Quantitative Magnetic Resonance Imaging in Light-Chain (AL) Amyloidosis: Preliminary Experience

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Purpose: To evaluate the utility of multi-parametric quantitative MRI, including T_2 relaxation times as well as diffusion coefficients, in diagnosing organ involvement in AL (immunoglobulin light chain) amyloidosis using *ex vivo* MRI of human autopsy specimens of myocardium, kidney, liver, and spleen using MR imaging at ultra-high field strength (11.7T).

Methods: This study utilized human AL amyloidosis autopsy tissue specimens obtained from the Amyloid Treatment & Research Program Tissue Repository at Boston University School of Medicine, maintained with IRB approval. Specimens of myocardium with varying disease severity as well as samples of liver, spleen, and kidney, along with control tissues, were included in this study. Frozen autopsy tissue specimens were thawed to room temperature in phosphate buffered saline (PBS; pH=7.4). A 20mm transmit/receive quadrature RF-coil was used to image the tissue specimens, which were placed in 15 mm glass vials along with smaller vials (6 mm diameter) containing both PBS (free from contamination related to the specimens) and olive oil to provide absolute aqueous and lipid T_2 and ADC references. The sample was temperature-controlled and all imaging was performed at 22.5±1°C.

Imaging experiments were performed using an 11.7 Tesla MRI scanner. For the purpose of deriving parametric T_2 maps, a multi-echo conventional spin-echo with the following parameters was employed: TE1=6.4ms, echo spacing=6.4ms, echoes=32, TR=4000ms. For purposes of deriving parametric ADC maps, a multi-slice spin-echo pulsed field gradient (PFG) pulse sequence with the following acquisition parameters was employed: TE=14.5ms, TR=2000ms, b-values = 4, 270, and 560 s/mm2. The following geometric parameters were utilized: voxel dimensions = 150x150x700µm3 (reconstructed pixel size = 75x75µm) and matrix size = 100x100. Five representative regions of interest (ROIs) were placed on the parametric T_2 and ADC maps by a single investigator. T_2 values of olive oil and ADC values of PBS were recorded given their relative similarity to the T_2 and ADC values of the organs measured.

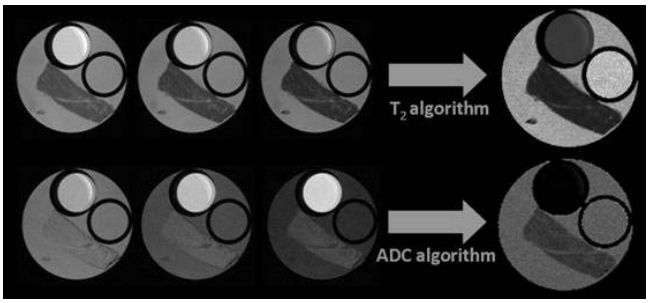

Figure 1. Directly acquired multi-echo TSE and DWI images used as to generate parametric T_2 (above) and AC (below) maps. Example includes myocardial specimen as well as reference vials containing olive oil (upper aspect of images) and PBS (rightward aspect of images).

The autopsy specimens were examined by histologically by a pathologist with expertise in grading the severity of organ involvement in AL amyloidosis. Sections stained with H&E and Congo red; definitive identification of amyloid deposition is based on the presence of apple-green birefringence following polarization of the congophilic deposits. The severity of amyloid deposition in the autopsy specimens was graded using the following scheme: 0, absence of amyloid deposition; 1+, perivascular amyloid deposition; 2+, perivascular and focal interstitial deposition of 2 or fewer high-power fields; 3+, prominent interstitial deposition of more than 2 high-power fields. T_2 and ADC values of tissues with amyloid deposition were compared to control specimens.

Results: Control specimens were from AL amyloidosis patients with histological proof of absence of disease involvement of that particular organ. The myocardial specimen was graded as 2+, while the kidney, liver, and spleen specimens were 3+. A single control specimen was compared with each involved specimen. A myocardial autopsy specimen with amyloid deposition limited to a perivascular deposition (1+) and a specimen with perivascular and focal interstitial deposition (2+) were included as well. A single severely involved (3+) specimen of the liver, spleen and kidney were included.

Significant differences in T_2 and ADC values were seen when comparing control and involved specimens of myocardium, spleen and kidney (all $p<0.0005$) (Table 1). Significant differences in ADC values were seen when comparing the control and involved specimens of liver ($p<0.0001$); no significant differences in T_2 values were found when comparing the liver specimens ($p=0.457$) (Table 1).

T_2 values of the olive oil had a mean value of 114.2+/-0.98ms, or a coefficient of variation (CV) of 0.0086. ADC values of the PBS solution had a mean value of 2.17+/-0.05x10-3 mm2/s, or a coefficient of variation (CV) of 0.021.

Conclusion: Deposition of amyloid protein in human autopsy specimens of patients with AL amyloidosis substantially affects ADC values in myocardium, liver, spleen, and kidney and T_2 values in myocardium, spleen and kidney. These findings offer the potential of developing a noninvasive imaging based methodology for diagnosing amyloid deposition in these organs.

Table 1. Comparison of T_2 and ADC values of human autopsy specimens of patients with AL amyloidosis.

Autopsy specimen		T_2 (ms)	p-value	ADC ($10^{-3}mm^2/sec$)	p-value
Myocardium	Amyloid – Interstitial	66.5 +/- 2.1	0.0014	1.31 +/- 0.04	<0.0005
	Control	76.0 +/- 3.9		1.46 +/- 0.04	
	Amyloid – Perivascular*	54.5 +/- 0.9	<0.0001#	1.16 +/- 0.10	<0.0001#
	Amyloid – Periascular**	71.0 +/- 4.4		1.53 +/- 0.06	
Liver	Amyloid	30.9 +/- 1.1	0.457	1.23 +/- 0.04	<0.0001
	Control	30.3 +/- 1.4		1.44 +/- 0.04	
Spleen	Amyloid	18.3 +/- 0.4	<0.0001	0.48 +/- 0.20	<0.0001
	Control	33.7 +/- 1.0		1.44 +/- 0.04	
Kidney	Amyloid	44.8 +/- 2.3	<0.0001	1.30 +/- 0.06	<0.0001
	Control	79.0 +/- 4.5		1.79 +/- 0.02	

*, ROI drawn in perivascular region; &, ROI drawn in myocardium, excluding perivascular region; #, comparison of values from perivascular regions versus non-perivascular regions