Non-contrast characterization of interstitial cardiac remodeling in chronic kidney disease patients

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Target Audience: Cardiologists, nephrologists, and myocardial tissue characterization researchers.

Purpose: This study aims to evaluate gadolinium free identification of myocardial fibrosis in chronic kidney disease (CKD) patients using native T1-mapping[1] and 2-point bSSFP[2]. **Background:** The development of cardiac fibrosis, which is routinely identified using late gadolinium enhancement (LGE) MRI is linked to arrhythmias, heart failure, and sudden death. Individuals with CKD suffer particularly high rates of mortality from non-ischemic heart failure with an emerging link to fibrosis, however, concerns over nephrotoxicity of gadolinium contraindicate such patients to LGE. The application of non-contrast fibrosis imaging in CKD patients could enable better diagnosis and empower research into anti-fibrotic therapies that currently cannot be evaluated. Mapping of native myocardial T1-relaxation times is emerging as a potential method for identification of fibrotic tissue[1]. Previously we developed a cine bSSFP method termed 2-point bSSFP to identify fibrosis and edema through the acquisition of pairs of differentially MT-weighted bSSFP images and demonstrated agreement with LGE and with measures of fibrotic density through mapping of the gadolinium partition coefficient[2]. In this ongoing study we sought to evaluate both techniques for myocardial tissue characterization in CKD patients. **Methods:** Five patients undergoing routine hemodialysis treatment for CKD (average age 57 ± 20 yrs.) and 5 healthy controls (52 ± 4 yrs.) volunteered to participate. Imaging was performed on a 1.5T Siemens Aera scanner (Erlanger, Germany) using a 12 channel chest array coil and 8 channel spine coil. A full stack of short axis images was acquired along the entire left ventricle. At each slice position, pairs of prospectively gated cine bSSFP images were acquired with flip angles of 5º and 45º. Specific sequence parameters included TR/TE = 35.64/1.25 ms; FOV = 300x300 mm^2; Matrix = 256x256; Slice Thickness = 8 mm; in-plane spatial resolution = 1.17mm x 1.1 mm, and the number of phases set to fill the cardiac interval. Native-T1 maps were acquired using a 5(3)3 modified Look-Locker (MOLLI) sequence with FOV=300x300 mm^2. Matrix = 256x256; slice thickness = 8mm; and flip angle = 35°. Two-point bSSFP data was analyzed by calculating maps of $\Delta S/S_0$ as $\Delta S/S_0=(S_{45}-S_5)/S_5*100$ (%), where S_i represents the signal intensity for each voxel at flip angle *i*. Myocardial borders were manually defined for maps of native-T1 and $\Delta S/S_0$, and maps were segmented according to the AHA standard model. Threshold values for native-T1 and $\Delta S/S_0$ were defined as mean plus 2 standard deviations over all myocardial segments in healthy controls. Mean native-T1 and $\Delta S/S_0$ values were calculated per group, and the number of myocardial segments with values above threshold was measured per individual. **Results:** Mean myocardial native-T1 relaxation times were 997.4 ± 44.6(ms) in healthy controls vs. 1055.6 ± 41.6(ms) in CKD patients (p<.0001), and mean $\Delta S/S_0$ values were 127.6 ± 31.3(%) in control vs. 143.8 ± 36.6 (%) in CKD patients (p<.0001). The threshold value determined from healthy controls for native-T1 was 1086.6 ms and for $\Delta S/S_0$ was 190.2%. Representative maps of native-T1 and $\Delta S/S_0$ in a healthy control and a CKD patient are shown in Figure A. In healthy controls, only 0.5% of all segments were classified as having elevated native-T1 relaxation times, and 0.6% as having elevated $\Delta S/S_0$, with an individual average of 2.7 ± 6.0% and .6 ± 1.2 % of myocardial segments exceeding threshold values for native-T1 or $\Delta S/S_0$ (Figure B). In CKD patients, 26.5% and 6.3% of all segments were classified as elevated by native-T1 and $\Delta S/S_0$, respectively. Individual patient proportions of elevated segments were 24.4 ± 19.8% for native-T1 (p<0.05 vs. control) and 6.3 ± 4.0% for $\Delta S/S_0$ (p = 0.09 vs. control). Both Native-T1 mapping and 2-point bSSFP revealed only 1 control patient with segments classified as elevated compared to 4 CKD patients. **Discussion:** Fibrotic tissue is characterized by increased extracellular water volume which lengthens native T1 and T2 relaxation times and reduces MT in affected voxels. Whereas native-T1 mapping directly measures the lengthened T1 of increased extracellular water volume, 2-point bSSFP combines effects of lengthened T2 and reduced MT to identify fibrotic and edematous tissue. In patients with CKD both native-T1 mapping and 2-point bSSFP revealed areas of myocardium with increased values that likely reflect fibrotic remodeling of myocardial interstitium. Significantly higher fibrotic burden calculated by T1-mapping compared to 2-point bSSFP likely reflects the effects of motion registration artifacts towards the base and apex in the hearts of CKD patients resulting in higher T1 values[1]. **Conclusions:** Both techniques hold promise for cardiac diagnosis of CKD patients currently contraindicated to standard of care LGE. **Acknowledgements:** The authors thank Dr. Hartmut Malluche, Ms.Nedda Hughes and Ms. Kimberly McClaughlin. M.V. and S.L. are supported by National Center for Advancing Translational Sciences, National Institutes of Health, grant number KL2TR000116 and by NIH CTSA UL1TR000117. This work also funded by American Heart Association Nation Affiliate grant 14CRP20380071. **References:** (1) Dabir et al. J Cardiov Magn Reson. 2014; 16, 69. (2) Leung et al Proc. ISMRM. 2014; 22, 235.

