Non-Contrast Myocardial Fibrosis Imaging using MT-weighted Balanced Steady State Free Precession MRI

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Target Audience: Cardiac MRI researchers and clinicians with a focus on tissue composition.
Purpose: To develop a cardiac MRI (CMR) method to image myocardial fibrosis ***without*** the use of gadolinium contrast agents.
Introduction: The development of myocardial fibrosis is increasingly linked to arrhythmia and sudden cardiac death (SCD)[1]. Late gadolinium enhanced (LGE) CMR has emerged as a reference standard for in vivo imaging of myocardial fibrosis with excellent prognostic ability, and when combined with a T1-mapping approach, can enable quantitative fibrosis imaging[2]. However, patients with acute and chronic kidney disease are considered contraindicated to LGE-CMR despite being at extremely high risk for cardiac events including SCD[3]. Recently, the magnetization transfer (MT) characteristics of balanced steady state free precession (bSSFP) imaging have been explored for imaging of edema following acute myocardial infarction[4]. We sought to exploit MT from fibrotic collagen to image myocardial fibrosis from pairs of differentially MT-weighted bSSFP cine images as a potential gadolinium-free and endogenous contrast based fibrosis imaging method.
Methods: 15 patients (7 men, 8 women, average age 54 ± 17 years) referred for clinical CMR examination were recruited to participate in the research protocol. All imaging was performed on a 1.5T Siemens Aera scanner (Erlanger, Germany) using a 12 channel chest array coil and an 8 channel spine coil. CMR of ventricular structure and global function was performed using a bSSFP sequence. In each patient, one mid-ventricular slice was selected and a set (Figure 1) of MT-weighted bSSFP cine images were acquired with minimal MT-weighting (excitation flip angle = 5º) and strong MT-weighting (flip angle = 45º). bSSFP imaging used a prospective acquisition with the number of cardiac phases optimized to fill the cardiac cycle. Additional parameters included TR/TE = 35.64/1.25 ms; FOV = 260x260 mm^2; Matrix = 256x256; Slice Thickness = 0.8cm; and in-plane spatial resolution was 1mm x 1mm. Maps of myocardial T1-relaxation times were acquired using a 5(3)3 modified Look-Locker imaging sequence (MOLLI) with FOV = 272 x 272mm; Matrix = 256*170; Slice thickness = 0.8cm; and flip angle = 35°. Afterwards, gadolinium-DTPA (0.2mmol/kg) was infused via an indwelling intravenous catheter at an average rate of 4mL/s. After 15 minutes, LGE images were acquired using an inversion recovery pulse sequence (FOV = 260x260mm^2; Matrix = 256x192; TR/TE = 796/3.28ms; Averages = 1; Flip Angle = 25°, TI =250-350ms for optimal nulling) followed by post-contrast 4(1)3(1)2 MOLLI imaging. Maps of the MT-ratio (MTR) index were calculated on a pixel-wise basis as MTR Index = $(S_{45}-S_5)/S_5*100$ (%), where S represents the signal intensity of a given voxel. MTR Index measurements over the first 2 and last 2 cardiac phases at end-diastole were averaged. The gadolinium partition coefficient (λ) was calculated from sets of MOLLI images acquired before (pre) and 15 minutes after (post) infusion of gadolinium-DTPA as $\lambda = (R1_{myocardium,post}-R1_{myocardium,pre})/(R1_{blood,post}-R1_{blood,pre})$. Non-enhanced myocardium was selected on LGE images and fibrotic myocardium was identified as pixels with signal intensity > 2 standard deviations above the un-enhanced mean signal. Myocardial regions of interest in fibrotic and healthy tissue were used to calculate mean MTR Index and mean λ for each patient.
Results: Patterns of fibrosis were detected with LGE-CMR in 8 patients, and were also present as elevated MTR Index in all 8 patients. Fibrosis imaging with MT-weighted bSSFP cine CMR demonstrated strong spatial correlation with patterns of enhancement at LGE-CMR in patients with (Figure 1) and without fibrosis (Figure 2). The average MTR Index was significantly higher in myocardial tissue regions defined as fibrotic at LGE-CMR when compared to healthy tissue (Figure 3). Myocardial tissue with MTR Index > 175% (mean + 2*SD of healthy tissue) demonstrated elevated λ (0.68 ± 0.13 [A.U.]) when compared to myocardium with MTR Index <175% (0.41 ± 0.17 [A.U.], P<0.05).

