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Characterizing the tumor microenvironment with reduced dynamic PET imaging in glioblastoma

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Keywords

PET, MRI, FMISO, Glioblastoma, Perfusion

Abstract

Glioblastoma multiforme (GBM) is the most common and aggressive brain tumor in adults. Owing to a high level of disease heterogeneity and common recurrence, 5-year survival is below 10% with a near 100% mortality rate. Early and accurate diagnosis of GBM is vital for disease staging and treatment planning. Such diagnosis is often made using dynamic contrast-enhanced magnetic resonance imaging (MRI) and positron emission tomography (PET). These imaging techniques not only outline the physical structure of the tumor but also indicate blood flow and oxygen content within its microenvironment. These features are clinically significant, as disease prognosis and treatment efficacy are modulated by hypervascularization and reduced oxygen content (hypoxia).

The most common strategy to identify hypoxia is PET imaging with the 18-fluoromisonidazole (FMISO) radiotracer. To add specificity to this assessment, dynamic PET studies have been implemented, mapping the kinetics of the tracer over time. However, proper dynamic scans often exceed two hours and require multiple blood samples, largely rendering them clinically infeasible and isolated to research studies.

We present a retrospective analysis of pseudo-dynamic FMISO PET images collected as part of a clinical trial exploring pembrolizumab therapy and FMISO imaging in glioblastoma patients. To improve patient experience and clinical feasibility, the study used a short (40-min) imaging protocol and no blood sampling. A linear dynamic model was applied to these reduced dynamic scans to differentiate between transient FMISO concentration governed by blood flow and chronic uptake indicative of true hypoxic tumor. By comparing parameters of this dynamic model to cerebral blood volume (CBV) measurements, we found statistically significant associations between CBV and dynamic parameters in healthy tissue, but not tumoral regions. Results suggest that this reduced imaging protocol might have potential in identifying perfusion mediated FMISO concentration, offering a more specific diagnostic tool with a reasonable clinical implementation.