Effect of Saturation Pulse Length on Parallel Transmission Based Amide Proton Transfer (APT) Imaging of Different Brain Tumor Types

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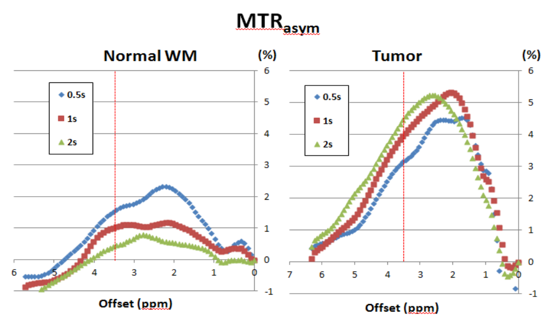
Introduction: Amide proton transfer (APT) imaging [1] employs the exchange between protons of free tissue water and the amide groups (-NH) of endogenous mobile proteins and peptides, imaged by a saturation transfer technique. It was demonstrated that the APT signal - defined as asymmetry of magnetization transfer (MT) at +3.5ppm relative to water - is increased in brain tumors and it could be clinically useful for the grading of glioma [2] and in differentiation of radiation necrosis and active/recurrent tumor [3]. In this imaging technique, the length of RF saturation (T_{sat}) is an important parameter for sensitivity. In APT imaging, the T_{sat} used in animal studies was usually a few seconds, however, it was typically limited to 0.5 - 1s on clinical scanners. Recently, a technique based on parallel RF transmission was demonstrated, which allows arbitrarily long RF pulses (~5s) via amplifier alternation in clinical scanners [4]. The purposes of this study were to initially evaluate the T_{sat} dependence of the APT contrast in human brain tumors and to demonstrate the efficacy of long T_{sat} achieved by the use of the parallel RF transmission based technique.

Materials and Methods: *Subjects:* Eleven patients with brain tumors (2 metastatic tumors, 3 high grade gliomas, 4 meningiomas, and 2 acoustic schwannomas) were included in this study. *MRI:* MRI was conducted on a 3T clinical scanner (Achieva TX 3.0T, Philips Healthcare, NL) using an 8-channel head coil for signal reception and 2-channel parallel transmission via the body coil. Acquisition software was modified to alternate the operation of the two transmission channels during the RF saturation pulse [4] and to allow a special RF shimming for the saturation homogeneity of the alternated pulse (identical mean B1 level per channel). Saturation pulse-trains: 50ms sinc-gaussian elements, $B_{1,rms}$=2.0μT. 2D fast spin-echo sequences with driven equilibrium [4] refocusing were used. The imaging parameters were as follows: T_{sat}=0.5/1.0/2.0s, TR/TE=5s/6ms, FOV (230 mm)^2, matrix 168^2, resolution $1.8\times1.8\times5$ mm^3, 25 saturation frequency offsets S[ω], ω=-6..6ppm (step 0.5ppm) and S_0 (ω=-160ppm), affording 2 minutes scanning time. δB_0 maps for off-resonance correction were acquired separately (identical geometry, 2D GRE, ΔTE=1ms, TR/TE=15ms/8ms, 16 averages, 33 sec). Maps of the MT asymmetry MTR_{asym}=(S[-3.5ppm]-S[+3.5ppm])/S0 were calculated with a point-by-point δB0 correction [4]. Region-of-interests (ROIs) were carefully placed in the entire area of Gd enhancing lesions within brain tumors as well as in normal cerebral white matter (WM).

