BEYOND EDEMA: MYOCARDIAL T2 IN CHRONIC MYOCARDIAL INFARCTION SWINE

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Target Audience: Cardiologist, Cardiac MRI scientist, Clinicians

Introduction:

T_2 correlates with pathologic processes within myocardial tissue. Recently, quantitative T_2 mapping has been shown more robust than qualitative clinical T_2-weighted (T_2W) imaging in many diseases though most effort has been directed at acute injury and visualization of edema.[2,3] Chronic myocardial infarction (MI), can also demonstrate altered T_2, as the fibrotic scar tissue, mainly consisting of collagen, increases the interstitial space per unit volume.[1] Yet there are limited reports of measurement of T_2 in chronic MI.[4,5] In this work, we explore quantitative T_2 measurement as a way to characterize chronic MI without extraneous contrast agent.

Methods:

Animal Model: Reperfused MI was induced by 120 min occlusion of the middle left anterior descending coronary artery in N=5 Yorkshire swine (*37-45 kg*). Imaging was performed 14-16 weeks post-MI. *MRI:* 3D whole-heart free-breathing T_2-mapping,[6] consisting of interleaved volumes were acquired with T_2Prep TEs = 0, 25, 45 ms (TR/TE 4/1.2 ms, flip angle 18°, 1.25×1.25×5.0 mm^3 voxels interpolated to 0.98×0.98×2.5 mm^3) was achieved at 3T (Achieva TX, Philips Healthcare). Post-contrast late gadolinium enhancement (LGE) was acquired using a 2D phase sensitive inversion recovery (PSIR)[7] sequence (TR/TE 5.3/2.6 ms, flip angle 18°, 1.25×1.25×5.0 mm^3 voxels interpolated to 0.98×0.98×5 mm^3). After *in vivo* MRI acquisitions one of the animal received second contrast injection and was excised. The heart was scanned with T_1-weighted (T_1W) spiled gradient echo (SPGR) sequence about 1 hr post infusion for infarct identification (TR/TE 12/2.2 ms, flip angle 18°, voxel size 0.25×0.25×0.5 mm^3). *Histology:* The heart was fixed and fully preserved in 10% formaldehyde. After preservation, the heart were sliced and photographed and histology with Masson's Trichrome staining was obtained. *Post processing:* 3D T_2 maps were calculated per voxel using linear regression of the log of the signal and poor fits (R^2<0.9) were rejected. Representative apical/middle/basal slices were chosen from each case for quantitative comparison. 90 radial segments of each slice (total 1350 segments of each type of images) were made to extract the mean T_2 or signal intensity (SI) from T_2 maps and LGE images. Otsu's method[8] was used to compute a global threshold which maximized the separability of classes in gray levels to differentiate MI from normal myocardium in LGE. Average T_2 value from infarct and normal area was analyzed by unpaired 2-tailed Student's *t*-test with significance defined as p<0.05.

Results:

Chronic infarct was detected in all animals by LGE. T_2 map showed excellent correlation with the myocardial distribution of infarct as evidenced by elevated T_2 and the correlation with hyper-enhanced infarct area from LGE (Fig 1). T_2 in infarct was significantly higher than that of normal myocardium (62.9±14.1 ms v.s. 46.3±4.7 ms, p = 0.0002) (Fig 2). High spatial resolution T_2 mapping enabled heterogeneity detection in and around the infarct area. Figure 3 showed that collagen penetrated into normal myocardium at the border zone of infarct in T_2 map (Fig 3A and B), which excellently matched with the *ex vivo* T_1W image and histology. Fine fibrosis structure can be appreciated in the zoomed in images (Fig 3 B and C) and the corresponding histology (Fig 3D).

Discussion:

The exact mechanism of myocardial T_2 enhancement in chronic myocardial scar is not copmletely understood. In scared myocardium, both water and collagen content have an impact on relaxation times. The relative water content and its distribution impact T_2 measurments. Water in myocardial scar tissue might be also more mobile than those in healthy myocytes. [9] In addition, there is a positive relationship between collagen content and T_2 measurments in cardiac muscles, in contrary to skeletal muscles and tendons. [10] This might explain at least in part, the differencs between the various tissues. It is not known yet, however, if T_2(W) is suitable to differentiate acute and chronic stage in MI. The substance in acute MI tissue is different from chronic fibrosis. Weighted images might be less reliable to differentiate the sophistic status because the accompanying changes of both T_1 and T_2 relaxation properties.[11] It was reported that T_2 in acute stage was extremely higher than the chronic stage, the corresponding reference values might be a approach for differentiating acute and chronic MI. Of note, in this study, we were limited to a window time of up to 4 months post MI, though the wound healing process was not completed yet. T_2 elevation mechanism in chronic MI needs to be further elucidated.

