# In vivo 3D High Resolution Cardiac Diffusion Weighted MRI using Motion Compensated Diffusion-prepared Balanced Steady-State Free Precession Approach: Preliminary Application in Hypertrophic Cardiomyopathy Patients

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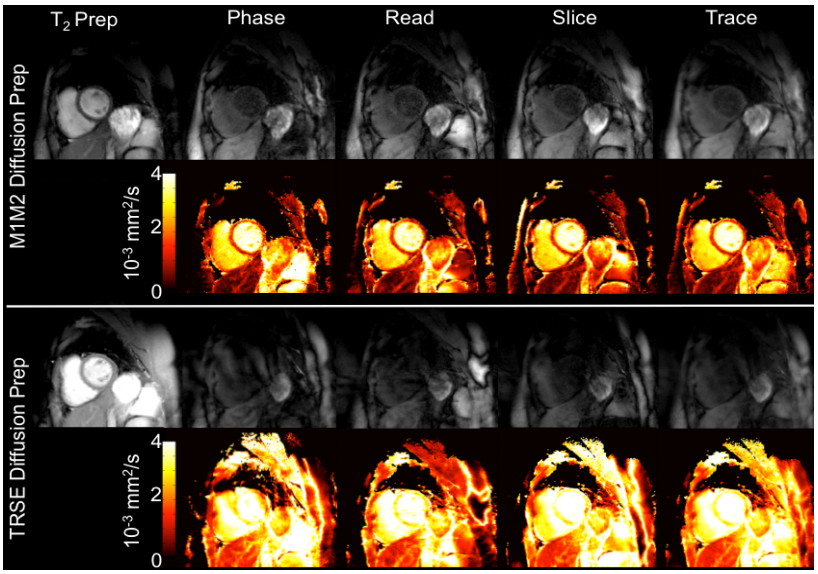
**Target Audience:** MR engineers, physicists, and clinicians (cardiologists and radiologists) interested in cardiac diffusion weighted MRI.

**Introduction:** Cardiac diffusion-weighted MRI has the potential to identify acute myocardial infarction, myocarditis, and myocardial fibrosis[1–3]. In studying diffusion MRI of myocardial fibrosis *in vitro*[3], the myocardial tissue microstructure exhibits fiber disarray that manifests in a stark increase (50-100% change for 20-70% fibrosis) in trace apparent diffusion coefficient (trADC). However, the presentation of the fiber disarray is commonly diffuse in non-ischemic hypertrophic cardiomyopathy (HCM) patients. This may affect the sensitivity of current *in vivo* cardiac diffusion MRI protocols[4,5] to reveal this signal change because they commonly have lower spatial resolution (voxel volume = 41 to 59mm$^3$). To address the possible partial voluming limitation, we developed a free-breathing bulk motion compensated diffusion-prepared segmented balanced steady-state free precession (bSSFP) technique capable of 3D high resolution *in vivo* cardiac diffusion-weighted MRI. For preliminary feasibility, we applied the proposed technique in HCM patients.

**Methods:** Diffusion-prepared sequences have the flexibility to diffusion encode with a multi-shot image readout. The diffusion preparation was optimized to reduce sensitivity to cardiac bulk motion with second order motion compensation (M1M2). The image readout consists of a 3D centric phase encoded segmented bSSFP acquisition that incorporates a prospective navigator. Ten healthy subjects were scanned twice (once in the beginning and at the end) on a 1.5T system (Siemens Avanto) using the proposed technique[6] (TR/TE=3.4/1.3ms, α=110°, 1.6x1.6x10mm$^3$ = 26mm$^3$, 4 slices, 40mm 3D slab, 5 linear ramp-up, b=450s/mm$^2$, $G_{diff}$=40mT/m). Diffusion preparation was applied in the diastolic phase with ($TE_{prep}$=115ms) and without (TRSE) ($TE_{prep}$=45ms) M1M2 using 3 orthogonal directions under varying off-resonance conditions. TrADC maps and the left ventricular (LV) trADC were calculated. For each slice, the LV was segmented into six AHA segments and segments were averaged across all slices. Additionally, we performed the proposed technique in HCM patients (N=2) using the same hardware and sequence parameters listed above. We compared trADC maps with phase sensitive inversion recovery (PSIR)[7] late gadolinium enhanced (LGE) images (TR/TE/TI=6.04/3.38ms/300ms, FA=25°, 1.4x1.7x6mm$^3$, 8 SAX) identifying elevated trADC and hyperintensity in LGE as fibrotic regions. TrADC of the fibrotic and remote regions were identified for each slice of each patient. Statistical significance was tested using two-tailed paired t-test for two mean comparisons and one-way ANOVA for multiple means comparisons.



