3D Fast Spin-Echo Amide Proton Transfer MR with Intrinsic Field Homogeneity Correction for Neuro-Oncology Applications

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Purpose – Amide proton transfer (APT)[1], an endogenous saturation transfer contrast, has recently gained attention as a molecular imaging approach in oncology and neurology. The APT signal (MTR asymmetry) reflects concentrations of amide (NH) containing proteins/peptides, which are significantly enhanced in active tumor tissue[2]. APT is expected to play an important role in the delineation and classification of active tumor tissue for therapy planning and monitoring, e.g. for the differentiation of radiation necrosis and active/recurrent tumor[3]. As the length of RF saturation (T_{sat}) is essential for sensitivity, but limited for clinical MRI systems (typically T_{sat}<1s), a technique based on multi-channel RF transmission was demonstrated recently[4], which allows arbitrarily long RF pulses via amplifier alternation. 3D coverage of the whole tumor or whole brain is an important requirement for the clinical application and fast spin-echo techniques with radial phase encoding have been shown[5] to provide high SNR in an acceptable 3D acquisition time (5 min). For the analysis of the MTR asymmetry (MTR_{asym}), precise information on the field inhomogeneity (ΔB_0) is required. A spin-echo Dixon acquisition technique was previously described to obtain simultaneous ΔB_0 information during APT-MRI without increasing the acquisition time[6]. In the present work, these approaches were combined for fast 3D APT imaging with intrinsic B_0 correction and evaluated in a volunteer study.

Methods – In vivo experiments were performed on a 3.0T MRI scanner (Ingenia, Philips Healthcare, The Netherlands) using a two channel body coil for transmission and a 15-channel head coil for reception. N=9 healthy volunteers were enrolled in the study, from whom informed consent was obtained. A pulsed RF saturation with T_{sat} = 2s was used, consisting of 40 single lobe sinc-gaussian pulse elements (50ms) at 100% duty cycle by alternate transmission via two RF channels[4] with $B_{1,rms}$=2.0μT. The Z-spectrum was sampled using 7 frequency offsets: ω=±3.1ppm, ω=±3.5 ppm, ω=±3.9ppm and ω=–160ppm (S_0). The timing of the acquisition window and the readout gradient was shifted (echo-shift ES) for different Z-spectral points: ±3.9ppm: ES=+0.4ms; ±3.1ppm: ES=–0.4ms; other: ES=0ms. The 3 images with positive saturation frequency offset were used for Dixon B_0 mapping[6]. Adaptive RF shimming was performed using a B_1 calibration pre-scan per RF channel for imaging/refocusing pulses and the saturation pulse. The following sequence was used: 3D fast spin-echo, driven equilibrium refocusing, turbo factor 183, centric profile ordering, FOV 212×184×66mm^3 , voxel size 1.8×1.8×4.4mm^3, TE = 6.2ms, TR = 7200ms, sensitivity encoding acceleration factor R=2 (left-right), total acquisition time 4½ min. Maps of MTR_{asym}=(S[–3.5ppm]–S[+3.5ppm])/S_0 were calculated with B_0 correction by Z-spectral interpolation[4] in the modified scanner reconstruction SW. For each volunteer, a cylindrical ROI was defined fitting into the brain for all 15 slices. Histograms of the asymmetry values were created for B_0 corrected and non-corrected images and evaluated with respect to center values c[%] and width w[%] using Gaussian fits.

