T1 pulse sequence optimization in a diabetic cohort

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Introduction: Diabetic cardiomyopathy (DCM) is increasingly recognized as contributing to the morbidity and mortality of diabetic patients. It is characterized by pathological ventricular remodeling, and occurs independently of myocardial infarction. This gradual remodeling of the left ventricular myocardium is characterized by diffuse fibrosis, myocyte apoptosis and hypertrophy. Quantitative MRI measurements of left ventricular remodeling processes have the potential to facilitate earlier diagnosis and allow therapeutic monitoring of patients with DCM. The Gd-DTPA partition coefficient or λ, defined as the tissue-to-blood ratio of extra-cellular volume fractions, should be valuable because changes in λ from control values of 0.3 reflect alterations in the extra-cellular volume, such as that seen in pathological ventricular remodeling.[2] Myocardial λ measurements use indices of endogenous (endog) and contrast-enhanced (ce) T1 in myocardium (myo) and ventricular blood (lv). Prior pre-clinical and clinical trials of acute and chronic infarction have noted gross λ fluctuations from control values between 50 and 240%.[1-3] This study evaluates methodological optimization for λ quantification in a clinical diabetic population using a novel single-point T1 strategy employing spiral imaging.

Methods: The targeted patients comprised two Type 1 and one Type 2 diabetics, with diabetes for greater than 10 yrs duration, without micro or macro-vascular complications, and with normal renal function (estimated GFR >60ml/min/1.73m^2). The MRI evaluation included T1, function, and infarct imaging, using a 1.5 Tesla GE Signa and a cardiac phased-array coil. Gd-DTPA administration consisted of bolus delivery (0.3 ml/kg) followed by low dosage continuous infusion (0.004 ml/kg/min). λ was quantified directly from measurements of T1 rather than T1-weighted signal intensity ($\lambda = (1/T1_{myo,ce} - 1/T1_{myo,endog}) / (1/T1_{lv,ce} - 1/T1_{lv,endog})$), following a 35 minute delay for Gd-DTPA equilibration. Functional imaging was completed following initiation of Gd-DTPA infusion to facilitate time-efficient scanning.

The T1 measurement uses a time-efficient, single-point, motion-insensitive, and multi-slice modification of the T1prep technique, where the inversion pulse is toggled on and off for subsequent pulse sequence iterations so that the difference signal is a T1-weighted monoexponential decay.[2] Unlike Look-Locker T1prep, in which T1-weighted magnetization is sampled in a single slice with a series of small-tip angle α pulses, the single-point design samples magnetization at single TI values as a series of 2D slices across the targeted 3D volume using a train of 90º spectral-spatial pulses and spiral readout gradients. Furthermore, the cardiac phase is kept consistent across TI values by time-shifting the preceding non-selective inversion pulse relative to the cardiac trigger and imaging sequence. Respiratory motion is compensated in a free-breathing acquisition using the Diminishing Variance Algorithm with the respiratory belt and an overscan factor of 3, so that a complete data set is acquired with corresponding respiratory positions and outlier spiral interleaves are iteratively replaced until the total scan time is increased 3-fold.[5] The inherent flow insensitivity in the sequence facilitates ventricular T1 quantification, while wash-in effects consequent of multi-slice acquisitions are minimized by ventricular T1 evaluation in the slice corresponding to the first spectral-spatial pulse. The T1 acquisition time was approximately 6min, yielding images at 2 TIs (TI_{endog} = 14, 1014ms; TI_{pc} = 14, 514ms) using 2nex, 3 RR intervals, and 1.63mm in-plane resolution (10 4096-point spiral interleaves over 32cm at 125kHz readout bandwidth). The slice thickness was 8mm.

Ejection fractions were measured using standard software (Mass+, Medis, NL). T1 analysis (xcinema, Stanford, CA) first quantified global λ, as the mean and reproducibility (2σ) of λ measurements across three 8-mm basal and mid-myocardial slices separated by 1cm. A Monte Carlo simulation of SNR and noise reproducibility guided evaluation of more regional λ, identifying the target SNR for reduction of thermal noise reproducibility (2σ) to 5%, assuming viable λ of 0.3 and a 0.38mM vascular Gd-DTPA concentration at steady-state. The lower 95% CI of the mean per voxel SNR was applied to calculate the minimal region-of-interest volume (ROImin) for thermal noise insensitive λ quantification. The mean and reproducibility (2σ) of per subject regional λ was calculated using 8 equally-spaced ROImin within each myocardial short-axis image.

Results: Subjects demonstrated globally reduced ejection fraction (47±1%) but without delayed hyperenhancement post Gd-DTPA infusion. The associated global λ values (±2σ) were 0.47±0.06. 0.44±0.04, and 0.42±0.04 suggesting the feasibility of confident detection of 10% λ shifts in global evaluation. The per voxel SNR values (mean±2σ) were 158±48 at the early TI. Monte Carlo simulation predicts a reduction of noise reproducibility to (2σ) to 5% for per voxel SNR of approximately 300 at the experimental TI values. This target SNR is achieved when ROIs contain 8 or more independent voxels, given a lower 95% confidence interval of the per voxel SNR of 110. Regional measurements presented significant spatial heterogeneity (0.46±0.14, 0.47±0.14, and 0.47±0.17) even following removal of outliers identified by λ shifts greater than 2.5σ from the mean on a per subject basis. A total of 12 outlier points were identified over the total 72 ROI data set. Anteriorly-located outliers displayed elevated $T1_{myo,ce}$ and reduced λ (λ±2σ =0.23±0.14, n=5), while lateral-posterior outliers displayed reduced $T1_{myo,ce}$ and elevated λ (λ±2σ=0.71±0.14, n=7).

Summary: Quantitative λ measurements were performed within a diabetic cohort using a cardiac-gated but free-breathing single-point spiral T1prep strategy. Mean λ appears to be slightly elevated to 0.44 from control levels of 0.3.[2] The spiral methodology appears to provide reproducibility (2σ) in global λ quantification which is on the order of 10%, which is the sensitivity target for monitoring diabetic remodeling. However, regional evaluation suggests that global measurements hide countering biasing mechanisms, with reproducibility on the order of 30% using thermal-noise-insensitive sampling volumes of 0.2cc. Higher fidelity imaging at lung, venous, and septal interfaces (shorter spiral interleaves, increased k-space resolution) should elevate λ reproducibility in future cohorts.

References: 1) Flacke, Radiology, 2001; 2) Foltz, MRM, 2006; 3) Pereira, MRM, 1999; 4) Loganathan, Int. J. Cardiovasc Imag, 2006; 5) Foltz, MRM, 2003.

Figure: Representative endogenous and contrast-enhanced single-point T1-weighted images within a basal myocardial short-axis slice, and the associated regressions for global myocardial and vascular ROIs.