High Spatial Resolution Myocardial T_2^* Mapping at 7.0 T Reveals Differences between Healthy Volunteers and Patients with Hypertrophic Cardiomyopathy

Till Huelnhagen[1], Fabian Hezel[1], Andreas Pohlmann[1], Andreas Graessl[1], Jan Rieger[2], Darius Lysiak[2], Christof Thalhammer[1], Peter Kellman[3], Marcel Prothmann[4], Jeanette Schulz-Menger[4,5], and Thoralf Niendorf[1,5]

[1]*Berlin Ultrahigh Field Facility (B.U.F.F.), Max-Delbrueck Center for Molecular Medicine (MDC), Berlin, Germany,* [2]*MRI.TOOLS GmbH, Berlin, Germany,* [3]*National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, United States,* [4]*Dept. of Cardiology and Nephrology, HELIOS Klinikum Berlin-Buch, Berlin, Germany,* [5]*Experimental and Clinical Research Center, a joint cooperation between the Charite Medical Faculty and the Max-Delbrueck Center, Berlin, Germany*

Target audience: This work is of interest for basic MR researchers, imaging scientists, clinical scientists, radiologists and cardiologists.

Purpose: Hypertrophic cardiomyopathy (HCM) is a genetic heart disease with a prevalence of 0.2-0.5% in the general population. HCM may cause sudden unexpected cardiac death in any age group. Myocardial disarray with myocyte hypertrophy and fibrosis are histopathologic hallmarks of HCM [1]. Cardiovascular magnetic resonance (CMR) is increasingly used for myocardial tissue characterization including late gadolinium enhancement (LGE) and T_1/T_2 mapping techniques [2, 3]. T_2^* sensitized MRI and T_2^* mapping provide alternative means for myocardial tissue characterization since microscopic susceptibility is related to tissue microstructure [4]. The linear relationship between magnetic field strength and microscopic susceptibility renders it conceptually appealing to pursue myocardial T_2^* mapping at ultrahigh fields [5]. Recognizing this opportunity, this work examines the capability of T_2^* mapping at 7.0 T to differentiate between normal myocardium and myocardial tissue affected by HCM. With the ultimate goal to provide an MR based biomarker that supports risk stratification of HCM.

Methods: Six healthy volunteers and 6 patients with confirmed HCM were examined using a 7.0 T whole body MR system (Siemens Healthcare, Erlangen, Germany) equipped with a gradient system (Siemens Healthcare, Erlangen, Germany, G_{max}=40 mT/m, slew rate=200 mT/m/ms). A 16 channel transceiver array tailored for CMR at 7.0 T was used for signal excitation and reception [6]. For all subjects 2D CINE FLASH imaging was performed for cardiac chamber quantification. For CINE T_2^* mapping a cardiac triggered interleaved multi-echo gradient-echo technique (TE = (2.04-10.20) ms, spatial resolution = (1.1x1.1x4.0) mm^3) was employed. Data acquisition was distributed over three breath-holds to cover 9 echo times and 19 to 24 cardiac phases [7]. A low flip angle (α=20°) was used to preserve myocardial signal. Midventricular short axis views of the heart were acquired. An MR stethoscope (MRI.TOOLS GmbH, Berlin, Germany) and pulse oximetry were applied for cardiac gating. All T_2^* sensitized images were de-noised with a spatially adaptive non local means filter [8] and co-registered. T_2^* mapping was conducted using a mono-exponential signal decay model. Fitting results with $R^2 < 0.5$ were excluded from T_2^* analysis to account for image artifacts and noise contributions. For myocardial T_2^* analysis only $0ms \leq T_2^* \leq 50ms$ was included. Differentiation between T_2^* of normal tissue and T_2^* of tissue affected by HCM T_2^* was performed using a histogram analysis along with cumulative frequency plots which can be interpreted as integrals of histograms.

