Three-dimensional (3D) Amide Proton Transfer (APT) Imaging of Human Brain Tumors at 3T

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Introduction

Amide Proton Transfer (APT) imaging[1] is a specific type of chemical exchange saturation transfer (CEST[2]) imaging that gives contrast due to endogenous mobile proteins and peptides and tissue pH. The clinical application of APT to neuroimaging of tumors is promising, but has so far been limited to single-slice acquisitions, due to various technical limitations, such as high RF power deposition and a long scan time. We have recently developed a relatively fast 3D gradient- and spin-echo (GRASE) approach[3] for APT imaging, using SENSE acceleration and a 32-channel phased-array head coil. In this abstract, we demonstrate the feasibility of applying this fast 3D APT sequence to patients with brain tumors at 3T.

Materials and Methods

Experiments were performed on a Philips 3T MRI scanner using body coil excite and a 32-channel phased-array coil for reception. The gradient- and spin-echo (GRASE) 3D sequence[3] consisted of three sections: RF saturation (800 ms duration and 2 μT amplitude), lipid suppression (asymmetric frequency modulated pulse), and GRASE 3D image acquisition (TSE factor of 22 in RL, EPI factor of 7 in FH). FOV = 212×186 mm^2; resolution = 2.2×2.2 mm^2; 15 slices of 4.4 mm thickness; SENSE acceleration factor of 2 in RL; TR = 3 s. To correct for B_0 field inhomogeneity effects, APT imaging were acquired with a six-offset protocol (±3, ±3.5, ±4 ppm from water; 2 to 8 averages).[1] The total scan time was 10 min 40 sec. SAR was 1.2W/kg. In data analysis, APT signals were calculated using a magnetization transfer ratio (MTR)-asymmetry analysis[1] at ±3.5ppm: $MTR_{asym}(3.5ppm) = S_{sat}(-3.5ppm)/S_0 - S_{sat}(+3.5ppm)/S_0$, where S_{sat} and S_0 are the image intensities without and with RF saturation. Nine brain tumor patients were recruited. All patients provided written informed consent as required.

Results and Discussion

Fig. 1 shows an example of APT and conventional MR images for a patient with histopathologically confirmed WHO grade-3 anaplastic astrocytoma (AA). Two gadolinium-enhancing lesions (red arrows) on the post-contrast T_1w images were both hyperintense on the APT images, compared to edematous tumor periphery (orange arrow) and surrounding normal-appearing white matter. Further, regions of increased APT extended outside of the tumor cores (identified by Gd-enhancement) and into the peripheral brain zones (likely non-Gd-enhancing tumor infiltration); however, the hyperintense APT areas were smaller than the lesions on T_2w and FLAIR. The average APT image intensity was consistently higher in the tumor core (n = 6) than in the peripheral edema ($p < 0.05$) and contralateral normal-appearing white matter (CNAWM; $p < 0.05$). The clear APT hyperintensity is a typical feature of high-grade gliomas, suggesting increased content of mobile proteins and peptides.

Fig. 2 shows a comparison between APT and standard MR images for high-grade (grade-3 and 4) and low-grade gliomas. The top row illustrates a case with a histopathologically confirmed WHO grade-3 glioma that showed **APT hyperintensity** (compared to CNAWM) but **no Gd enhancement**. In contrast, the middle row gives a case with a confirmed grade-2 astrocytoma that showed **Gd enhancement** but **APT iso-intensity** (with scattered punctate areas of minimal hyperintensity), compared to the CNAWM. All high-grade gliomas studied (n = 6), including one without Gd enhancement (Fig. 2, top row), had markedly increased APT signals. However, all low-grade gliomas (n = 3) were consistently iso-intense on APT (Fig. 2, middle and bottom rows). The average APT image intensity was significantly higher for high-grade gliomas than for low-grade gliomas ($p < 0.05$). These results suggest that APT has the potential to accurately distinguish high grade from low grade tumors.

Conclusions

These early results suggest 3D APT imaging at 3T is feasible in patients with brain tumors, and that the APT signal is able to identify high grade brain tumors, as well as distinguish high- vs. low-grade lesions. 3D APT may be a valuable addition to the MRI armamentarium for the accurate characterization of human brain tumors.

(1) Zhou et al. MRM 2008;60:842. (2) Ward et al. JMR 2000;143:79. (3) Zhu et al. MRM 2010;64:638.

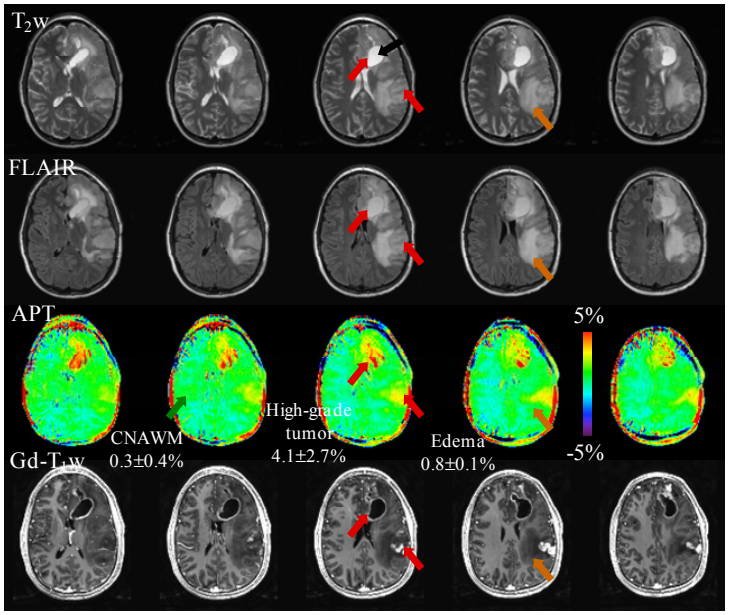

Fig. 1. APT and conventional MR images for a patient with a multi-focal grade-3 AA. Red arrow: tumor core; black: cystic cavity; orange arrow: peritumoral edema; green arrow: CNAWM. APT imaging shows that the tumor cores (red arrow) are hyperintense.

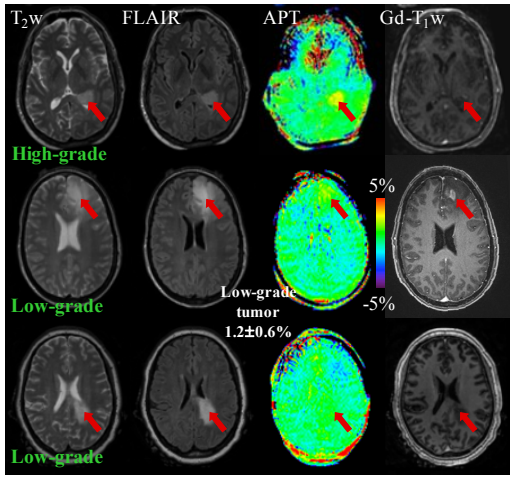

Fig. 2. (top row) A brain lesion that showed no Gd enhancement, but was found to be a high-grade glioma at the time of pathology. Such lack of Gd enhancement has been shown to occur in 10% of GBM and 30% of anaplastic astrocytomas. However, APT hyperintensity is clearly visible in the lesion. **(middle row)** A brain lesion that showed Gd enhancement, but was found to be a low-grade glioma at the time of pathology. It is important that APT shows iso-intensity to minimal hyperintensity within the lesion. **(bottom row)** Typical APT and conventional MRI characteristics for a patient with a low-grade glioma (no Gd enhancement, APT isointensity).