Application of native myocardial T1 mapping in subjects with coronary microvascular dysfunction and no obstructive coronary artery disease

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Target Audience: MR scientists, cardiologists, and radiologists interested in myocardial T1 mapping and/or coronary microvascular dysfunction.

Background: Women with signs and symptoms of myocardial ischemia and no obstructive coronary artery disease (CAD) often have coronary microvascular dysfunction (CMD) evidenced by the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE) clinical studies [1,2]. Despite the absence of obstructive CAD, CMD is associated with a higher risk of adverse cardiac events including heart failure compared to healthy women and its clinical implications and treatment are currently important topics in non-invasive cardiology [1-3]. To date, the association of diffuse myocardial fibrosis and CMD has remained unexplored. In this study, we aimed at evaluating the presence of fibrosis in a cohort of subjects with suspected CMD using native myocardial T1 mapping. Elevated native T1 values are known to be suggestive of diffuse myocardial fibrosis, e.g. in hypertrophic and dilated cardiomyopathies [4,5]. We hypothesized that the native myocardial T1 would be abnormally elevated in WISE subjects with signs and symptoms of ischemia and suspected CMD, indicating the presence of diffuse myocardial fibrosis.

Methods: Symptomatic women (n=16) with no obstructive CAD (defined as ≥ 50% epicardial stenosis in at least one artery) and objective evidence of myocardial ischemia enrolled in a single site cohort of the NHLBI-sponsored WISE-Coronary Vascular Dysfunction study were evaluated. Subjects with evidence of left ventricular dysfunction, left ventricular hypertrophy, or valvular/structural heart disease were excluded.

In all subjects, T1 mapping using a vendor-provided 5(3)3 MOLLI sequence for the mid-ventricular slice was performed at 1.5T (Magnetom Avanto, Siemens Healthcare). The MOLLI acquisitions (8 inversion times (TIs) following 2 inversion pulses) were ECG-triggered and obtained during an end-expiration 11-heartbeat breath-hold. T1 maps were generated following on-line automatic motion correction of the 8 acquired TI images [6,7]. The mean myocardial T1 value for each subject was measured using a standard myocardial segmentation scheme. For comparison, the average native T1 value for normal controls (n=62) as previously reported in the literature [8] was used, all measured using the same vendor-provided MOLLI sequence on the same type of scanner (1.5T Magnetom Avanto, Siemens Healthcare). The native T1 values for symptomatic WISE women were compared to the reported normal controls using a one-sample t-test.

Results: The mean age of WISE subjects was 55±11 years with an average BMI of 23.5; 31.3% of subjects had hypertension and 6.3% had diabetes. All subjects had preserved ejection fraction (mean EF: 63%). No focally elevated native T1 region was observed in any of the subjects. A representative T1 map is shown in Figure 1. The published normal control group was 51.6% female with an average age of 43.6±17.4 and average BMI of 26.5. The mean native myocardial T1 values in the symptomatic WISE women were higher compared with normal controls (1043.7 ± 40 ms versus 964.6 ± 35.3 ms, $p < 0.01$), shown in Figure 2.

Discussion: Native T1 values in women with signs and symptoms of ischemia and no obstructive CAD were significantly elevated compared with normal values reported in the literature, consistent with the presence of diffuse myocardial fibrosis. Future studies using age- and sex-matched normal controls are needed to confirm these initial findings; however a recent multi-center study of native T1 reference values in normal subjects (Philips platform) showed no relationship between native T1 and age or sex (within 15 ms) at 1.5T [9]. The mean native T1 value for normal subjects from the multi-center study was 950±21 ms, which nearly matches the normal values used in this study.

Conclusion: Native T1 values in women with signs and symptoms of ischemia and no obstructive CAD were significantly elevated compared with normal values reported in the literature. Our initial findings suggest the presence of diffuse myocardial fibrosis in this population. The presence of diffuse myocardial fibrosis may elucidate a potential underlying mechanism leading to heart failure and other adverse events in patients with CMD, with important therapeutic implications.

References: [1] Gulati et al. Arch Intern Med 2009;169(9). [2] Pepine et al. J. Am. Coll. Cardiol. (JACC) 2010;55(25). [3] Crea et al. Eur Heart J. 2014;35:1101-1111. [4] Dass et al. Circulation: Cardiovasc Imaging 2012;5:726-33. [5] Puntmann et al. JACC: Cardiovasc Imaging 2013;6:475-84.[6] Xue et al. MRM 2013;69(5). [7,8] Kellman et al. JCMR 2012;14:63,14:64. [9] Dabir et al. JCMR 2014;16(69).

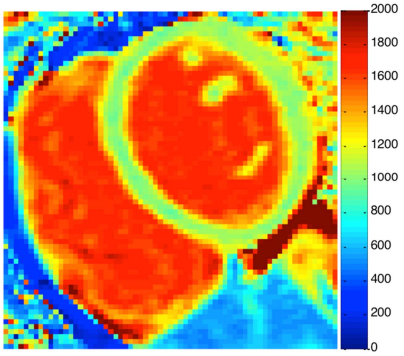

Figure 1. Native T1 map from a WISE subject with coronary microvascular dysfunction (CMD) with average native T1 of 1060.6±69.3 ms, significantly elevated from the normal reference mean (964.6±35.3 ms).

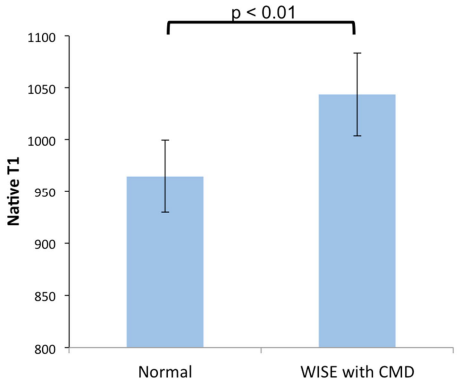

Figure 2. Native myocardial T1 for symptomatic WISE subjects with suspected coronary microvascular dysfunction (CMD) are higher compared with normal controls (mean values: 1043.7 ms versus 946.6 ms, $p < 0.01$).