Editorial: Structural, Metabolic, and Physiologic MR Imaging to Study Glioblastomas

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Glioblastoma (GBM) is the most common and fatal primary malignant brain neoplasm in adults (1). The current standard of care treatment for GBM comprises maximal safe surgical resection followed by concurrent chemoradiation therapy (CCRT) and maintenance chemotherapy with temozolomide. Despite aggressive multimodal treatment the prognosis has remained poor (2). Recently, novel therapeutic approaches such as immunotherapy (3) and electric field therapy (4) have been introduced. Currently, several clinical trials are in progress to evaluate the safety profile and therapeutic efficacy of these new frontiers in fight against this devastating and life-threatening disease.

In the field of neuro-oncology, diagnosis and treatment response evaluation remain highly dependent on neuroimaging methods. While conventional magnetic resonance (MR) imaging sequences provide valuable information about the anatomic details and blood-brain-barrier (BBB) integrity, they lack specificity in characterizing gliomas as these neoplasms are highly heterogeneous both in spatial and temporal dimensions. Continuous developments in metabolic and physiologic MR imaging techniques have provided new insights into understanding underlying tumor biology and tumor microenvironment (5–9). Taken together, these techniques have been utilized to make the correct diagnosis, prognosis, evaluation of treatment response to both established and novel therapeutic regimens, and identification of new molecular targets for fostering the discovery of new treatments. Additionally, an emerging field of "radiomics" has the potential to change the ways in which advanced MR imaging techniques can be utilized more efficiently (10). This Research Topic was launched to collect high-quality manuscripts to advance our knowledge on clinical utilities, existing challenges, and limitations of using metabolic and physiologic MR imaging techniques in characterizing GBMs. A total of twelve manuscripts (nine original research and three review articles) were finally accepted for publication under this Research Topic.

ORIGINAL RESEARCH ARTICLES

The leakage of the contrast agent into the extravascular extracellular space (EES) during the dynamic susceptibility contrast (DSC)-perfusion MRI affects the signals produced in two
investigated Kumar et al. (2022)). Identified endothelial cell-enriched genes from transcriptome classification GBM patients into short-term and long-term survival groups. The investigators concluded that evidence for the value of regular interval imaging is currently lacking. At the same time, the authors indicated that evidence for the value of regular interval imaging remains crucial in neuro-oncology. An expert panel comprising of professionals from data science, health economics, trial management of adult brain tumors, and patient representatives extensively reviewed the current evidence on the use of interval imaging to monitor brain tumors, and summarized their findings in a review article. The investigators concluded that evidence for the value of regular interval imaging is currently lacking. At the same time, the authors indicated that ongoing collaborative efforts might provide some evidence to optimize monitoring imaging biomarkers for the standard of care brain tumor management (Booth et al.).

A review article by Kumar et al. comprehensively showcased the clinical potentials of emerging metabolic imaging techniques such as 3D-echoplanar spectroscopic imaging, 2D-correlation spectroscopy, and chemical exchange saturation transfer imaging (PET) and other inherent shortcomings associated with this technique, Mangalore et al. explored whether high “b” value diffusion-weighted imaging (DWI) and 18FDG-PET can provide similar or complementary information in detecting malignant brain lesions. The investigators obtained comparable sensitivity and specificity for DWI and 18FDG-PET derived parameters and concluded that DWI could act as a surrogate for 18FDG-PET in the diagnosis of brain tumors.

Despite the clinical importance, the accurate distinction between GBMs and solitary metastasis often remains challenging as these entities exhibit similar features on conventional neuroimaging. To address this issue, Zhang et al. designed a clinical trial and developed an integrated radiomics model by incorporating DWI-derived ADC and 18FDG-PET derived standardized uptake value (SUV). This integrated model provided significantly better diagnostic performance than the utilization of any single imaging parameter alone.

Using multivariate logistic regression analyses, Wong et al. developed a mathematical model by incorporating multiple clinical features and imaging factors (DWI-derived ADC, contrast-enhancement size, whole-tumor size) in predicting malignant transformation of low-grade gliomas. This model had an accuracy of 84% from the training group and 85% from the validation group.

In a seminal study, Cui et al. investigated the prognostic significance of metabolic alterations from the postoperative peritumoral edematous zone (PEZ) in GBMs. Authors proposed that an elevated choline/N-acetyl aspartate ratio in PEZ can be considered as an independent risk factor for predicting early tumor recurrence. Moreover, this metabolic abnormality was also associated with poor prognosis and adverse clinical outcomes in patients with GBM.

By leveraging the utility of unique brain functional connectivity information obtained from resting-state functional MRI combined with machine learning algorithms, Lamichhane et al. classified GBM patients into short-term and long-term survival groups with high sensitivity and specificity (precision prognostics).

**REVIEW ARTICLES**

Determining the utility of interval imaging (i.e., imaging at pre-planned time-points to assess tumor status) in brain tumor management remains crucial in neuro-oncology. An expert panel comprising of professionals from data science, health economics, trial management of adult brain tumors, and patient representatives extensively reviewed the current evidence on the use of interval imaging to monitor brain tumors, and summarized their findings in a review article. The investigators concluded that evidence for the value of regular interval imaging is currently lacking. At the same time, the authors indicated that ongoing collaborative efforts might provide some evidence to optimize monitoring imaging biomarkers for the standard of care brain tumor management (Booth et al.).

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in several neuro-oncologic applications. The authors also provided a detailed head-to-head comparison of these three metabolic techniques.

In another review article, Gonçalves et al. provided an overview on the potential utilities of advanced MR imaging techniques for studying pediatric GBMs.

Altogether, the studies published in this special issue have highlighted the importance of using advanced MR imaging and PET imaging techniques in redefining and reshaping our understanding of GBMs. Collectively, these techniques provide crucial information about the tumor microstructure, microvasculature, and metabolism, thus offering opportunities for optimizing clinical care of glioma patients. "Radiomics" is a relatively young and evolving field, and has a tremendous potential to provide meaningful biological understandings of imaging features for further improvement in the clinical outcomes and quality of life of these patients. However, the widespread translation of advanced imaging and radiomics methods into the routine clinical workflow has been slow due to some technical challenges. We believe that standardization as well as harmonization of data acquisition and post-processing procedures will strengthen the clinical applications and advance progress toward developing and validating new imaging biomarkers in the field of neuro-oncology.

**AUTHOR CONTRIBUTIONS**

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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