Conclusion:

Myocardial T_2 mapping has the potential to noninvasively characterize chronic MI size, location and transmurality without exogenous contrast agents. The observed changes in T_2 may generally apply to any collagenous scar tissue, an important idea since collagen, though present in relatively small amounts even in normal tissue, strongly influences cardiac function.[12] Hence, native T_2 is a promising imaging probe to assist the further understanding on the myocardial tissue characterization.

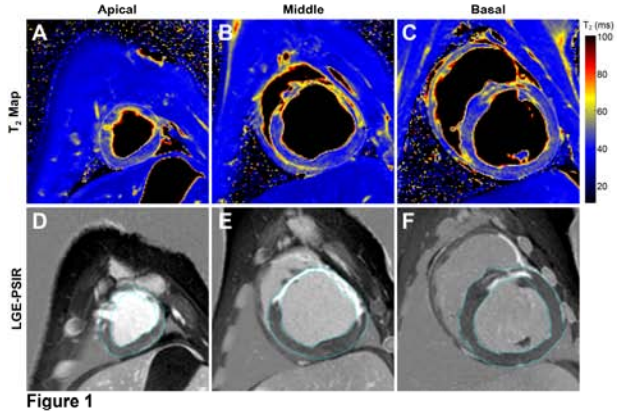

Figure 1

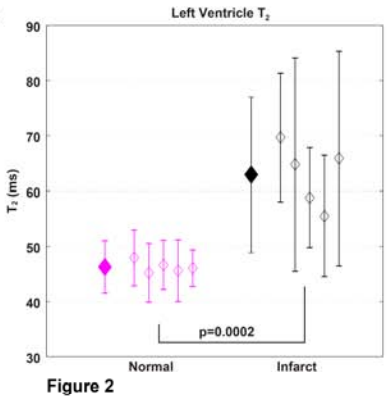

Figure 2

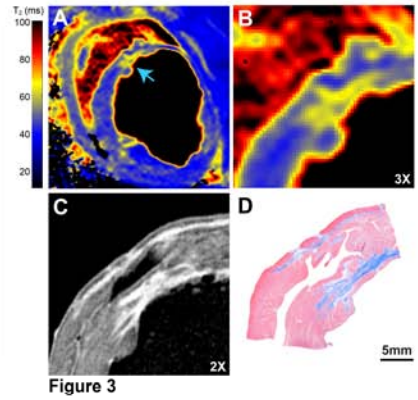

Figure 3

Figure 1: Representative T_2 map (A-C) and corresponding LGE-PSIR (D-F) for three short axix slices from apex and mid-cavity and base.

Figure 2: Comparision on the T_2 between normal myocardium and infarct identifed from corresponding LGE. Unpaired 2-tailed Student's *t*-test result shows singificant difference between the average T_2 from nomal myocardium and infarct. Solid symboles denote group averages.

Figure 3: Comparison of T_2 map (A) with zoomed inside (blue arrow, B) acquired *in vivo* on an animal 4 months post MI with equivalent slices from *ex vivo* T_1W SPGR (C) and Masson's Trichrome stain (D). Note correspondence of collagen deposition as visible on D with the increased T_2 value observed with A and B.

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References: [1] Lima et al. Circ 1995 92:1117; [2]Verhaert et al. JACC Card Img 2011 4:269; [3] Zia et al. Circ Card Img, 2012 5:566; [4] Krauss et al. Eur J Radiol. 1990 11:110; [5] Pflugfelder et al. JACC 1986 7:843; [6] Ding et al. ISMRM 2011; [7] Kellman et al. MRM 2002 47:372; [8] Otsu et al. Automatica. 1975 11:285; [9] Witschey et al. MRM 2010 64:1453; [10] Scholz et al. Inv. Radiol. 1989 24:893; [11] Ugander et al. JACC Card Img 2012 5:596; [12] Janicki et al. Adv Exp Med Bio. 1993 346:291;