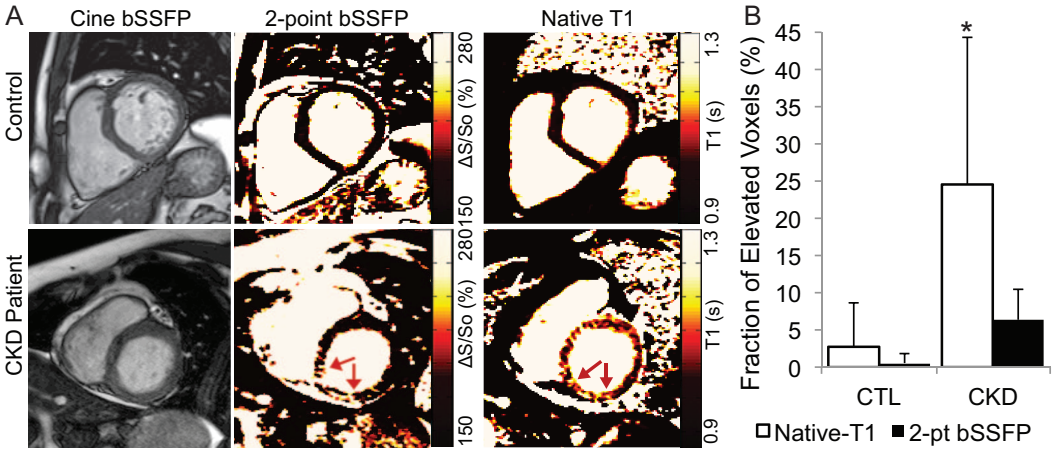

Figure. A. Representative basal slices from a healthy volunteer (control) and a patient with chronic kidney disease (CKD). 2-point bSSFP revealed areas of enhancement along the inferior RV insertion point (red arrows) in the CKD patient, which was also observed via native-T1 mapping (red arrows). Elevated T1 is also observed in the septum. **B.** Both techniques revealed a greater number of enhanced myocardial segments in CKD patients.