Reproducibility of Contrast Enhancement Parameters in Carotid Atherosclerosis

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Introduction

High resolution MRI of the carotid artery is a valuable investigational tool for evaluating atherosclerotic plaque composition and the particular plaque features that relate to plaque rupture. Recently, contrast enhanced (CE) MRI of plaque using gadolinium agents has emerged as a new tool for plaque analysis because CE-MRI enhancement occurs for several important plaque features, including fibrous regions [1,2] and regions with neovasculature [2,3]. One very appealing aspect of CE-MRI for plaque analysis is the potential to extract quantitative parameters of enhancement that reflect overall plaque stability and may one day be used in assessing clinical risk. Already, dynamic CE-MRI coupled with kinetic modeling has been shown to elicit the extent of neovasculature [3] and macrophages [4], both of which reflect plaque inflammation, a possible precursor to rupture. These techniques are especially promising for use in clinical trials to quantify the effect of pharmaceutical agents, but first, the reproducibility of the measurements must be investigated. In this study, we evaluate the test-retest repeatability of two parameters derived from kinetic modeling of dynamic CE-MRI of plaque: the partial volume of plasma v_p and the transfer constant K^{trans}.

Methods

In vivo MRI examinations of eight carotid arteries with atherosclerosis and greater than 50% vessel stenosis were conducted at two time points. The time between the two examinations ranged from one to 13 days with an average separation of 7 days. The carotid imaging protocol included a 2D time-of-flight dynamic sequence (spoiled gradient echo; TR/TE=100/3.5ms; matrix=256x144; FOV=16x12cm; 6 slices; 10 time frames), wherein a dose of 0.1 mmol/kg of a gadolinium contrast agent (Omniscan, Amersham Health, Oslo) was injected coincident with the second image in the sequence. Within each MRI slice, the inner and outer boundaries of the plaque were drawn. Kinetic modeling of the plaque response to the contrast agent was then performed to measure the partial volume of plasma (v_p) and the transfer constant (K^{trans}) of the plaque as a whole, and for individual slices. Kinetic modeling was based on a two compartment model with reflux neglected and used change in signal intensity of the plaque and lumen as surrogates for concentration [see 3]. Images obtained at the two time points were matched and analysis was performed only on those images that were common to both sets. The interscan reproducibility of these measurements was evaluated by computing the intraclass Pearson's correlation coefficient (r), the sample standard deviation (σ), and the coefficient of variation (σ/μ).

Results

Twenty-four matched locations were available for this analysis. Figure 1 shows an example of data obtained at the two time points. Figure 2 shows the overall reproducibility of v_p and K^{trans} at the slice level. The corresponding intraclass correlations were 0.72 and 0.82, respectively. The reproducibility statistics showed closer agreement for v_p (r=0.91) when the plaques were analyzed as a whole (all slices together). As summarized in Table 1, plaque level v_p and K^{trans} values had standard deviations (1.4% and .012 min^{-1}) that were well below the average values (8.8% and 0.070 min^{-1}).

Conclusions

This experiment shows that CE-MRI of carotid atherosclerosis is capable of generating stable quantitative characterizations of plaque enhancement over multiple scans. The relatively wide ranges of v_p (typically between 0% and 20%) and K^{trans} (between 0 and 0.15 min^{-1}) observed are suggestive that different plaques respond very differently to gadolinium contrast agents and that this difference may prove clinically significant. The previously established link between these parameters and signs of inflammation add further evidence to support this hypothesis [3,4]. The contrast enhancement parameters are also potentially valuable for clinical trials of therapies that target plaque inflammation. The significance of these results for a single patient are, however, marginal for clinical decision making. If further studies indicate a link between enhancement and plaque stability exist, new MRI protocols for higher signal-to-noise ratios and more sophisticated kinetic modeling techniques will be required to improve reproducibility for the individual patient.

References

1. Wasserman et al. *Radiology*. 223:566-73, 2002.
2. Yuan et al. *JMRI*. 15:62-7, 2002.
3. Kerwin et al. *Circulation*. 107:851-6, 2003.
4. Kerwin et al. ISMRM abstract, 2004.

Table 1. Reproducibility statistics for dynamc CE-MRI variables (whole plaque composite)

Dynamic parameter	Intraclass r	σ	μ	Coefficient of variation
v_p	0.91 (p<0.002)	1.4%	8.8%	16%
K^{trans}	0.80 (p<0.02)	0.012 min^{-1}	0.070 min^{-1}	17%

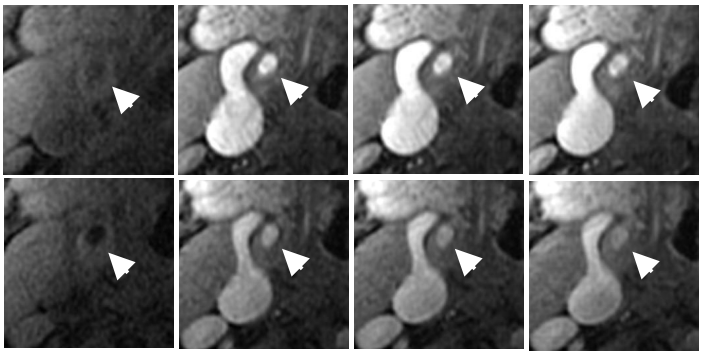

Figure 1. Qualitative reproducibility: dynamic CE-MRI of same artery (arrow) on two different days showing the first 4 time points in the sequence.

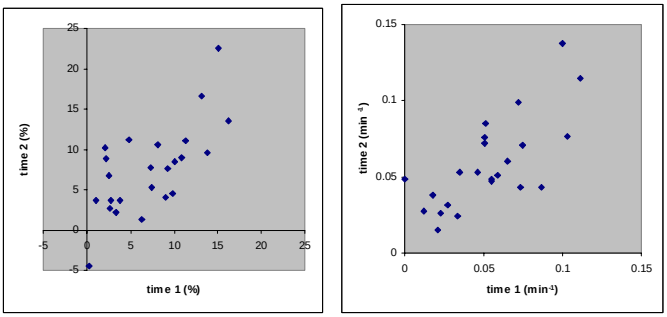

Figure 2. Quantitative reproducibility: comparison of slice-level v_p (left) and K^{trans} (right) measured from two different scans