Magnetic Susceptibility Anisotropy of the Myocardium

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Purpose: Anisotropic magnetic susceptibility has been found in brain white matter and kidney. This anisotropy can be characterized by the method of susceptibility tensor imaging. Here, we report that magnetic susceptibility of the heart is also anisotropic and is associated with myocardial organization. Myocardial fiber orientation and structure is an important determinant of myocardial stress and strain[1] and is altered by cardiac disease[2]. The helical organization of myocardial fibers throughout the heart has been characterized using diffusion tensor MRI and verified with histology. In this study, we determined the relationship between the magnetic susceptibility and the DTI-based fiber orientation of myocardial tissue. The origins of the observed bulk magnetic susceptibility anisotropy (MSA) in myocardium can be related to the microscopic anisotropy of peptide bonds in myofibrillar proteins that has long been understood[3,4]. Given the high-resolution capability of gradient echo phase, imaging susceptibility anisotropy of the heart would aid in assessing myocardial fiber integrity and alterations induced by cardiac diseases and disorders.

Methods: An adult, male C57BL/6 mouse was anesthetized with Nembutal and perfused via jugular vein at a rate of 8 ml/min by a peristaltic pump with 1) 40 ml of 0.2% heparin in 0.9% saline solution, 2) 150 ml of 10% formalin to fix the tissue, and 3) 20 ml of 1.3% agarose gel. After the gel solidified, the heart was harvested and stored for three days in 10 mM PBS. Following data acquisition, the specimen soaked for four days in a solution of 10 mM PBS and 2.5 mM Gd-HP-DO3A. Pre- and post-contrast MR image data were acquired at 9.4 T using 1) a 3-D spoiled-gradient-recalled sequence with multiple echoes (n = 16 and 8, respectively) and 2) a diffusion tensor imaging protocol: one spin-echo scan with b = 0 s/mm^2, and 12 diffusion-encoded spin-echo scans with b = 1850 s/mm^2 (see Table 1 for more details). Mean voxel-wise susceptibility was calculated from the GRE multi-echo phase data. Lastly, in order to relate susceptibility and fiber orientation, a myocardial fiber angle map was calculated from the angle between the major eigenvector of the diffusion tensor and the magnetic field direction.

Results: Fig. 1 shows a color fractional anisotropy image and a susceptibility (χ) map of the mouse heart specimen following Gd enhancement. Perpendicular myocardial fibers appear more diamagnetic relative to parallel fibers. Fig. 2 plots the magnetic susceptibility of the segmented myocardium voxels against $\sin^2\theta$. Myocardial tissue exhibits MSA ($\chi_{0°} - \chi_{90°}$) of 3.3±0.1 ppb, which is an order of magnitude smaller than in brain white matter. Following Gd enhancement, the MSA of myocardium was measured at 24.2±0.2 ppb.

Discussion: Qualitatively and quantitatively, fiber orientation correlates very well with magnetic susceptibility contrast (Figs. 1-2). Though small, myocardial MSA is discernable in susceptibility images acquired at high field. This bulk anisotropy is in agreement with the observed microscopic susceptibility anisotropy of peptide bonds within the axially aligned fibrillar proteins of the myocyte[4]. Isolated muscle tissue orients with the fiber axis parallel to magnetic fields[3] due to its high content of organized myofibrillar proteins. These proteins–myosin, tropomyosin, and actin–contain a large number of α helices and β pleated sheets[5], both of which are more diamagnetic radially than axially due to the angle between the symmetry axis and the vector normal to the peptide planes[4]. This susceptibility anisotropy appears to be augmented by contrast agent, though the mechanism behind Gd-enhanced MSA in myocardium is less clear. Earlier studies have shown that compartmentalization of Gd-DTPA in the extracellular space of muscle tissue yields a significant T_2 reduction in extracellular water, but not intracellular water[6]. In this case, Gd would suppress the signal of the susceptibility-isotropic extracellular space, yielding greater MSA. Alternatively, the increased MSA may be induced by a local magnetic field generated by the contrast agent in the organized tissue matrix. Further work is underway to elucidate the origins of this enhancement since contrast agents are likely to similarly improve susceptibility tensor imaging of the myocardium.

