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Differentiating Glioma Recurrence and Pseudoprogression by APTw CEST MRI

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Abstract

Objectives: Recurrent glioma is highly treatment resistant due to its metabolic, cellular, and molecular heterogeneity and invasiveness. Tumor monitoring by conventional MRI has shortcomings to assess these key glioma characteristics. Recent studies introduced chemical exchange saturation transfer for metabolic imaging in oncology and assessed its diagnostic value for newly diagnosed glioma. This prospective study investigates amide proton transfer-weighted (APTw) MRI at 3 T as an imaging biomarker to elucidate the molecular heterogeneity and invasion patterns of recurrent glioma in comparison to pseudoprogression (PsPD).

Materials and methods: We performed a monocenter, prospective trial and screened 371 glioma patients who received tumor monitoring between August 2021 and March 2024 at our institution. The study included IDH wildtype astrocytoma and IDH mutant astrocytoma and oligodendroglioma, graded according to the WHO 2021 classification. Patients had received clinical standard of care treatment including surgical resection and radiochemotherapy prior to study inclusion. Patients were monitored by 3 monthly MRI follow-up imaging, and response assessment was performed according to the RANO criteria. Within this cohort, we identified 30 patients who presented with recurrent glioma and 12 patients with PsPD. In addition to standard anatomical sequences (FLAIR and T1-w Gd-enhanced sequences), MRI included APTw imaging. After sequence co-registration, semiautomated segmentation was performed of the FLAIR lesion, CE lesion, resection cavity, and the contralateral normal-appearing white matter, and APTw signals were quantified in these regions of interest.

Results: APTw values were highest in solid, Gd-enhancing tumor parts as compared with the nonenhancing FLAIR lesion (APTw: 1.99% vs 1.36%, P = 0.001), whereas there were no detectable APTw alterations in the normal-appearing white matter (APTw: 0.005%, P < 0.001 compared with FLAIR). Patients with progressive disease had higher APTw levels compared with patients with PsPD (APTw: 1.99% vs 1.26%, P = 0.008). Chemical exchange saturation transfer identified heterogeneity within the FLAIR lesion that was not detectable by conventional sequences. There were also focal APTw signal peaks within contrast enhancing lesions as putative metabolic hotspots within recurrent glioma. The resection cavity developed an APTw increase at recurrence that was not detectable prior to recurrence nor in patients with PsPD (APTw before recurrence: 0.6% vs 2.68% at recurrence, P = 0.03).

Conclusions: Our study shows that APTw imaging can differentiate PD and PsPD. We identify previously undetectable imaging patterns during glioma recurrence, which include alterations within resection cavity associated with disease progression. Our work highlights the clinical potential of APTw imaging for glioma monitoring and further establishes it as an imaging biomarker in neuro-oncology.