Optimization of Post Contrast T1 Mapping Time for Diagnostic Assessment of Myocardial Amyloid

Mitchell Anthony Cooper[1], Thanh D. Nguyen[2], Jonathan Weinsaft[3], Matthew Maurer[4], Suzanne Lentzsch[4], Heather Landau[5], Jiwon Kim[5], Sattar Gojraty[3], Silvina Dutruel[2], Martin Prince[2], and Yi Wang[2]

[1]*Biomedical Engineering, Cornell University, Ithaca, New York, United States,* [2]*Radiology, Weill Cornell Medical College, New York, NY, United States,* [3]*Cardiology, Weill Cornell Medical College, New York, New York, United States,* [4]*Columbia University, New York, New York, United States,* [5]*Memorial Sloan Kettering Cancer Center, New York, New York, United States*

TARGET AUDIENCE Researchers and clinicians performing cardiac MRI to characterize non-ischemic cardiomyopathies.

PURPOSE Cardiac amyloidosis is a non-ischemic cardiomyopathy in which insoluble proteins accumulate in the extracellular space of the myocardium, resulting in heart failure and death. The current gold standard for the diagnosis of cardiac amyloid is endomyocardial biopsy, an invasive procedure not well suited for screening purposes or serial assessment. Myocardial T1 mapping after the administration of gadolinium (Gd) contrast, which distributes within the myocardial extracellular space, has emerged as a noninvasive tool to detect and potentially quantify severity of cardiac amyloid (1-3). However, optimal imaging time points for maximizing post-contrast T1 differences between healthy and amyloid affected myocardium have not been established. The purpose of this study was to identify optimal T1 mapping time for amyloid diagnosis by performing numerical simulation of a tracer kinetic model as well as by measuring myocardial T1 at serial time points in healthy and amyloid positive patients.

METHODS Numerical simulation of the myocardial Gd concentration time curve was performed using a tracer kinetic model proposed by Henrik et al (4). The arterial input function was simulated using the local density random walk (LDRW) model with input parameters reported previously (5). Normal and diseased ECV was assumed to be 0.26 and 0.5 (3).

The cardiac MRI protocol (1.5 T) included 2 components – CINE imaging (SSFP) for cardiac structure/function, and T1 mapping for myocardial tissue characterization. T1 mapping was performed in two groups: (1) "amyloid +" subjects, defined by biopsy-proven systemic amyloid with associated remodeling suggestive of cardiac involvement (left ventricular [LV] hypertrophy and/or atrial dilation); (2) normative controls without risk factors for amyloid or cardiovascular disease. 13 subjects (6 amyloid +, 7 controls) were studied (42±20 years, 46% male); all amyloid affected subjects had biopsy-confirmed systemic disease with associated remodeling suggestive of cardiac involvement. T1 mapping was d using a conventional modified Look-Locker inversion recovery (MOLLI) sequence (flip angle = 30°; matrix 256x128; parallel imaging reduction factor = 1.5; linear view ordering; 6 Kaiser-Bessel ramp preparation; 17 heart beat acquisition), with T1 calculated using an established formula ($T1 = T1^{*}$ (B/A-1), where $T1^{*}$, A, and B were obtained via three-parameter exponential fit). [Gd] was determined using $1/T_{1,POST} = 1/T_{1,PRE} + R*[Gd]$ where the T1 relaxivity R = 4.3/sec/mM (4). To evaluate time-dependent differences in myocardial T1, MOLLI was acquired at sequential time points: pre-contrast (for concentration determination) and 3, 5, 10, 14, 20 minutes following intravenous administration of Gd (0.2 mmol/kg). T1 ROI analysis was performed for all subjects in the septal wall of the LV.

RESULTS Simulation predicted a peak difference in myocardial [Gd] between healthy and amyloid myocardium at approximately 1.5 min post contrast (Fig.1). Table 1 summarizes the cardiac parameters between the two imaging groups. Amyloid subjects had higher LV mass, lower myocardial contraction fraction, and larger left atrial area than controls, but similar LV end-diastolic volume, stroke volume, and LVEF. MOLLI was successfully acquired in all subjects at each time point: T1 differed significantly (all $p \leq 0.05$) between amyloid and control groups at all times (Fig.2). However, magnitude of difference temporally decreased following gadolinium administration (Fig.3): T1 differences between patients and controls were maximal at 3 minutes post-contrast (145±31 vs. 317±24 msec, $p << .05$) with progressive decrements thereafter, as evidenced by 54% relative difference between groups at 3 minutes and only a 37% difference at 20 minutes following Gd infusion.

DISCUSSION MOLLI-quantified myocardial T1 yields maximal difference between amyloid-affected subjects and normative controls within 3 minutes following gadolinium administration. Current findings support use of early post-contrast MOLLI T1 mapping for identification of cardiac amyloid.

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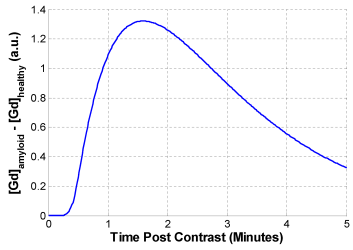

Figure 1. Simulated Gd concentration difference between healthy and diseased myocardium.

Table 1. Comparison of cardiac structure and function parameters measured by MR in amyloid patients and controls.

	Amyloid (n=6)	Healthy (n=7)	P value
LV mass [gm]	185 ± 47	107 ± 42	<0.01
Contraction fraction	0.32 ± 0.07	0.85 ± 0.22	<0.001
Left atrial area [cm^2]	24 ± 6	18 ± 4	0.05
LV end-diastolic volume [ml]	111 ± 31	137 ± 41	0.24
LV stroke volume [ml]	62 ± 14	90 ± 28	0.05
LV ejection fraction [%]	57 ± 10	66 ± 4	0.1

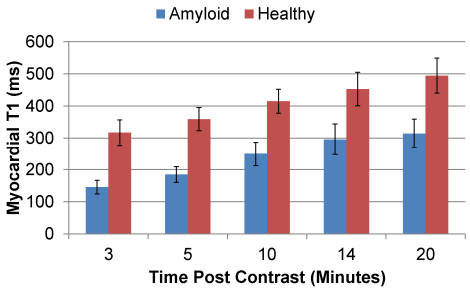

Figure 2. Temporal changes of myocardial T1 times for amyloid patients and healthy controls following a 0.2 mmol/kg Gd injection.