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Leveraging Hybrid FLT-PET/MR Imaging to Distinguish Tumor Progression from Radionecrosis in Brain Metastasis Patients Post-Radiosurgery

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Abstract
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Abstract

Objectives:

An estimated 20% of stereotactic radiosurgery (SRS) patients relapse and experience tumour progression (TP) within 6 months of treatment. SRS patients may also be afflicted by radionecrosis (RN), a radiation-induced tissue injury virtually indistinguishable from TP via routine treatment follow-up scans. Currently, invasive post-surgical histopathology remains the only gold-standard confirmation of TP/RN5. Thus, non-invasive imaging techniques with strong diagnostic accuracy are urgently required to improve patient stratification while minimizing harm. However, the historic rate of image-based TP/RN differentiation accuracy lies at a modest 54%, impeding the widespread full adoption of image-based protocols in clinical practice due to suboptimal performance3. To bridge this gap, we aim to establish an image-based PET/MR classification protocol to distinguish tumour progression from radionecrosis in patient lesions post-SRS at a ⩾80% diagnostic accuracy/sensitivity/specificity threshold across implemented classification methods.

Methods:

To date, 10 adult patients with confirmed TP or RN have been enrolled in our study. All patient datasets were co-acquired within the same session using the hybrid PET/MR imaging platform. 18F-Fluorothymidine (FLT) was employed as a PET imaging radiotracer with approval for experimental use. Acquired static and dynamic PET datasets were analyzed using two methods: (i) a conventional static PET maximum standard uptake value (SUVmax) estimation and, (ii) compartmental modelling of a 20-minute dynamic PET acquisition (dPET). dPET time-activity curves were fitted reversible and irreversible two-compartment models, with the best-fitting model selected using the Akaike Information Criterion. Additional kinetic parameters (net flux – Ki, distribution volume – Vd; phosphorylated fraction – Pf) were calculated from fitted compartment parameters (k1, k2, k3 and k4). The classification performance of SUVmax values versus dPET kinetic parameters was assessed to distinguish which protocol differentiates TP from RN most accurately. MRI t1-weighted, t2-weighted and diffusion-weighted imaging (DWI) sequences were co-acquired in the same frame of reference as PET acquisitions. All sequences were co-registered to a planning t1-weighted MRI reference, with lesion contours propagated across all sequences. Using the PyRadiomics open-source package, a comprehensive set of 107 radiomic features were extracted for each MR sequence and for static PET acquisitions. A one-way ANOVA analysis was performed on normalized radiomic features with respect to the ground truth patient condition (TP/RN) to select for statistically significant features ($p < 0.05$) to be used in future AI model classification.

Results:

The FLT-dPET derived kinetic parameters Ki and Pf suggest that dPET analysis can distinguish TP from RN in post-SRS lesions (0.063±0.043; 0.304±0.204 and 0.002±0.0; 0.004±0.001 respectively, $p < 0.05$), whereas RN cannot be separated from background FLT uptake in healthy tissues ($p > 0.05$). Significant radiomic features for classification ($p < 0.05$) selected by ANOVA f-score feature selection are related to textural and voxel intensity metrics, hinting at the importance of intensity-based image data for TP/RN classification and corroborating the relative inefficacy of geometrical features at distinguishing TP from RN.

Conclusion(s):

Our study examined the accuracy of FLT-PET and MR protocols in classifying between TP and RN in post-SRS brain metastasis lesions. Direct comparison of classifier accuracy can advise future development of image-based protocols to favour patient stratification. Although effective treatments exist for both TP and

RN cases, robust stratification is crucial due to the substantial divergence in treatment approaches.