

APT-CEST post Gadolinium. Should it be avoided? Comparison of pre- & post-Gadolinium CEST on glioma at 3T.

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Synopsis

This study compares APT-CEST between pre- and post-gadolinium in patients with gliomas at 3T, and evaluates the feasibility of performing CEST after administration of T1 contrast. The results of the study demonstrate that Gd administration does not significantly affect the quality of the APT-CEST image, encouraging the acquisition of CEST data, even after the administration of T1 contrast agents.

Introduction

In the last few years, chemical exchange saturation transfer (CEST) imaging has emerged as a metabolic marker for MRI, with great promise in the field of neuro-oncology. APT-CEST has shown to correlate with tumour grading¹ as well as to provide useful clinical information such as differentiation of radiation necrosis from tumour recurrence². Tissue relaxation can alter APT-CEST contrast and as such the recommendation is to perform it prior to the administration of contrast agent^{3,4}. However, this can be practically difficult as clinical exams tend to be prioritised over changes in protocol for research. Some MRI vendors require modification of the scanner software to run CEST sequences, which further complicates the inclusion of CEST half way through the clinical exam. This study compares APT-CEST between pre- and post-gadolinium in patients with gliomas at 3T, and evaluates the feasibility of performing CEST after administration of T1 contrast.

Methods

Patients: Seven patients with suspected glioma were recruited with informed consent for APT-CEST pre- and post- Gadolinium (Gd). Three patients underwent follow up imaging with a total of 11 studies included for analysis. **Volunteers:** Nine healthy volunteers were also recruited to assess repeatability of APT within subjects. Time between APT-CEST scans was identical as in patients but no Gd was administered. All studies were conducted on a Siemens mMR biograph. APT-CEST was acquired with a gradient echo based snapCEST acquisition⁵, where a 3s (50% duty cycle) was used at two different powers ($B_1 = 0.75, 1.25\mu\text{T}$) for B_1 correction. A WASAB1 scan⁶ was also acquired for field homogeneity corrections. APT-CEST was calculated as the normalised asymmetry at 3.5ppm and corrected for both B_0 and B_1 field inhomogeneity⁷. T1 maps were acquired with an inversion recovery method ($TI=0.1\text{s}, 0.235\text{s}, 0.550\text{s}, 1.3\text{s}, 3\text{s}$ and 7s , $TR=10\text{s}$) using the same readout as for APT-CEST. **Analysis:** In patients, regions of interest (ROI) of the 'non-enhancing', 'enhancing' and 'necrotic core' in the tumour and healthy 'white matter' (WM), were segmented from T2w-FLAIR and T1w-postGd images (Figure 1). In volunteer subjects WM was segmented from the T2w-FLAIR. For all ROIs, APT-CEST signal was compared pre- and post- Gd. Bland Altman plots and histogram analysis was performed for both APT-CEST and quantitative T1 maps. In order to assess the effect of Gd in APT-CEST, the normal variation was estimated from the healthy volunteer cohort.

Results

Pre- and post- Gd APT-CEST images displayed very similar features, highlighting the same areas of the brain in both scans. The range of contrast in different gliomas that APT-CEST was able to produce remained mostly unaffected post administration of Gd as seen in figure 1. ROI based histogram analysis in figure 2 illustrates the variation pre- and post- contrast in the APT-CEST. All ROIs (in rows) show extensive overlap between the two time-points. Pairwise t-test on the mean signal of each patient in different ROIs revealed no significant difference ($p>0.05$) in the core, non-enhancing and WM regions. Low significant difference ($p<0.05$) was found in the enhancing tumour region (row 2). A near identity (1:1) correlation was found between the pre- and post- Gd APT-CEST scans ($y=1.07x+0.00$, $r^2 = 0.96$, $n= 43$) as shown in figure 3 (left). Based on the contrast required to differentiate WM versus non-enhancing lesions, the 'maximum allowed difference' for APT was set at ± 0.005 . With this limit the Bland-Altman plot (figure 3, right) shows a 95% agreement between pre- and post scans (41 out of 43 points). Healthy volunteers display the same degree of variation as patients with Gd administration. In contrast, the scatter plot of the quantitative T1 (figure 4), show both enhancing and core regions to be severely biased due to the Gd administration with a mean difference of 700ms.

Discussion and Conclusion

The consistency of the APT-CEST even in regions with significant T1 reduction post Gd, supports the idea that the APT signal originates mostly from the intracellular volume, where Gd does not permeate. Further quantitative analysis would need to account for the blood volume (an interstitial space in cases of blood brain barrier leakage) in order to accurately estimate the impact of Gd in the APT contrast. Nonetheless, the results of this study demonstrate that Gd administration does not significantly affect the quality of the APT-CEST image, encouraging the acquisition of CEST data, even after the administration of T1 contrast agents.