	MTR_{asym} (3.5ppm)				ΔMTR_{asym} (3.5ppm) Tumor- Normal WM		
	T_{sat} 0.5s	T_{sat} 1.0s	T_{sat} 2.0s		T_{sat} 0.5s	T_{sat} 1.0s	T_{sat} 2.0s
Metastasis (n=2)	2.7±1.0%	4.3±0.2%	4.9±0.2%		1.1±1.0%	2.9±1.2%	4.1±0.6%
High grade glioma (n=3)	3.1±0.3	3.9±1.0	4.5±2.2		1.6±0.6	2.9±0.9	4.0±2.1
Meningioma (n=4)	2.6±1.0	3.0±1.0	2.4±0.9		1.1±1.0	1.9±1.1	1.9±0.1
Acoustic schwannoma (n=2)	3.2±0.2	4.1±0.2	4.8±1.6		1.7±0.7	2.6±0.2	4.1±1.5

Table 1: MTR_{asym} [%] and APT contrast between normal white matter and tumor (ΔMTR_{asym}) was evaluated in 4 different types of brain tumors and for 3 different lengths of the RF saturation (Tsat).

Results and Discussion: Table 1 shows MTR_{asym} (3.5ppm) and the APT contrast ΔMTR_{asym} (3.5ppm)= MTR_{asym} (tumor) - MTR_{asym} (WM) in each tumor type and for the three T_{sat} values. Both MTR_{asym} (3.5ppm) and ΔMTR_{asym} (3.5ppm) were increased with the length of T_{sat} and became maximum at T_{sat} of 2.0s in all types of tumor except for meningioma (maximum at T_{sat}=1.0s). **Figure 1** shows the spectra of MTR_{asym} and ΔMTR_{asym} averaged in the group of high grade glioma (n=3) for normal white matter and brain tumors. In normal white matter, MTR_{asym} was decreased as T_{sat} became longer. Because this effect is visible on the whole range of saturation frequency offsets, it could be attributed to a stronger overall contribution of the native asymmetry of the macromolecular MT effect with increasing T_{sat}. In contrast, MTR_{asym} (3.5ppm) in the tumor was consistently increased with the length of T_{sat}. As a consequence, ΔMTR_{asym} (3.5ppm) also increased with T_{sat} and reached maximum at T_{sat} of 2.0s. Interstingly, the largest APT tumor to WM contrast was observed at frequency range of 2 to 3.5 ppm. **Figure 2** demonstrates a representative case of high grade glioma (GBM). The tumor core with Gd enhancement shows a high APT signal, which is increased at longer T_{sat}. Background signal in normal brain is decreasing at longer T_{sat} and serves for a higher contrast.



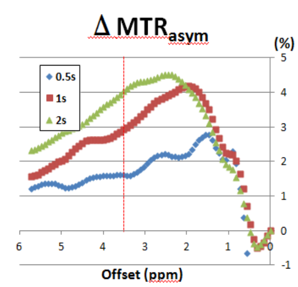


Figure 1. MTR_{asym} spectra, and ΔMTR_{asym} spectra acquired using three different T_{sat} values and averaged in the group of high grade glioma (n=3) for normal white matter and tumor tissue.

Conclusion: The APT contrast was enhanced with the use of longer T_{sat} (>1s), which was enabled by the parallel RF transmission, in most types of tumor investigated in the study. Meningioma showed a different trend and it might reflect different pathological or chemical features of this tumor. A further study will perform detailed comparisons among different tumor types and a histopathological analysis in larger number of subjects. Our results underline the importance to enable long T_{sat} on clinical scanners for sensitive APT-MRI and to optimize sequences under realistic conditions *in vivo*.

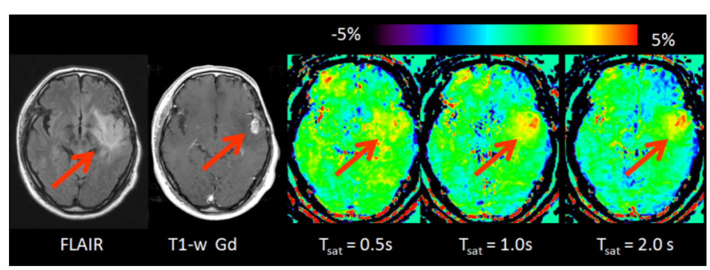


Figure 2. 52 year-old male with a GBM. The enhancing lesion shows high APT signal. APT contrast is increasing with T_{sat} by MTRasym increase in the tumor and decrease in normal white matter.

References

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4. Keupp J et al., ISMRM 19:710 (2011)