

Estimation of the Myocardial Extracellular Volume Fraction from Dynamic Contrast-Enhancement Measurements and Comparison with Partition Coefficient Measurements

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Introduction: Recent studies have shown that myocardial T1 after administration of an extracellular Gd-based contrast agent and the myocardial partition coefficient represent novel biomarkers of diffuse fibrosis, which may be not recognized by standard methods for imaging delayed contrast enhancement [1-2]. Such novel markers of diffuse fibrosis and remodeling of the extracellular matrix could be useful for detecting and monitoring the progression of cardiac diseases and heart failure, and reduce the need for myocardial biopsies. The myocardial partition coefficient, when corrected by the blood hematocrit, provides an estimate of the extracellular volume fraction (v_{ec}), which is independent of the contrast dosage. It is nevertheless time-consuming to accurately measure the myocardial partition coefficient by multiple pre- and post-contrast T1 measurements. In this study we investigated the possibility of determining the v_{ec} with a single dynamic imaging acquisition at rest using a bolus injection of an extracellular contrast agent [3].

Methods: The study was conducted in 20 patients (11 with congenital heart disease; 9 with idiopathic dilated cardiomyopathy) and 12 normal controls in a 3 Tesla MRI system (Philips Medical Systems). Multiple (3 to 5) T1 measurements were made in each study with a Look-Locker cine technique with an inversion time (TI) resolution of 40 ms and segmented gradient-echo acquisition (TR/TE/flip angle = 3.4/1.7 ms/12°; slice thickness = 8 mm; 176 x 140 matrix; 40 ms per segment; FOV = 380 x 320-380 mm; SENSE factor of 2) and using a total Gadolinium-based contrast dosage of 0.1 mmol/kg (Omniscan, GE Healthcare). Dynamic contrast enhancement was measured with a single-shot gradient echo pulse sequence with non-slice selective saturation-recovery magnetization preparation (TR/TE/flip angle: 2.4/0.98 ms/ 20°; 160 x 140 matrix; field of view ~ 380 mm and 80% rect. FOV factor). The myocardial partition coefficient for Gd-DTPA (λ_{Gd}) was determined from the T1 measurements by fitting a least squares regression line to R1 values in tissue (R1t) vs. R1 in the blood pool (R1b). An example is shown in Figure 1a. The extracellular volume fraction was calculated as $\lambda_{Gd} \cdot (1-Hct) \cdot \rho$, where Hct is the blood hematocrit and ρ the specific density of myocardial tissue ($\rho=1.05$ g/ml). Signal intensity curves for myocardial contrast enhancement were fit to a two-space model of blood-tissue exchange implemented in the JSIM modeling environment (<http://physiome.org/jsim/>), with v_p and v_{isf} , representing the plasma and interstitial volume fractions, respectively, F_p the plasma blood flow, and PS the permeability surface area product. The parameters v_{isf} , F_p , and PS were optimized with a Simplex algorithm, and v_p was kept constant at a default value of 0.045 ml/g. The extracellular volume fraction was estimated from the optimal parameter values as $v_{ec} = v_p/(1-Hct) + v_{isf}$. Bland-Altman analysis was used to compare the estimates of v_{ec} .

Results: An example of the fit of dynamic contrast enhancement data to the two-space JSIM model is shown in Figure 2b. The estimates of v_{ec} from the T1 measurements averaged 0.28 ± 0.06 (mean \pm SD) vs. 0.29 ± 0.05 ($p=0.46$, $N=29$). The 95% confidence limits for agreement between individual measurements ranged from -0.08 to 0.06 (Bland Altman plot). Fits were repeated for a range of plasma volumes from 0.03 to 0.07. The v_{ec} estimate, representing essentially the sum of interstitial space and plasma volume was relatively insensitive to these changes of v_p (coefficient of variation for $v_{ec} = 3.4 \pm 2.5$ %), while the plasma flow changed had relative variation of 7 ± 6.6 % over the same range of v_p . If the distribution volume of Gd-DTPA was estimated from the signal intensity ratios in tissue and blood pool one minute after contrast injection, then v_{ec} tended to be underestimated, and the flow-adjusted estimate obtained with JSIM avoided this bias.

Discussion: Multi-slice measurements of myocardial contrast enhancement by dynamic imaging provide an efficient method to determine the distribution volume for an extracellular contrast agent, compared to multiple T1 measurements. The main determinant for the precision of v_{ec} obtained from dynamic contrast enhancement is the contrast-to-noise. Further optimization of contrast-to-noise and contrast injection parameters may allow in the future the replacement of multiple time-consuming T1 measurements by a single multi-slice dynamic contrast enhancement measurement.

References:

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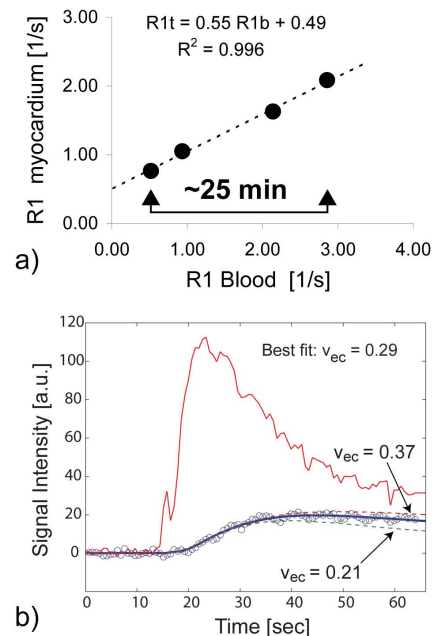


Figure 1