Acknowledgements

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References

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Figures

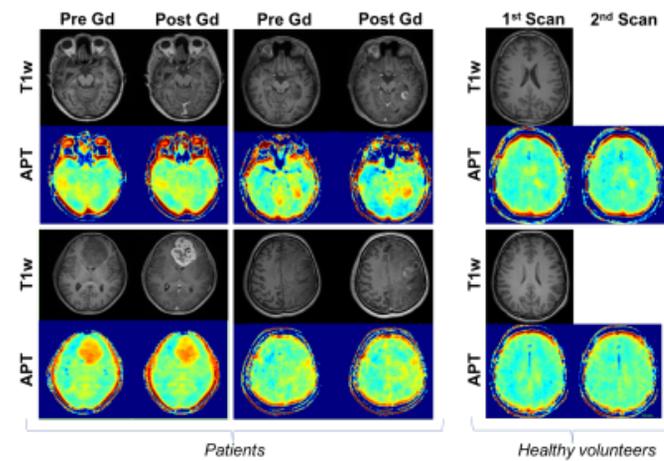


Figure 1: Pre- and post-Gd APT-CEST and T1w images of four patients (left). APT-CEST and T1w images of two healthy volunteers. Time between 1st and 2nd ATP scans was the same as in patients, but no Gd was administrated (right)..

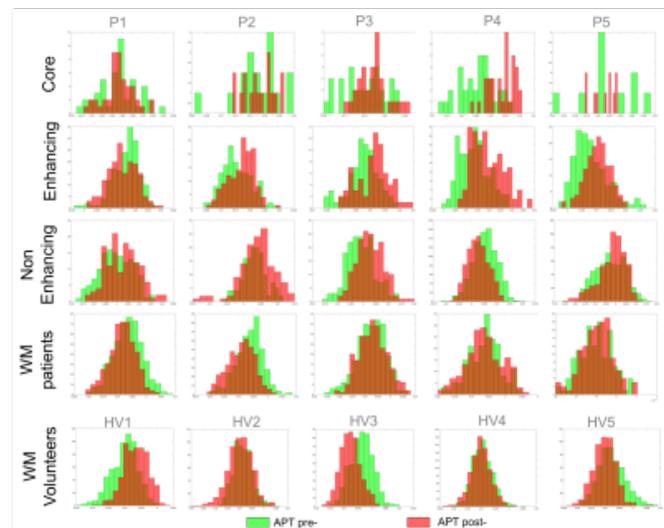


Figure 2 Histograms of the APT-CEST signal pre-(in green) and post-Gd (red) in 5 different patients for all the segmented ROIs. Columns represent different patients. Each row corresponds to different ROI. Bottom row displays the histogram in the WM ROI for 5 healthy volunteers with no Gd between the two scans.

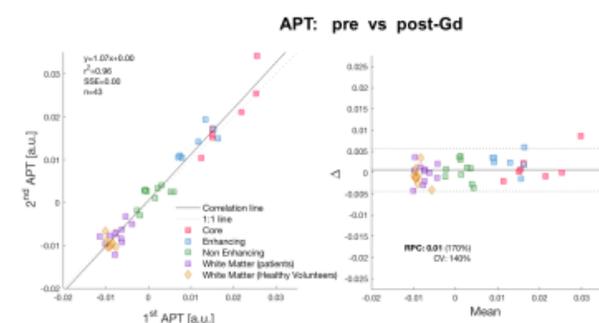


Figure 3: Correlation and Bland-Altman plot of the pre- and post-Gd APT-CEST signal for all ROIs and participants. Volunteer subjects (shown as diamonds in the graph) did not have Gd injection.

T1: pre vs post-Gd

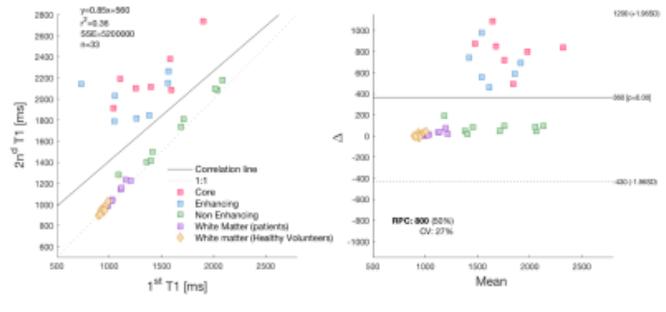


Figure 4: Correlation and Bland-Altman plot of the pre- and post-Gd T1 values for all ROIs and participants. Volunteer subjects (shown as diamonds in the graph) did not have Gd injection.