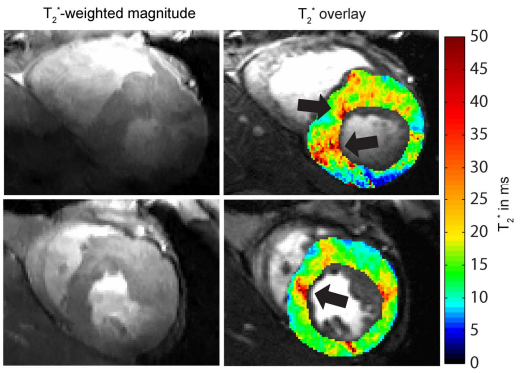

Figure 1: Mid-ventricular short axis views of the heart of two HCM patients. T_2^* weighted magnitude image **(left)** (TE=2.04ms) and myocardial T_2^* map superimposed to a 2D FLASH CINE image **(right)**. Focal regions of increased T_2^* are marked by arrows.

Results: T_2^* averaged over all myocardial segments and cardiac phases of the mid-ventricular short axis view was found to be elevated in HCM patients versus healthy volunteers. Healthy subjects yielded a median T_2^* of approximately 13.1ms. In comparison, HCM patients revealed a median T_2^* of approximately 17.5ms. Highest T_2^* values were found in the septal segments of the HCM patients as depicted in Figure 1. Some HCM patients also showed focal regions of increased T_2^* as depicted in Figure 1 for anteroseptal and inferoseptal segments. Figure 2 shows histograms together with cumulative frequency plots of myocardial T_2^* derived from healthy volunteers and HCM patients. A clear shift of the histogram peak toward higher T_2^* was observed for HCM patients. This observation manifests itself in a significant rightward shift in the cumulative frequency plots. The broader peak in the histogram obtained from the HCM patients represents a greater heterogeneity in T_2^* versus normal myocardium.

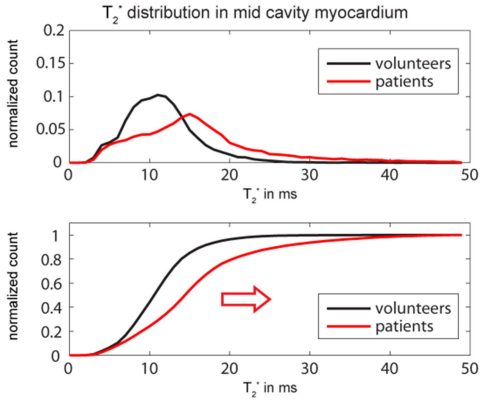

Figure 2: Histogram and cumulative frequency plot of T_2^* in mid cavity myocardial short axis views. Combined data from six healthy volunteers and six HCM patients for all cardiac phases.

Discussion: To the best of our knowledge this is the first patient study report on cardiac MR at 7.0 T. While the multi-breath-hold acquisitions used in our study remain a concern and demand faster T_2^* mapping techniques our results underline the basic feasibility of high spatial resolution T_2^* mapping in patients at 7.0 T. Our results demonstrate that myocardial T_2^* is elevated in HCM patients versus healthy volunteers. While the biophysical and (patho)physiological mechanism triggering this T_2^* difference remain to be unraveled potential mechanisms include changes in (i) myocardial microstructure, (ii) myocardial perfusion or oxygenation and (iii) macroscopic morphology. Since microscopic susceptibility increases with field strength, thus making the field perturbation effect of myocardial micro-structure and BOLD effects more pronounced, T_2^* mapping at 7.0 T might be beneficial to address the T_2^* sensitivity-constraints reported at 1.5 T and at 3.0 T.

Conclusion: This is the first patient study report on cardiac MR at 7.0 T. High spatial resolution myocardial T_2^* mapping at 7.0 T reveals differences between healthy volunteers and patients with hypertrophic cardiomyopathy. This observation holds the promise to provide means for an MR based biomarker for the risk stratification of HCM.

References: [1] Noureldin et al. (2012) JCMR 14:17, [2] Ferreira et al. (2014) J Thorac Imaging 29(3):147. [3] Treibel et al. (2014) Curr Cardiovasc Imaging Rep 7(3):9254, [4] Ziener et al. (2012) MRM 30(4):540, [5] Meloni et al. (2013) MRM, [6] Thalhammer et al. (2012) JMRI 36(4):847, [7] Hezel et al. (2012) PLoS One 7(12):e52324, [8] Manjon et al. (2010) JMRI31(1):192.