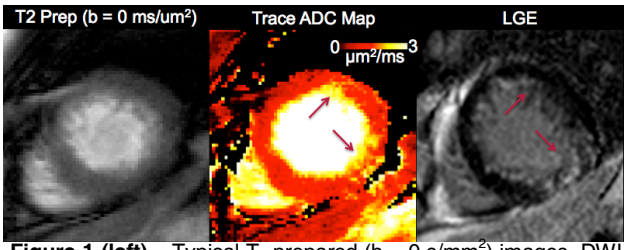




**Figure 1 (left)** – Typical $T_2$ prepared (b = 0 s/mm$^2$) images, DWI (b = 450 s/mm$^2$) in three orthogonal directions, and ADC maps for M1M2 (top) and TRSE (bottom) diffusion preparation. M1M2 diffusion-prepared images clearly depict myocardium with minimal artifacts and reasonable myocardial trADC values. TRSE diffusion-prepared images present ghosting artifacts and signal drop out due to bulk motion corruption.

**Figure 2 (top)** – T2 prep (b = 0 ms/um$^2$), Trace ADC map, and LGE image showing fibrosis in anteriolateral and inferolateral walls. Elevated regions in trADC map and feather-like hyperintensity in LGE are in spatial agreement (red arrows). In this slice, mean trADC in the fibrotic and remote regions were 1.7±x10$^{-3}$ mm$^2$/s and 1.1±x10$^{-3}$ mm$^2$/s, respectively.

**Results:** M1M2 diffusion-prepared scans resulted in LV trADC values of 1.5±0.4x10$^{-3}$ mm$^2$/s (population SD) that were reproducible yielding no statistical differences (p=0.54). Regional differences between six AHA segments were not statistically significant across all subjects (p=0.97). M1M2 diffusion-prepared images showed no ghosting artifacts and/or signal fallout. Under certain substantial off-resonance frequencies (e.g +200Hz), the proposed method failed in yielding both T2prep and DW images when bSSFP-related banding formed. The non-motion compensated diffusion-prepared scans yielded LV trADC values of 6.6±0.9x10$^{-3}$ mm$^2$/s and diffusion-prepared images with severe bulk motion-induced artifacts. In HCM patients, the trADC maps demonstrated agreeable spatial correlation in identifying regions of fibrosis with LGE. The difference in trADC values of fibrotic and remote regions were statistically significant when comparing all slices from both patients, $p < 0.05$ (1.8±0.3x10$^{-3}$ mm$^2$/s and 1.3±0.2x10$^{-3}$ mm$^2$/s, respectively).

**Discussion:** The LV trADC values derived with M1M2 motion compensation diffusion preparation were consistent with previously reported values ranging from 0.8 to 2.4 x10$^{-3}$ mm$^2$/s[4,5,8]. Regional differences in LV trADC values were not statistically significant for all healthy volunteers. The uncompensated diffusion preparation measurements yielded LV trADC values that were vastly greater suggesting motion corruption. In HCM patients, the spatial correlation between the trADC map and the LGE were visually in concordance. The mean trADC of fibrotic regions were ~40% greater than remote regions and found statistically significant when comparing across all slices.

**Conclusion:** We developed a novel free-breathing bulk motion compensated diffusion-prepared segmented bSSFP technique capable of 3D high resolution *in vivo* cardiac diffusion-weighted MRI. Preliminary application in HCM patients revealed diffusion change in LGE-identified fibrotic regions with a 40% increase in trADC. A potential application of the proposed diffusion technique is non-contrast imaging of myocardial fibrosis in HCM patients.

**References:** [1] Wu, et al. Circ (2006). [2] Potet, et al. Radiol (2013) [3] Pop, et al. Phy M Biol. (2013) [4] Nielles-Vallespin, et al. MRM (2012) [5] Rapacchi, et al. Inv Radiol (2011). [6] Nguyen, et al. MRM (2013). [7] Kellman, et al. MRM (2002) [8] Gamper, et al. MRM (2007)