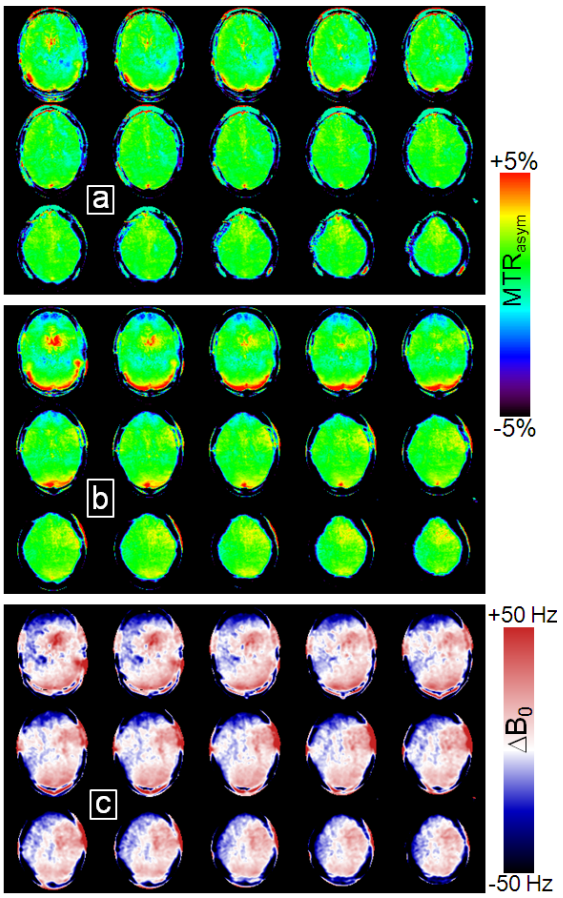

Figure 1: 3D APT-MRI with intrinsic homogeneity correction via Dixon B_0 mapping on a healthy volunteer brain. (a) Collection of all 15 slices for the obtained homogeneous MTR_{asym} map with B_0 correction. (b) Asymmetry analysis prior to B_0 correction. (c) Obtained 3-point Dixon B_0 map.

Results and Discussion – Fig. 1a shows the 3D APT imaging results (all slices) of a selected volunteer. For comparison, asymmetry analysis prior to B_0 correction is shown in Fig. 1b, which clearly shows areas of positive and negative bias. The result of Dixon 3-point B_0 mapping is shown in Fig. 1c. The areas of biased asymmetry in Fig.1b correspond well to the larger magnetic field deviations found in the B_0 map. The B_0 correction yields a homogeneous APT signal with high SNR throughout the brain (Fig.1a), except for some small areas in the lower brain. In preparatory phantom experiments it was found that larger values ES≥0.5ms should be avoided, because small spatial intensity variations are observed in the Z-spectral images, which become apparent in the MTR_{asym} maps after B_0 correction. The effects were negligible for the chosen ES of 0.4 ms, but further investigation is needed to identify the origin. Histogram analysis was performed on all slices – one example is shown in Figure 2. The histograms were closely approximated by Gaussian distributions in all cases. As a central result, reproducible center MTR_{asym} values c=(1.0±0.2)% were found throughout the volunteer series showing narrow distributions with w=(1.3±0.2)% for the normal brain areas (GM,WM,CSF). For comparison, non-corrected asymmetry data (like Fig.1b) showed shifted center values c_{NC}=(1.3±0.3)% and a wider distribution range w_{NC}=(1.7±0.4)%. As pathological MTR_{asym} values are expected in the range of 3-8% for the applied saturation settings (high grade glioma[2,7]), the obtained homogeneity in the B_0 corrected APT images forms a solid basis for sensitive tumor tissue characterization.

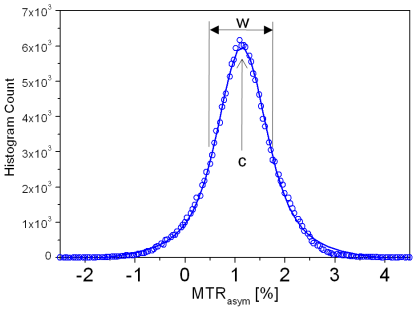

Figure 2: Example histogram analysis to assess spatial APT homogeneity. The center (c) and width (w) of the Gaussian distributions were analyzed for all volunteers.

References – **1**. Zhou J et al., Nat Med.9:1085(2003). **2**. Wen Z et al., Neuroimage 51:616(2010). **3**. Zhou J et al., Nat Med.17:130 (2011). **4**. Keupp J et al., Proc. ISMRM 19:710(2011). **5**. Doneva M et al., Proc. ISMRM 21:4233(2013). **6**. Keupp J et al., Proc. ISMRM 20:4185(2012). **7**. Togao O et al., Proc. ISMRM 21:955(2013).