Does it affect the quantification if amide proton transfer imaging is performed pre- or post-gadolinium contrast agent administration?

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Target Audience: Clinicians and researchers who are interested in performing amide proton transfer (APT) imaging within a protocol that requires the administration of gadolinium contrast agents.

Purpose: Gadolinium contrast agents (Gd-CA) are widely used in clinical MRI imaging to increase the signal-to-noise ratio (SNR) for perfusion assessment. It is well known that the administration of Gd-CA will reduce the relaxation time, T_1 [1, 2]. APT imaging is an emerging chemical exchange saturation transfer (CEST) MRI technique for pH mapping that has applications in stroke and cancer diagnosis [3]. The APT ratio (APTR), based on the concept of magnetization transfer asymmetry analysis (MTR_{asym}), is T_1 dependent [4], hence may be affected by the presence of residual Gd-CA post contrast imaging. However, to date no study has compared the differences in APT imaging before and after Gd-CA administration to determine whether the effect is significant or the sensitivity to contrast is of concern. In this study, APT data were acquired in patients with vertebrobasilar disease pre- and post- contrast to examine the extent of T_1 change on APTR.

Methods: Four patients who had undergone surgical carotid stenosis removal provided informed consent and were scanned using a pulsed APT sequence at 3T (Siemens Verio) before and after an intra-venous bolus injection of 0.1 mmol/kg 0.5M chelated Gd contrast agents followed by a 20 ml saline flush. Single-slice transverse imaging was performed mid brain with TR/TE = 4000/26 ms, matrix 80 x 80 and slice thickness = 5 mm. Saturation was achieved using 50 Gaussian pulses of duration 20 ms with 20 ms spacing to achieve an equivalent continuous saturation B_1 value of 0.535 μT (average power). Data were acquired for saturation frequency offsets from -4.5 to 4.5 ppm with 0.3 ppm increment plus a reference image with no saturation (unsaturated data), resulting in 32 volumes acquired in 2 min 55 s.
Motion artefacts were corrected using FLIRT in the FSL package [5] using 2D registration with three degrees of freedom and the unsaturated image was used as the reference. B_0 inhomogeneity was corrected using the shift in water centre frequency obtained by fitting the Bloch equations to the collected CEST data. MT ratio (MTR) was calculated according to $MTR = 1 - S(\Delta\omega)/So$, where $\Delta\omega$ refers to saturation frequency offsets at ± 3.5 ppm and So is the unsaturated signal. APTR, defined as MTR(3.5ppm) – MTR(-3.5ppm), was also calculated. Differences in the images of pre and post contrast were shown by subtraction after aligning them using FLIRT. Two-tailed t-tests were performed on the APTR in white and grey matter (WM & GM) that had been segmented from the unsaturated image using FAST in the FSL package [6], to examine whether the CA had significant effect on the APT signal. In order to exclude the artefacts and noise near the boundary of the brain area, only APTR values within ± 0.05 (5%) were included for the t-tests (APT effect should be within this bound at 3T [3]).

