Characterization of Multiple Sclerosis Lesions through a Quantitative study of Perfusion using a Gadolinium Contrast Agent

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Introduction

While Magnetic Resonance Imaging (MRI) has been used widely to confirm the diagnosis of Multiple Sclerosis (MS), conventional MRI techniques have shown a limited ability to demonstrate pathological changes that are characteristic of the disease [1]. Standard MRI in MS includes various types of contrast (T_1-weighted, T_2-weighted, etc.), as well as imaging after the injection of gadolinium (Gd) contrast agents (CAs). Gadolinium enhancement is indicative of a breakdown in the blood brain barrier (BBB), therefore visually enhancing lesions have been interpreted as active and it has been suggested that the presence of both enhancing and non-enhancing lesions is an indication of dissociation over time. In this study, we analyzed the pattern of enhancement in hypointense non-enhancing MS lesions, isointense non-enhancing MS lesions, enhancing MS lesions and normal appearing brain matter with Dynamic Contrast Enhanced (DCE) MRI using a two compartment model.

Materials and Methods

In this ongoing study we retrospectively analyzed clinical 3T MRI data from 37 patients from a pool of 160 patients diagnosed with MS. As part of the clinical scans, patients underwent DCE MRI on a 3T scanner (Achieva, Philips) using a Gd based contrast agent (Magnevist, Bayer Healthcare, dose: 0.1 mmol/kg, injection rate: 0.5 ml/s). DCE MRI was performed using a RF-spoiled Fast Field Echo (FFE) sequence (TR/TE: 8/4 ms; FA = 20°; FOV = 230 mm; matrix: 256x256; in-plane resolution: 0.9x0.9 mm^2; slice thickness: 10 mm; 20 slices centered 5 mm apart; acquisition time: 6.7s per time point for 50 time points with an 8-channel coil). DCE MRI data analysis was performed using an IDL based (ITT Inc, Boulder, CO) in house developed software. For this preliminary analysis, 109 regions of interest (ROIs) have been defined in the DCE datasets in locations that correspond to lesions identified on the FLAIR (Fluid Attenuated Inversion Recovery) images (Figure 1a). Each lesion ROI was categorized as isointense (49 lesions from 26 patients), enhancing (15 lesions from 9 patients), or hypointense (25 lesions from 16 patients). A control ROI was defined for each lesion in tissue that corresponds to normal appearing brain tissue in the FLAIR images on the contralateral side of the brain (when possible) to the lesion (Figure 1b) or next to the lesion. Signal enhancement curves for each ROI were evaluated using Brix's two compartment model [2], enabling quantification of the following pharmacokinetic parameters: exchange rate (k_{ep}[min^{-1}]); amplitude (*Amp*); and the elimination rate (k_{el}[min^{-1}]). Student's paired t-tests were performed to compare the pharmacokinetic parameters extracted from the different lesion ROIs to those from their matched controls.

Results

Statistically significant differences were seen in the mean values of *Amp* and k_{el} from the enhancing lesions and *Amp* from hypointense lesions when compared to those from their matched controls. Table 1 shows the mean values and the level of significance. There are quantifiable differences in the perfusion characteristics of enhancing lesions (Fig 1d), hypointense lesions, and normal appearing brain matter (Fig 1c). Enhancing lesions consistently showed a rising enhancement (negative k_{el} value) after the initial uptake of Gd (Fig 1d).

Table 1: Mean extracted *Amp* and k_{el} values for enhancing, hypointense, and isointense lesions vs. their matched controls. The p-values are for a two-sided paired Student's t-test (Bold represents statistically significant differences ($p<0.05$)).

	Enhancing Lesions		*Hypointense Lesions*		*Isointense lesions*	
	Lesion	*Control*	*Lesion*	*Control*	*Lesion*	*Control*
Amp	**0.227**	**0.068**	**0.089**	**0.064**	0.067	0.067
p- value	**$8.318 \cdot 10^{-5}$**		**0.028**		1.000	
k_{el}	**-0.127**	**0.269**	0.099	0.139	0.112	0.126
p-value	**0.026**		0.370		0.412	

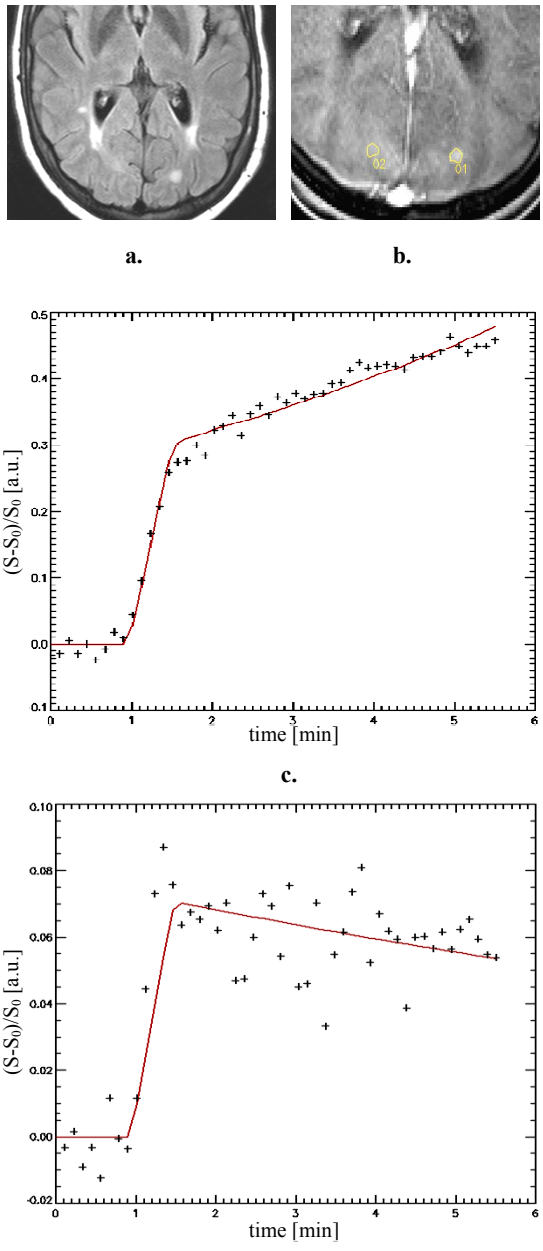

Figure 1: Typical Enhancing MS Lesion vs. matched control **a.** Transverse FLAIR image of the brain of a MS patient **b.** Lesion and control ROI definitions in a T_1-weighted image after Gd injection (01 is enhancing lesion ROI, 02 is control ROI). Signal enhancement over time and Brix Two compartment model curve of best fit for **c.** enhancing lesion ROI (*Amp* = 0.300, k_{el} = -0.112) and **d.** control ROI (*Amp* = 0.072, k_{el} = 0.069).

Discussion

Gd based contrast agents show more than just the presence of enhancing lesions in MS patients. DCE MRI is capable of detecting perfusion differences across different types of MS lesions and normal appearing brain tissue. The results of this preliminary analysis support the notion that DCE MRI could lead to a better understanding of the mechanisms and pathophysiology of MS lesions.

References

1. *J Neuroimaging* 17, 50S-55S, 2007 **2.** *J Comput Assist Tomogr* 15, 621-628, 1991