

Assessing metabolic heterogeneity and invasion patterns in glioma recurrence by APTw CEST MRI

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INTRODUCTION:

Recurrent glioma has dismal prognosis due to its heterogeneity and highly invasive growth. Tumor monitoring by conventional MRI has shortcomings to assess these key tumor characteristics. Recent studies introduced chemical exchange saturation transfer (CEST) for metabolic imaging in newly diagnosed glioma. This prospective study investigated Amide Proton Transfer (APT) CEST MRI at 3 Tesla to elucidate the heterogeneity and invasion patterns of recurrent glioma.

METHODS:

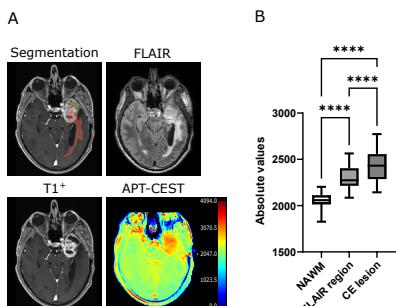
We performed a monocenter, prospective trial and enrolled 371 glioma patients who received tumor monitoring by MRI in our department between August 2021 and March 2024. Within this cohort we identified 43 patients who presented with recurrent glioma on follow-up imaging. Study sequences included fluid-attenuated inversion recovery (FLAIR), T1w Gd contrast-enhanced mPRAGE and APTw CEST imaging. Standard sequences were co-registered with APTw CEST and segmentations of the FLAIR lesion, CE lesion, resection cavity, contralateral normal appearing white matter and of CEST hotspots were performed to quantify CEST dynamics.

RESULTS:

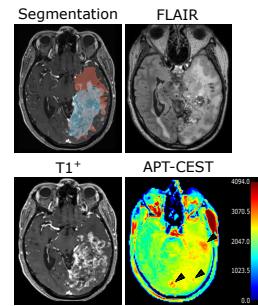
APTw CEST values were highest in solid, contrast enhancing tumor parts compared to the pure FLAIR lesions. APTw CEST demonstrated heterogeneity within the FLAIR lesions that was not detectable by conventional sequences. We further identified focal CEST signal peaks within contrast enhancing areas as potential metabolic hotspots within recurrent glioma. Interestingly, we identified APTw CEST alterations within the resection cavity in recurrent glioma which were not detectable prior to recurrence.

DISCUSSION:

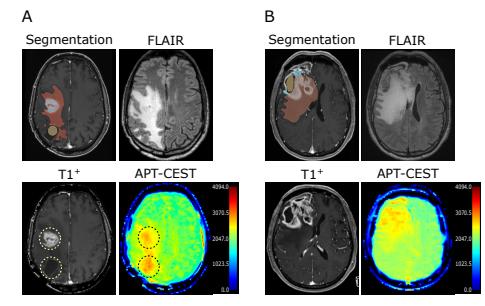
APTw CEST provides information beyond conventional MR sequences with marked heterogeneity in FLAIR lesions, metabolic hotspots in areas of contrast enhancement and de-novo CEST alterations in the resection cavity. These findings may help to further understand and differentiate patterns of recurrent glioma.



APTw signal increase is most pronounced in the contrast enhancing tumor. **A:** Segmentation masks, T1 post contrast, FLAIR imaging and CEST maps are shown for a representative patient with glioma recurrence. **B:** Quantification of APTw revealed the most significant increase in the contrast-enhancing (CE) lesion, with a milder increase observed in the FLAIR lesion.



APTw CEST imaging reveals metabolic hotspots that were not discernible with conventional sequences, where Gd-enhancing areas are widespread and diffuse. This finding might emphasize the capability of APTw CEST imaging to detect distinct metabolic signatures within glioma recurrence.



A,B: Representative images of two distinct patterns of APTw CEST signals in the FLAIR lesion. Some patients demonstrated an increased ATPw signal, suggesting tumor cell infiltration along white matter tracts, e.g. from resection cavity to Gd enhancing tumor recurrence (**A**). In contrast, other patients showed an increased APTw signal only within the contrast-enhanced (CE) lesion.