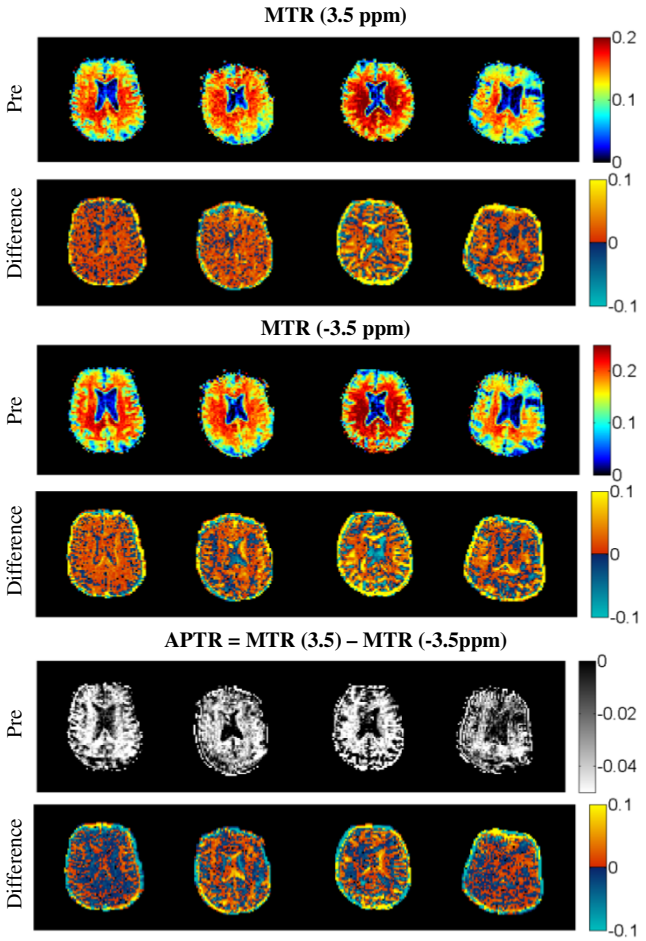

Fig. 1: Top row of each section shows the pre-images: MTR(3.5ppm), MTR(-3.5ppm) and APTR (from top to bottom). Their respective differences ($MTR/APTR_{pre}$ – $MTR/APTR_{post}$) are shown directly below the pre-images.

Results: Fig. 1 shows the pre contrast images and their differences (pre – post). From the results, it is clear that Gd-CA had an influence on the whole APT spectrum where both the MTR signals at ± 3.5 ppm decreased after the administration when compared to the pre-Gd data (more positive differences) as a result of the T_1 change. The mean and standard deviation of APTR in WM and GM before and after CA infusion are plotted in Fig. 2; WM APTR of patient 1 and GM APTR of patient 4 showed significant change after Gd-CA infusion at a 5% significance level.

Discussion: Although APT imaging was performed some time (< 10 mins) after the perfusion imaging, residual of Gd-CA still appeared to affect the quantification of APTR. Significant difference in APTR was found in some of the patients scanned. A previous study [2] has shown that MTR is sensitive to the change of T_1 induced by the Gd-CA. In theory, APTR should be less sensitive to this effect because it is an asymmetry analysis, but the results in this study suggest that Gd-CA may asymmetrically affect the APT spectrum, possibly related to nuclear overhauser effects (NOE) at the negative offsets.

Conclusion: This study suggests that APTR values after the passage of Gd-CA do not necessarily match those observed pre contrast despite being an asymmetry measure that might make it insensitive to changes in T_1. For quantitative APT imaging, this implies that it will be necessary to acquire APT data prior to the contrast agent administration to avoid any misinterpretation of the APT effect or for inter-subject comparison.

References: 1. Sharma *et al*., JMRI. 23:323-330, 2006. 2. Jones *et al*., JMRI. 3:31-39, 1993. 3. van Zijl *et al*., MRM. 65:927-948, 2011. 4. Zhou *et al.*, Nat. Med. 9:1085-1090, 2003. 5. Jenkinson *et al*., NeuroImage, 17(2):825-841, 2002. 6. Zhang *et al*., IEEE Trans Med Imag, 20(1):45-57, 2001.

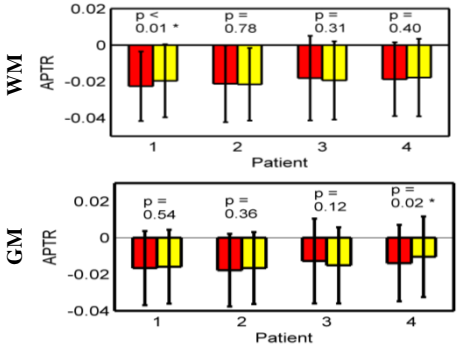

Fig. 2: Mean and standard deviation of patient APTRs, where the top row is for the WM region and the bottom one is for the GM. p values refer to the t-test results and asterisks (*) indicates that the results were significantly different at a 5% significance level.