Comparison of 3D acquisition techniques for amide proton transfer in brain tumor applications

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Introduction: Amide proton transfer (APT)[1] is a novel contrast mechanism enabling molecular MR imaging of proteins as well as the assessment of local pH. Clinical applications of APT imaging are often limited to a single slice acquisition due to the long scan time needed for multiple acquisitions at different saturation offset frequencies as well as SAR limitations. A fast 3D acquisition protocol for APT based on 3D gradient and spin echo (GRASE) readout was previously proposed that enables APT with whole brain coverage in clinically acceptable time[2]. These studies were mainly focused on low resolution scans with a large number of acquired saturation offset frequencies and short saturation time T_{sat} < 1s. Parallel transmission based APT enables long saturation pulses at 100% duty cycle at clinical systems and it was recently shown[3] that an optimal CNR efficiency for APT can be achieved at $T_{sat} \approx 2$s. The purpose of this work is to investigate the application of 3D APT sequences with optimized saturation length and whole brain coverage. 3D GRASE and fast spin echo (TSE) sequences for APT are compared in phantom and in vivo studies.

Methods: Phantom and in vivo experiments were performed on 3T MRI scanners (Ingenia and Achieva TX, Philips Healthcare, Best, The Netherlands) using a two channel body coil for transmission and a 13-channel/8-channel head coil for reception, respectively. An optimized RF saturation length T_{sat} = 2s was performed using 40 single lobe sinc-gaussian shaped pulse elements, 50ms each. Six offset frequencies around $\Delta\omega = \pm 3.5$ppm, step size 0.4ppm, and S_0 (ω = -160ppm) were acquired. The phantom consists of 6 vials (30ml) filled with a mixture of egg white, water and Magnevist (Bayer Healthcare), with protein concentrations of 0.6% up to 7%, which were adjusted to equal T1 relaxation (T1=1.1±0.03s) via the Magnevist concentration. 3D acquisitions were performed with FOV 230×230×95mm^3 and voxel size 1.8×1.8×5mm^3. The following sequences were performed in the phantom experiments: 3D TSE, turbo factor 256, centric profile ordering, TE = 6ms, TR = 7712ms. 3D GRASE, with turbo factor of 64 in the phase encoding direction, TR =3575ms and EPI factors of 5 (TE = 8.6ms,), 7 (TE = 10ms), 9 (TE = 12ms), and 17 (TE = 20ms) in the slice encoding direction. 2D single shot TSE for a central slice was performed for reference. A SENSE factor of 2 was applied in all sequences. MTR asymmetry maps $MTR_{asym} = (S_{-\Delta\omega} - S_{+\Delta\omega})/S_0$ were corrected for δB_0 obtained from a separate B_0 measurement.

Based on the results of the phantom experiments, i*n vivo* comparison between the 3D GRASE (EPI factor of 9), 3D TSE and 2D TSE APT acquisition was performed in tumor patients. Informed consent was obtained from the tumor patients and the protocol was approved by the institutional review board.

Protein %	2D TSE	3D TSE	GRASE EPI 5	GRASE EPI 7	GRASE EPI 9	GRASE EPI 17
0.6	1.6±0.3	1.8±0.3	1.5±0.2	1.4±0.3	1.5±0.2	0.8±0.6
1.0	2.2±0.4	2.6±0.3	2.5±0.3	2.3±0.2	2.3±0.3	2.2±0.5
1.7	5.0±0.3	5.7±0.3	5.6±0.3	5.4±0.3	5.7±0.3	4.7±0.4
2.8	7.1±0.3	7.4±0.3	6.2±0.3	6.1±0.5	6.7±0.4	5.5±0.5
4.4	9.9±0.4	9.9±0.5	9.1±0.4	9.1±0.4	9.2±0.4	8.1±0.4
7.0	12.5±0.3	12.6±0.4	11.9±0.4	11.2±0.5	11.5±0.4	10.6±0.7

