Measurement of tissue extracellular volume in health and amyloidosis using Equilibrium contrast MRI

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Purpose: Diffuse extracellular expansion occurs in a wide range of diseases and is frequently the result of diffuse fibrosis or amyloid deposition. Equilibrium MRI (EQ-MRI)[1] has been shown to accurately quantify diffuse myocardial interstitial expansion[2], however the principles of this technique are generalisable to other organs. Systemic amyloidosis is a condition in which the interstitium becomes expanded by deposition of abnormal amyloid proteins[3]. The aim of this study was to utilize Equilibrium MRI (EQ-MRI) to measure the extracellular volume fraction (ECV) within a set of healthy tissues; and demonstrate an increase in ECV in tissues known to accumulate abnormal amyloid protein.

Methods: Healthy volunteers (n=40) and patients with systemic AL Amyloidosis (n=67) underwent EQ-MRI after giving informed consent according to local ethics procedures. Extracellular volume fraction (ECV) was measured in the myocardium, liver, spleen, biceps brachialis and paravertebral muscles. Equilibrium imaging was performed using a primed contrast infusion (a bolus of 0.2ml/kg at 3ml/s followed 15 minutes later by an infusion of 0.133ml/hr for 30 minutes)[1]. Tissue T1 was measured within single slices acquired through the lower chest and upper abdominal using a multi–breath-hold, spoiled gradient echo, fast low angle shot (FLASH) inversion recovery technique (slice thickness 8mm, TR 2000ms, TE 3.15ms, flip angle=21°, field of view 400x260mm, increasing inversion times (TI) per breath-hold of 140 ms, then 200 to 1000 ms in 100-ms increments subsequently corrected for repeat time – fig 1). Regions of interest were drawn within each tissue and ECV calculated for each using the formula: $ECV_{tissue} = (1\text{-heamatocrit}) \times \Delta (1/T1)_{tissue} / \Delta (1/T1)_{blood}$

Variation in ECV between tissues was assessed using the Friedman test in both the healthy and amyloid groups. ECV measurements in the heart, liver, spleen and muscle of healthy volunteers were compared with those in the Amyloidosis population using a Mann-Whitney U test.

Results: Median ECV in healthy heart, liver, spleen, biceps and paravertebral muscle measured 0.22, 0.27, 0.33, 0.11 and 0.09 respectively; compared with 0.41, 0.31, 0.37, 0.16, 0.16 in the amyloid patients. A Freidman test demonstrated significant variation in overall ECV measured within these tissues ($p<0.0001$). There was a statistically significant increase in ECV within all organs in the amyloidosis group compared with healthy volunteers (fig. 2).

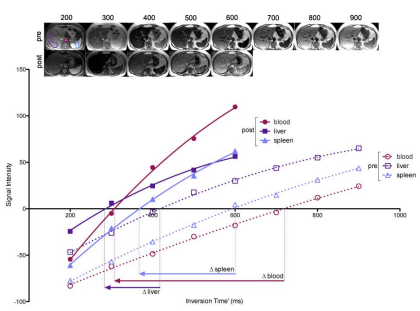

Figure 1. Images acquired at increasing inversion times and tissue signal intensity plotted with phase restored. From the inversion recovery curves, change in T1 can be determined

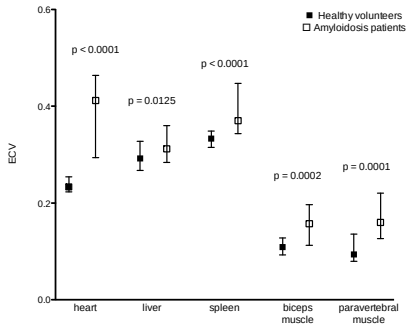

Figure 2. Comparison of tissue ECV measured in healthy subjects and amyloidosis patients (median and IQR)

Discussion: Equilibrium contrast MRI can be used to evaluate extracellular volume within tissues and can demonstrate variation in ECV between these tissues. Tissue ECV in patients with amyloidosis is significant higher than that measured in healthy volunteers.

Conclusions: Equilibrium contrast MRI could provide an alternative method for diagnosis and tissue evaluation in diseases that cause extracellular expansion, particularly for organs in which invasive biopsy is technically difficult or associated with a significant complication risk; for example in the liver and heart.

References:

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