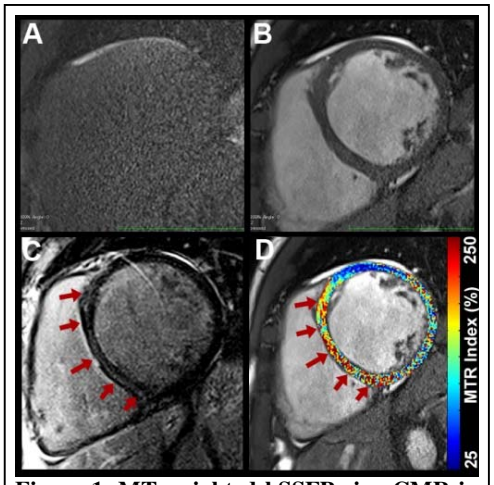

Figure 1. MT-weighted bSSFP cine CMR in a patient with non-ischemic dilated cardiomyopathy and LGE. (A) Reference end-diastolic bSSFP image acquired with flip angle = 5°. **(B)** MT-weighted bSSFP end diastolic image acquired with flip angle = 45°. **(C)** Late gadolinium enhancement (LGE) image reveals significant mid-wall fibrosis in the septum (red arrows). **(D)** Map of magnetization transfer ratio (MTR) calculated from images A and B, **prior to infusion of gadolinium**, reveals increased MTR in the septum in close spatial agreement with LGE image (C).

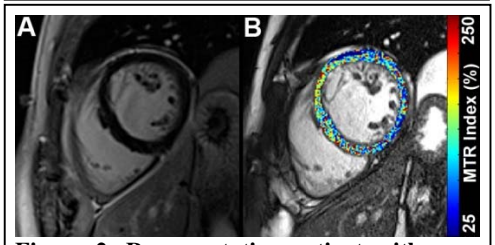

Figure 2. Representative patient with non-ischemic dilated cardiomyopathy without LGE. (A) LGE examination revealed no fibrosis. **(B)** MTR Index is uniformly low across the heart of this patient.

Discussion: Heightened MTR Index correlated strongly with myocardial fibrosis as identified by enhancement at LGE-CMR, and was further confirmed by quantitative measurement of elevated λ. Maps of MTR Index demonstrated strong spatial correlation with LGE-CMR in patients with non-ischemic dilated cardiomyopathy (Figures 1 and 2), hypertrophic cardiomyopathy, prior myocardial infarction, and left bundle branch block (not shown).

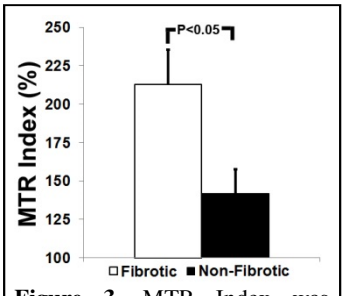

Figure 3. MTR Index was higher in myocardial tissue regions identified as fibrotic at LGE-CMR compared to healthy tissue (mean ± SD).

Conclusion: MT-weighted bSSFP enabled rapid and totally non-invasive imaging of left ventricular fibrosis in close agreement with standard of care LGE-CMR and without the use of gadolinium based contrast agents. Although this warrants confirmation in a larger number of patients, this novel technique is ideally suited to enable diagnosis and risk-stratification in large patient populations currently excluded from LGE-CMR but known to be at high risk of SCD, including the increasing number of patients with diabetes and CKD.

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References: **(1)** Wu et al. JACC. 2008; 51(25):2414-21. **(2)** Sibley et al. Radiology. 2012; 265(3): 724-32. **(3)** Scheitinger et al. JACC Imaging. 2008; 1(4):450-456. **(4)** Weber et al. MRM. 2009; 62(3):699-705.