Differentiation between glioblastoma and solitary brain metastases using APTw and perfusion MRI

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INTRODUCTION:

Brain tumors are one of the most aggressive forms of cancer, associated with poor prognosis and survival (1). Differentiating different types of brain tumors is important for treatment planning and management. However, solitary brain metastases (MET) and glioblastomas (GBM) might be difficult to distinguish using conventional magnetic resonance imaging (MRI) alone (1). Methods investigating perfusion or chemical exchange saturation transfer (CEST) MRI might provide additional value in presurgical prediction and subsequent management. Dynamic susceptibility contrast (DSC) MRI has previously shown increased cerebral blood volume (CBV) and increased blood-brain barrier (BBB) leakage (K_2) in GBM compared to MET (2). In addition, amide proton transfer weighted (APTw) CEST imaging has shown increased values in GBM compared to MET (3-5). Our study aimed to evaluate whether APTw MRI alone or combined with DSC MRI, using both CBV and the leakage parameter K_2, improves the diagnostic accuracy in distinguishing GBM and MET.

METHODS:

After informed consent was obtained, 21 adult patients with brain tumors (confirmed with diagnostic imaging, surgery or biopsy and molecular characterization as 13 GBM and 8 MET) were examined on a 3T Siemens scanner. The APTw sequence used a saturation module of 5 hyperbolic secant pulses of 100 ms with 4 interpulse delays (61 ms), and a B_1 of 2 μT. A Z-spectrum was obtained by applying the saturation module at 21 frequency offsets ±610 Hz (±5 ppm) in steps of 0.5 ppm, with the unsaturated reference image (S_0) acquired at an offset of -150 ppm relative to water. DSC MRI images were acquired using a gradient echo echo-planar imaging sequence with a repetition time of 1243 ms. A Gd-based contrast agent (Clariscan®, GE HealthCare) was administered (0.1 mmol/kg) 15 s after the initiated dynamic series at an injection rate of 5 mL/s. Both APTw and DSC MRI images were post-processed using software from Olea Medical® (Olea Medical Solutions, La Ciotat, France), including B_0 correction and integral asymmetry-based calculation of the APTw maps, as well as tracer kinetics and leakage correction to calculate CBV and K_2 (6). Regions of interest (ROIs) were placed in the whole tumor and contralateral normal-appearing white matter (NAWM). Mean values of CBV (normalized with NAWM), K_2 and APTw intensity were obtained and compared between GBM and MET using Mann-Whitney U tests, and receiver operating characteristic curves for diagnostic accuracy.

RESULTS:

Mean APTw values were significantly higher in GBM (2.88±1.00 %) compared to MET (1.98±0.80 %) ($p<0.05$). There was no significant difference between GBM and MET by normalized CBV (2.73±1.46 vs 2.43±2.05) or K_2 (1.34±2.87 min^{-1} vs 2.05±2.93 min^{-1}). APTw had the highest area under curve (AUC) at 0.76 to differentiate GBM and MET at optimal cut-off value 3.17 %, compared to CBV (AUC 0.59), K_2 (AUC 0.43) or a combination of the three metrics (AUC 0.26).

DISCUSSION:

Previous studies, differentiating GBM from MET, have either used APTw or perfusion imaging alone, with only few combining the metrics (5). We found that APTw shows better performance in distinguishing GBM from MET, compared to CBV or K_2, or a combination of the three. Additionally, the mean APTw values across ROIs in the whole tumor were increased in GBM compared to MET, consistent with previous research, where ROIs have been placed in the tumor core, contrast-enhancing region or peritumoral edema (3-5). Similarly, our findings indicate limitations in using K_2 as a diagnostic marker, possibly due to high variance (7). This study is limited by the cohort size and heterogeneity of the MET group, with primary tumors from lung adenocarcinoma and malignant melanoma, reducing generalizability and statistical power. In addition, the total saturation time was shorter in the APTw sequence compared to recent recommendations (8).

CONCLUSION:

APTw imaging showed the best diagnostic accuracy in distinguishing GBM and MET, and higher values in GBM, compared to CBV and BBB leakage measurements from DSC MRI, or a combination of the three metrics. Future studies should validate the findings in larger homogenous cohorts.

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