Conclusion: Magnetic susceptibility and fiber angle data were acquired from a mouse heart *ex vivo* to demonstrate the imaging of myocardial MSA. This anisotropy likely stems from the peptide bonds within the myoctye's highly organized fibrillar proteins. Gd increased the apparent susceptibility anisotropy of image data, but additional work in this area is required to uncover the exact cause.

References: [1] Waldman LK et al, Circ Res 1988;63:550-562. [2] Tezuka F, Tohoku J Exp Med 1975;117:289-297. [3] Arnold W et al, Proc Natl Acad Sci 1958;44:1-4. [4] Worcester DL, Proc Natl Acad Sci 1978;75:5475-5477. [5] Torbet J et al, FEBS Lett 1984;173:403-406. [6] Adzamli IK et al, Magn Reson Med 1989;11:172-181. Work funded by NIBIB P41 EB015897 and NIBIB T32 EB001040.

Table 1 Scan parameters for the four MR experiments

Scan	Contrast Agent (mM Gd)	Array Size (voxels)	Res (μm)	Flip Angle (°)	TR (ms)	$TE_1/\Delta TE/TE_n$ (ms)
GRE	0	256^3	45	35	200	1.7/3.0/46.7
GRE	2.5	256^3	45	50	50	1.7/3.0/22.7
DTI	0	64^3	180	90/180	2000	23.6/-/-
DTI	2.5	256^3	45	90/180	100	11.8/-/-

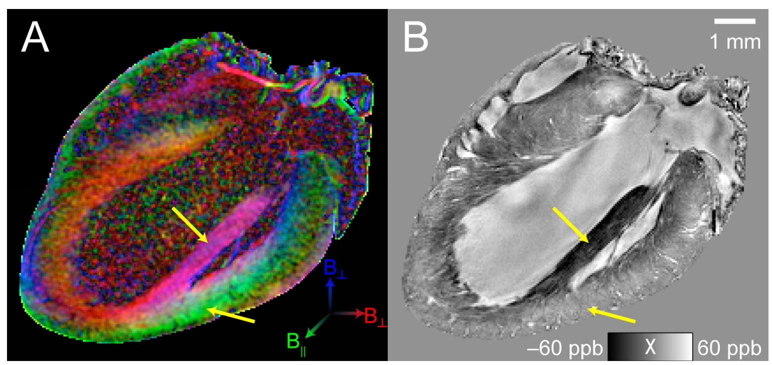

Fig. 1 A) DTI fractional anisotropy and B) magnetic susceptibility data acquired from a Gd-stained mouse heart specimen at 9.4 T. Muscle fibers that are perpendicular to B_0 (blue and red) appear more diamagnetic than parallel fibers (green) due to the magnetic anisotropy of myocardium.

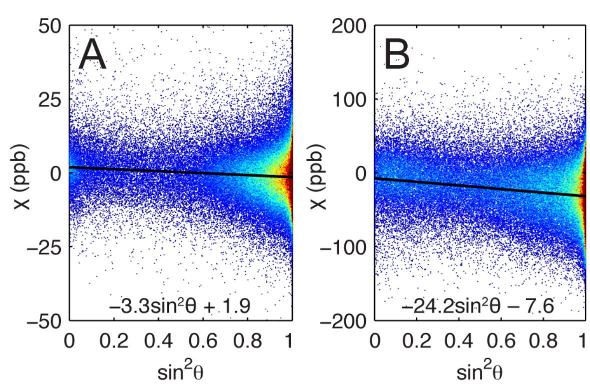

Fig. 2 Tissue susceptibility as a function of myocardial fiber angle A) before and B) after contrast enhancement. Gd increases the magnetic susceptibility anisotropy of myocardium. Only 5% of the voxel data is displayed.