Evaluation of Cardiac Amyloidosis with T1 Mapping

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Introduction: Amyloidosis is a systemic clinical disorder characterized by extracellular deposition of insoluble fibrillar proteins in multiple organ systems including the heart. Cardiac involvement is present in up to 90% of patients with the most common form of the disease, and 50% of patient have heart failure as their first presenting symptom [1]. CMR is becoming a key modality for non-invasive evaluation of cardiac amyloidosis, and a diffuse pattern of delayed enhancement (DE) and reduced T_1 post gadolinium contrast have been associated with poor outcomes [2]. When the T_1 of the myocardium is similar to that of the of the blood pool the diagnosis can sometimes be uncertain by conventional DE imaging. Post contrast T_1 measurements have been useful, but they are affected by multiple factors such as timing after gadolinium (Gd) administration, and renal clearance. Determination of the partition coefficient (λ) or volume of distribution (Vd) of Gd has been applied to detect diffuse cardiac fibrosis in multiple cardiac pathologies, but has not be applied to quantitative evaluation of extracellular protein deposition in cardiac amyloidosis in patients. The goal of this project was to use a modified MOLLI T_1 mapping technique before and after gadolinium administration to determine λ and Vd of gadolinium and to compare these values to those of normal subjects. We hypothesize that these parameters will be markedly elevated in amylodosis due to the expansion of the extracellular space and will provide a quantitative assessment of cardiac amyloidosis.

Methods: T_1 mapping was performed in 5 subjects (63±9 years) with suspected cardiac amyloidosis as part of their clinical evaluation and in 7 healthy volunteers (50±10 years) on a 1.5T MR scanner (Magnetom Avanto, Siemens Healthcare) using a modified 3-5 MOLLI pulse sequence consisting of 2 inversions and 3 recovery beats between inversions. Images were acquired in 3 subsequent heartbeats following the first inversion, and in the 5 heart beats following the second inversion resulting in 8 images acquired over 11 heart-beats. Typical MOLLI sequence parameters included: TE/TR/FA 1.1 ms/2.5ms/35°, FOV= 340 x 260, resolution 1.8mm x 1.8mm, thickness 8mm. T_1 was determined pre-contrast and approximately 20 minutes following injection of 0.15 mmol/kg Gd-DTPA. Hematocrit (Hct) was measured in all volunteers, and the Hct closest to the day of the CMR study was used for the amyloid patients. T_1 maps were calculated and manually segmented using an in-house MATLAB program. λ was determined from the slope of a plot of $1/T_1$ of the myocardium versus $1/T_1$ of the blood. Vd was calculated as λ*(1-Hct). Values were compared between groups using 2-tailed unpaired t-tests.

Results: Amyloid was confirmed by biopsy in 3 subjects (1 renal, 2 heart) and suggested by elevated plasma light-chains in the setting of heart failure and diffuse LGE by CMR in the other two subjects. Figure 1 shows T_1 maps pre and post contrast from a representative normal control and the five subjects with cardiac amyloidosis. Table 1 shows a comparison of the T_1 mapping parameters between the amyloid patients and normal subjects. The T_1 of the blood pool is significantly higher in amyloid patients both pre and post contrast, and the T_1 is significantly increased in the myocardium pre-contrast. These parameters are roughly 10-20% higher than that of the normal controls. The λ and Vd are significantly increased in the amyloid patients, and these parameters are increased by 75% and 82% as compared to the normal subjects.

Table 1: Comparison of T_1 mapping parameters

	Amyloid (n=5)	Controls (n=7)	P value
T1 LV pre	1773±133	1509±85	0.03
T1 myo pre	1144±49	962±42	<0.001
T1 LV post t	485±18	408±42	0.002
T1 myo post	503±61	544±36	0.15
λ Gd	0.78±0.18	0.44±01	0.01
Vd Gd	0.51±09	0.28±01	0.005

Conclusions: The λ and Vd of Gd are significantly increased in patients with amyloid reflecting the increased extracellular space which is occupied by amyloid proteins. These parameters have not been utilized previously in the clinical evaluation of cardiac amyloidosis and may provide an index of overall disease burden. Furthermore, we demonstrated significant increases in T_1 pre-contrast in both the myocardium and blood pool in amyloid patients. This may potentially aid in the diagnosis of cardiac amyloid in patients who cannot receive Gd-DTPA due to renal insufficiency. Further research is warranted to see if λ and Vd can predict adverse outcomes in cardiac amyloidosis.

References

[1] Selvanayagam JB et al, JACC,50(22):2101-10, 2007
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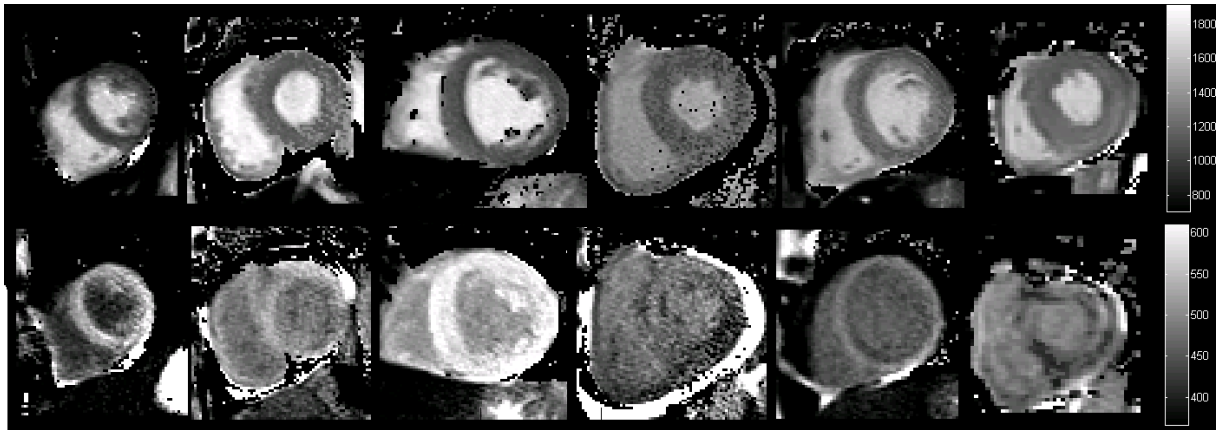

Figure 1: T1 images pre contrast (top row) and post contrast (bottom row) from a normal subject and the 5 subjects with cardiac amyloidosis. The corresponding Vd are 0.29, 0.49, 0.36, 0.55, 0.51, and 0.63 respectively