Quantitative Magnetization Transfer Imaging in Relapsing Multiple Sclerosis

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Background

Magnetization Transfer (MT) Imaging has become an important technique for characterizing lesions and to detect even subtle morphologic damage in patients with multiple sclerosis (1). So far MT has been quantified by the MT ratio (MTR) which is only a relative and composite measure of many processes contributing to spin relaxation.

Purpose

We recently have developed a method which allows for a more specific assessment of the major determinants of the MTR (2,3). We now have measured these variables in different types of MS lesions and investigated their relation to commonly reported MTR values.

Theory

Under the assumption of full RF saturation of protons bound to macromolecules such as the myelin lipids and proteins, MTR becomes solely a function of two parameters:

$$MTR = k \cdot T1_{free} / (1 + k \cdot T1_{free}) \qquad [1]$$

where k is the first order transfer rate and $T1_{free}$ is the native relaxation time of the bulk water in the absence of MT. $T1_{free}$ can be obtained with the knowledge of k and $T1_{sat}$ which is the apparent T1 under full RF saturation of the bound pool:

$$T1_{free} = 1/(1/T1_{sat} - k) \qquad [2]$$

The parameters MTR, k and $T1_{sat}$ can be estimated from a FastPACE experiment combined with pulsed RF saturation (2,3).

Subjects and Methods

Nine patients (6 women, 3 men, aged 25 to 50 years) with clinically definite MS and 8 healthy controls (4 women, 4 men, aged 18 to 45 years) were studied. All patients suffered from a relapsing-remitting course and had an Expanded Disability Status Scale (EDSS) score ranging from 1.0 to 5.0.

Conventional MR imaging and quantitative MT imaging were performed on a 1.5T unit (Gyroscan ACS-NT, Philips) using the standard head coil. The standard protocol included dual-echo spin echo imaging (TR=2060 ms, TE=20/80 ms) and precontrast and postcontrast T1-weighted spin echo imaging (TR=510 ms, TE=14 ms). The postcontrast scan was performed 5 minutes after intravenous application of 0.1 mmol/kg Gd-DTPA in MS patients only. Quantitative MT analysis was performed with a FastPACE sequence (TR=580 ms, α_1=45°, α_2=90°, phase cycling=90°/0°).

Parameter maps showing MTR, k and $T1_{sat}$ were calculated pixel by pixel using the modulus and phase images of the PACE acquisition as described in reference 2. $T1_{free}$ maps were calculated according to Eq.[2].

Conventional imaging was used to identify the following tissue categories: Normal appearing white matter (NAWM), diffuse white matter changes and focal non-acute and acute lesions. Focal non-acute lesions were subdivided according to their hypointensity on T1-weighted images as isointense, mildly (intensity > gray matter) and markedly hypointense (intensity < gray matter). Acute lesions were subdivided into densely enhancing lesions and ring enhancing lesions. Areas of marked hyperintensity around enhancing lesions which disappeared on follow-up scans were considered to reflect edema.

Results

In volunteers we analyzed 64 white matter regions considered as normal (NWM). In MS patients we analyzed a total of 296 areas. Quantitative results are summarized in Table 1.

While the MTR was significantly reduced in NAWM and dirty WM when compared to NWM, $T1_{free}$ was increased in dirty WM only. Focal non-active lesions showed a gradual decline of MTR and k values with greater T1-hypointensity. Inversely, $T1_{free}$ was noted to increase with T1-hypointensity. Different and more complex patterns could be observed within active lesions. While the MTR was lowest in ring enhancing lesions and highest in edema, $T1_{free}$ was lowest in densely enhancing lesions and highest in edema.

Overall, the transfer rate k correlated very well with the MTR when excluding edema and dirty WM. However, the transfer rate was more sensitive for tissue changes.

	Type	N	MTR [%] Mean(SD)	$T1_{free}$ [ms] Mean(SD)	k [sec^{-1}] Mean(SD)
Control					
	NWM	64	48.7(1.2)	670(51)	1.43(0.10)
Multiple sclerosis					
Diffuse Changes	NAWM	72	46.6(1.8)	664(49)	1.32(0.10)
	dirty WM	6	46.2(2.2)	721(29)	1.19(0.09)
Focal lesions					
Non Active	T1-isointensity	75	37.5(3.6)	803(68)	0.76(0.12)
	mild T1-hypointensity	79	33.1(4.3)	910(71)	0.55(0.11)
	marked T1-hypointensity	43	25.9(6.8)	1159(168)	0.32(0.11)
Active	dense enhancement	10	35.2(3.5)	822(30)	0.66(0.11)
	ring enhancement	8	25.2(4.1)	1048(237)	0.34(0.11)
	edema	3	39.2(2.6)	1250(20)	0.51(0.06)

Table 1: results of quantitative MT analysis in MS and controls

Conclusion

Although this study was performed with a limited number of MS patients, our results already demonstrate the potential of quantitative MT analysis. While MTR and k provide some redundant information the highest gain in additional information can be obtained from $T1_{free}$,which can be used as a relative measure for the water content. This information is particularly of high interest in areas where the interpretation of a pure MTR analysis is ambiguous, i.e. NAWM and acute lesions. Quantitative MT analysis offers a more detailed insight into MT dynamics and therefore could also serve better to monitor specific therapeutic interventions than the MTR.

References

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