Table 1: Average APT signal (MTR asymmetry) for different protein concentrations using different imaging sequences. 3D TSE and GRASE with EPI factor up to 9 show comparable results with the 2D TSE scan

Results & Discussion: The average MTR asymmetry values for each vial with different protein concentration and each sequence are given in Table 1. All considered imaging sequences yield a comparable contrast, with an exception for the GRASE acquisition with EPI factor of 17, which shows a systematic decrease of contrast due to the significantly longer TE. Figure 1 shows APT images using 2D TSE, 3D TSE and 3D GRASE acquisitions as well as a Gd T1-weighted and a T2 weighted image in a tumor patient (left acoustic tumor). Both TSE and GRASE based images show elevated signal in the tumor area. However, the TSE image shows a much more homogeneous signal and less noise. Although the GRASE acquisition has a shorter scan time (1:47min for 3D GRASE vs 5:30min for 3D TSE), the SNR difference is much larger than what could be compensated by introducing averaging in the GRASE scan to equalize the scan time of the two sequences. ROI analysis in a homogeneous white matter in the tumor patient example yields MTR asymmetry of 1.7±0.8% for TSE and 1.4±3.4% for GRASE, thus 4 times higher standard deviation.

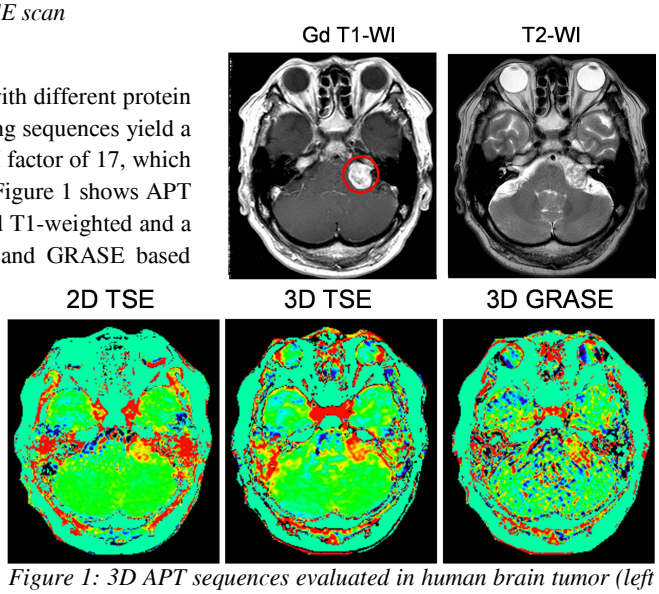

Figure 1: 3D APT sequences evaluated in human brain tumor (left acoustic tumor) Gd T1 weighted image (tumor is indicated by red circle), T2 weighted image, APT using 2D TSE, 3D TSE and 3D GRASE are shown. APT contrast is elevated in both the TSE and GRASE based APT weighted images. TSE shows much better SNR and homogeneous healthy tissue signal.

Although both TSE and GRASE acquisition sequences lead to comparable results in phantom experiments, the phantom does not reflect the complex MT contrast behavior in brain tissue. The large difference between the 3D TSE and GRASE based acquisitions in vivo is likely due to the stronger magnetization transfer effect with long saturation time (T_{sat} = 2s). This leads to a decreased signal amplitude in particular for the GRASE sequence, which is T2* weighted. The usually longer T1 times in tumor tissue could additionally influence the contrast in TSE. A detailed assessment of these effects will be a subject of further investigations.

Conclusion: Using a saturation length T_{sat} = 2s, the 3D GRASE APT acquisition leads to very low SNR. Although 3D TSE sequence requires longer acquisition times, using a centric profile ordering, high turbo factor and SENSE factor of 2, a 5:30min APT protocol largely covering the brain is achievable that delivers comparable image quality to the 2D acquisition.

References:

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