, 5 ms; Δ, 20 ms; b-value, 0 and 1063 s/mm^2; direction of applied diffusion-weighting gradients, 6. Image resolution was 0.50 × 0.16 × 0.16 mm^3 for fetal hearts and 1.0 × 1.0 × 1.0 mm^3 for adult hearts. Myofiber orientation in each voxel was estimated as the direction of the primary eigenvector. Helix angle and transverse angle of myofibers were respectively calculated as the angle between the fiber orientation and the transverse plane and circumferential directions.[1] The transmural distribution of helix angle in the septum and standard deviation of transverse angle at the LV and RV fusion site were quantified. Upon the completion of MRI, hearts were sliced at 5 μm thickness and stained with hematoxylin and eosin for histological analysis.

Results: Fig. 1 shows DTI determined myofiber helix angle in mid-gestation and pre-born fetal hearts and adult pig hearts. Myofiber structure in both group of fetal hearts were apparently different from that of adult pig hearts at septum (Fig. 1A-C). Quantitative analysis showed that the zero-crossing point of septal helix angle in both groups of fetal heart was substantially closer to LV endocardial surface than that of adult heart (Fig. 1D), suggesting higher contribution of RV myofibers in the septum of fetal hearts. Fig. 2 shows DTI determined myofiber transverse angles at the LV and RV fusion site. The higher contribution of RV myofibers in the septum of fetus pig hearts was clearly appreciated on the transverse angle maps (Fig. 2A-C). Quantitative analysis showed higher standard deviation of transverse angle in both groups of fetal heart than that in adult hearts, (Fig. 2D), reflecting more contribution of RV myofibers to the fusion site in fetal hearts. Histology results (Fig. 3) showed that circumferential myofibers shifted from LV side of septum in the fetal hearts to RV side in the adult hearts, validated the DTMRI results shown in Figure 1.

Discussion and Conclusions: Our results demonstrated that the contribution of RV myofibers in septum was higher in fetus pig hearts than adult pig hearts. The current observations were in agreement with that RV and LV respectively plays a dominant role in pre- and post-natal circulation. These marked cardiac structural differences reflected the plasticity of myocardial fiber development in response to the programmed differential contractile functions before and after birth.

Reference:

[1] Chen J, Liu W, Zhang H, Lacy L, Yang X, Song SK, Wickline SA, Yu X, Regional ventricular wall thickening reflects changes in cardiac fiber and sheet structure during contraction: quantification with diffusion tensor MRI. *Am J Physiol Heart Circ Physiol* 289: H1898-H1907, 2005

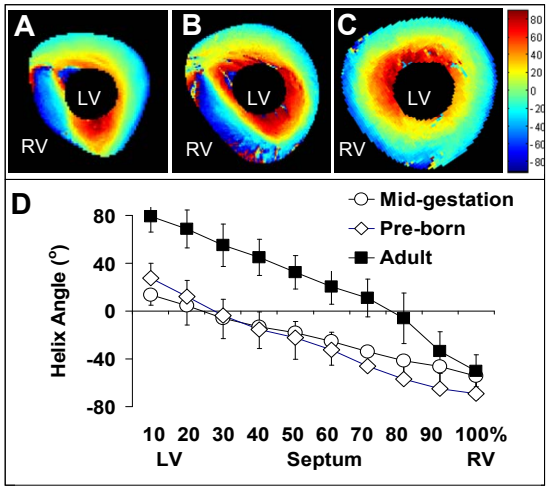

Figure 1. Helix angle mapping of mid-gestation (A), pre-born (B) and adult (C) pig hearts on the short-axis plane. Quantifications of transmural helix angle distribution in septum (region between LV and RV) were plotted in D.

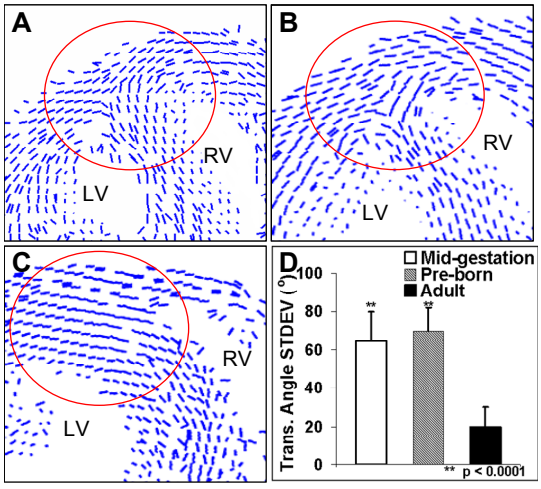

Figure 2. Myofiber projection mapping on heart short-axis plane in mid-gestation (A), pre-born (B) and adult (C) pig hearts. Circle shows LV-RV fusion sites, of which standard deviation of transverse angle were quantified in D.

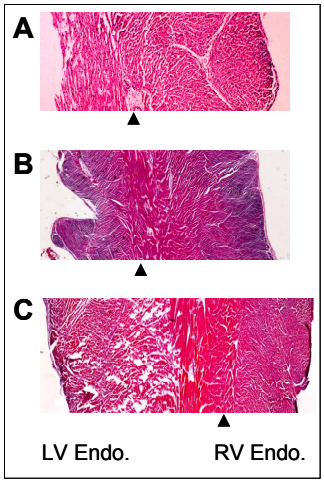

Figure 3. Histology of septum region in mid-gestation (A), pre-born (B) and adult (C) pig hearts. ▲ shows helix angle zero-crossing point, or location of circumferential myofibers.