Preliminary evaluation of the short term reproducibility of dynamic contrast enhanced (DCE) MRI in patients with carotid atherosclerosis

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Introduction

Several studies highlighted the pivotal role of inflammation in the pathogenesis of atherosclerosis[1]. Dynamic contrast enhanced (DCE) MRI has been shown to correlate to plaque inflammation in atherosclerotic rabbits and patients[2,3]. This technique has been shown to have excellent reproducibility and to be a good read-out for anti-inflammatory therapies in atherosclerotic rabbits. These results are encouraging and suggest a potential role for DCE-MRI in future clinical practice for the assessment of progression and/or regression of human plaques and as a surrogate imaging marker in clinical drug trials. However, DCE-MRI studies in patients are much more challenging than in animals, due to patient motion and signal dependence on surface coils sensitivity profile. Therefore, the reproducibility of this technique has to be evaluated in patients.

We present a preliminary study of the inter-scan reproducibility of DCE-MRI in patients with carotid atherosclerosis.

Methods

MRI Imaging: Three patients underwent carotid MR imaging at baseline and one week after baseline scan using a 1.5T clinical scanner and a 4-channel carotid array. Twelve non-overlapping black blood T1W, T2W and PDW cross sectional slices were obtained in the common carotids for plaque characterization[4]. DCE-MRI was performed on one selected axial slice (chosen as the slice with the greatest degree of wall thickening) using a double inversion recovery (DIR) black blood turbo spin echo (TSE) sequence (100 images, time resolution = 4.8 s). After a 24s delay from the beginning of the DCE-MRI acquisition (5 pre-contrast images), 0.1 mmol/Kg of Gd-DTPA was injected with a power injector followed by a 20 ml saline flush. Following DCE-MRI acquisition, a post-contrast T1 weighted image of the same slice chosen for DCE imaging was acquired for tracing of the vessel wall. All patients were imaged using the exact same protocol one week after baseline scan. Slice matching of DCE-MRI slices between sessions was achieved by evaluating anatomical fiducial markers (carotid bifurcation and cervical spine) in T1, T2 and PDW multi-slice scans.

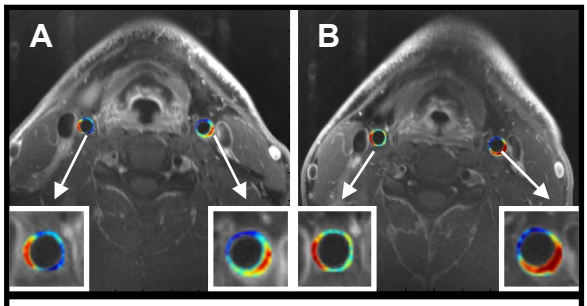

Fig 1: Representative overlay of AUC map on T1W post-contrast image of one patient. Panel A, baseline scan. Panel B, 1 week scan

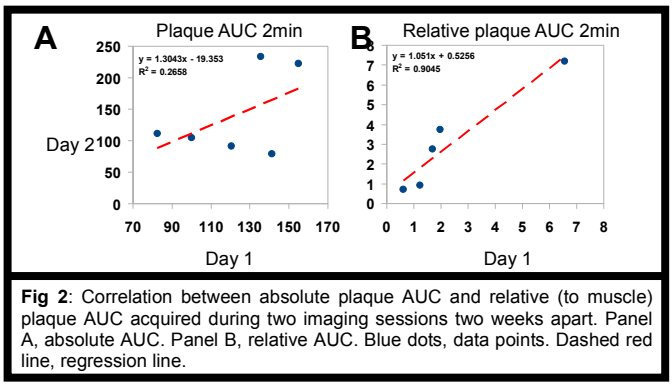

Fig 2: Correlation between absolute plaque AUC and relative (to muscle) plaque AUC acquired during two imaging sessions two weeks apart. Panel A, absolute AUC. Panel B, relative AUC. Blue dots, data points. Dashed red line, regression line.

Image analysis: Intra-series registration and de-noising of the DCE-MRI time series was performed by using the Kalman filtering, registration and smoothing (KFRS) algorithm[5]. Contrast agent uptake was evaluated by calculating the pixel-by-pixel area under signal intensity versus time curve (AUC) at different time points (1, 2 and 7 minutes after injection) by numerical integration via the trapezoidal rule. In order to ensure proper calibration of the signal between consecutive scans, AUC measured in the carotid wall was also divided by the AUC in the ipsi-lateral sternocleidomastoidl muscle, thus obtaining a relative AUC measure. Both carotids were analyzed in all three patients, for a total of 6 independent data points.

Statistical Methods: Intra-class correlation coefficients (ICC) with 95% confidence intervals were calculated to test inter-scan variability between baseline and one week AUC. The reproducibility of absolute plaque and muscle AUC and relative AUC measures was evaluated.

Results

Statistical analysis show **excellent reproducibility of relative AUC** calculated 2 and 7 minutes after contrast agent injection (ICC respectively 0.972 and 0.755, $p<0.05$). Relative AUC calculated at 1 minute after contrast agent injection showed poorer reproducibility. Sternocleidomastoid muscle AUC showed good reproducibility for all measures (ICCs > 0.7, $p<0.1$). Plaque absolute AUC, showed very poor reproducibility (see **Table 1**).

AUC Plaque (D1 vs. D2)			**AUC Muscle (D1 vs. D2)**			**Relative AUC (D1 vs. D2)**		
AUC 1min	**AUC 2min**	**AUC 7min**	**AUC 1min**	**AUC 2min**	**AUC 7min**	**AUC 1min**	**AUC 2min**	**AUC 7min**
ICC = 0.225 R = 0.158 p = 0.765	ICC = 0.521 R = 0.516 p= 0.295	ICC = 0.566 R = 0.423 p = 0.404	ICC = 0.91 R = 0.835 p = 0.078	ICC = 0.878 R = 0.838 p = 0.076	ICC = 0.733 R = 0.870 p = 0.055	ICC = 0.784 R = 0.656 p = 0.229	**ICC = 0.972** **R = 0.951** **p = 0.013**	**ICC = 0.755** **R = 0.970** **p = 0.006**

Table 1: ICCs, R and p-values are reported. Significant correlations are flagged in bold.

Conclusions

DCE-MRI of atherosclerosis has the potential to become a useful surrogate marker of plaque progression/regression in future clinical practice. In this preliminary study we investigate the reproducibility of DCE-MRI in patients with carotid atherosclerosis. We show excellent reproducibility of the AUC by DCE-MRI in the carotid arteries when normalized by ipsi-lateral muscle uptake. Despite being preliminary, this study shows promising results. We anticipate that more extensive evaluation of DCE-MRI reproducibility in carotid atherosclerosis could determine if this technique could be a useful tool for the evaluation of human atherosclerosis.

References

1) Moreno PR et al, Circulation 1994; 2)Kerwin WS et al, Circulation 2003; 3) Calcagno C et al, ATVB 2008 4) Mani V et al, Radiology 2004; 5) Kerwin WS et all, Magn Reson Med, 2002