Quantification of macromolecular albumin-Gd-DTPA contrast using 3D cardiac T1 mapping in normal myocardium

Vandoorne Katrien[1], Moriel H Vandsburger[2], Hagit Dafni[3], Michal Neeman[4], Gustav J Strijkers[1], and Klaas Nicolay[1]
[1]Biomedical NMR, Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands, [2]Physiology, University of Kentucky, Lexington, Kentucky, United States, [3]Veterinary Resources, Weizmann Institute of Science, Rehovot, Israel, [4]Biological Regulation, Weizmann Institute of Science, Rehovot, Israel

Target audience: Cardiovascular magnetic resonance researchers. **Purpose:** This study aimed to develop a method to quantify the dynamics of a blood pool contrast agent for mapping the myocardial microvascular density and the rate of extravasation from blood vessels at the myocardium using *in vivo* dynamic contrast enhanced (DCE) MRI. **Methods:** C57BL/6 mice (n=8) were imaged at a 9.4T Bruker experimental scanner, using a 72-mm-diameter volume transmit coil with a phased-array surface coil (Bruker Biospin, Ettlingen Germany). Three-dimensional (3D) Intragate FLASH images of the entire heart with retrospective gating were acquired before and after intravenous injection of macromolecular albumin-Gd-DTPA (10mg/mouse in 200µl; Relaxivity= r_1=130mM^{-1}s^{-1}; SyMO-Chem, Eindhoven, The Netherlands). A series of T1-weighted 3D-FLASH images were acquired with increasing flip angle to determine the endogenous myocardial T1 relaxation times prior to contrast agent administration in 8 mice. Afterwards, albumin-Gd-DTPA was injected through an indwelling tail vein catheter at a rate of 50µl/min. Consequently the dynamics of the contrast agent in n=4 mice was imaged by 4 consecutive scans with flip angle = 13º. In addition, a series of images were acquired with the same array of excitation flip angles as before in order to confirm changes in myocardial T1 relaxation times in 8 mice. MRI parameters included: flip-angles =2 º, 5 º, 8 º, 11 º, 13º as described before(1,2). Additional parameters included RF pulse of 1ms sinc pulse (10lobes, 20kHz); FOV 30x30x10; Matrix128x64x15 with zerofilling to 128x128x15; TE=1.784; TR=10; repetitions=22; and Scantime=4min. For the navigator slice parameters included RFpulse=1.5ms; Gauss pulse (Bandwidth=1830kHz); slice thickness=3mm. Pixel-by-pixel analysis was performed in MATLAB (Mathworks, Natick, MA, USA) to calculate the concentration of albumin-Gd-DTPA in a ROI that contained the myocardium for selected midventricular slices as described before (2). Fractional blood volume (fBV) and permeability surface area product (PS) values were calculated from a linear regression of the first 15min, after normalizing the concentration of contrast material in the selected ROI (the myocardium) by the concentration in the hepatic vein. **Results:** Preliminary results showed comparable precontrast T1 (1.75s±0.04) as previously published (1) (Fig. 1). Postcontrast T1 measured using precontrast T1 and the contrast agent's r_1 (0.72s±0.07) was almost identical to postcontrast T1 calculated based on variable flip angles (0.72s±0.06) (1,2). Fractional blood volume (fBV: 0.20±0.03) and permeability surface (PS: 0.005min^{-1}±0.009) were quantified for normal myocardium (Fig. 1, 2). **Discussion:** Cardiac MR T1 mapping (1) and the use of 3D cardiac T1 mapping to monitor the accumulation of contrast agents 24 hours after contrast injection in a murine myocardial infarction, has been described (3). Here, we quantify the characteristics and dynamics of the macromolecular contrast agent in blood vessels of healthy myocardium. **Conclusion:** In the future, this method will enable measurements of initial rate of extravasation of high-molecular-weight contrast materials specifically in tissues with high permeability, such as the infarcted myocardium. Therefore, this method using high-molecular weight contrast agent might allow quantification of permeability and has the potential to determine disease progression.

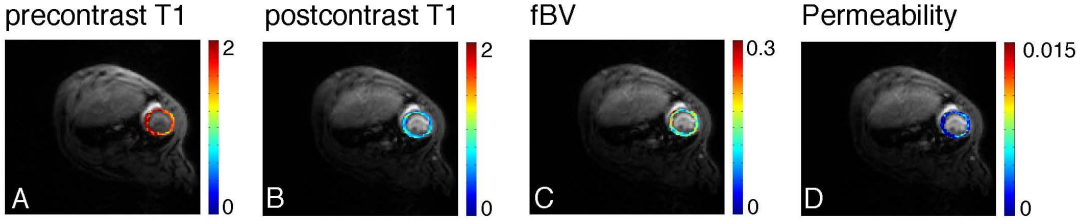

Figure 1. Representative midventricular slice of normal myocardium with an overlay of a parametric map of A) precontrast T1, B) postcontrast T1, C) fractional blood volume (fBV) and D) Permeability (PS)

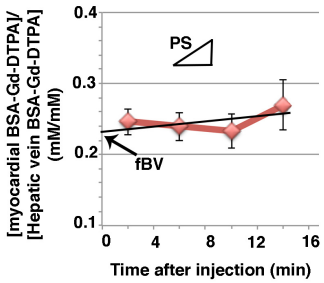

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Figure 2. Time-course of the ratio of [albumin-Gd-DTPA] in myocardium and hepatic vein using in vivo DCE-MRI for 16 minutes post contrast (4 time points). From the linear regression the intercept with the y-axis indicates the fractional blood volume (fBV) and the slope demonstrates the permeability surface area (PS).