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Review Article

Beyond conventional imaging: Advancements in MRI for glioma malignancy prediction and molecular profiling

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Highlights

- Modern MRI techniques are key in diagnosing and guiding glioma treatment.
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- Standardizing MRI protocols remains challenging, needing more research and collaboration.
- Differentiating tumor recurrence from pseudoprogression is crucial; advanced MRI often needs biopsy validation.

Abstract

This review examines the advancements in magnetic resonance imaging (MRI) techniques and their pivotal role in diagnosing and managing gliomas, the most prevalent primary brain tumors. The paper underscores the importance of integrating modern MRI modalities, such as diffusion-weighted imaging and perfusion MRI, which are essential for assessing glioma malignancy and predicting tumor behavior. Special attention is given to the 2021 WHO Classification of Tumors of the Central Nervous System, emphasizing the integration of molecular diagnostics in glioma classification, significantly impacting treatment decisions. The review also explores radiogenomics, which correlates imaging features with molecular markers to tailor personalized treatment strategies. Despite technological progress, MRI protocol standardization and result interpretation challenges persist, affecting diagnostic consistency across different settings. Furthermore, the review addresses MRI's capacity to distinguish between tumor recurrence and pseudoprogression, which is vital for patient management. The necessity for greater standardization and collaborative research to harness MRI's full potential in glioma diagnosis and personalized therapy is highlighted, advocating for an enhanced understanding of glioma biology and more effective treatment approaches.

Introduction

Gliomas represent the most prevalent type of primary brain tumor, with an age-adjusted average incidence rate of 6.03 per 100,000 individuals [1]. Typically, patients manifest symptoms such as seizures or focal neurological impairments, prompting the need for diagnostic imaging, primarily in the form of an MRI scan, which reveals the presence of the tumor.

Brain MRI, which includes T2-weighted, T2/Fluid attenuated inversion recovery (FLAIR) sequences, as well as 3D T1-weighted sequences before and after administering a gadolinium-based contrast agent (GBCA), is the gold standard method for detecting a brain tumor [2]. MRI techniques can offer supplementary insights into biophysical properties, such as tumor cell density using diffusion-weighted imaging (DWI), the infiltration of white matter using diffusion-tensor imaging (DTI), and the architecture of microvessels using perfusion-weighted imaging (PWI) [[3], [4], [5], [6]]. In addition, PWI can be utilized to identify metabolic hotspots in specific tumor tissue sampling. This technique is very valuable when considering biopsy instead of surgical resection [7].

Nevertheless, gliomas nearly always recur despite aggressive treatments, highlighting the critical need for early tumor recurrence diagnosis to optimize patient care and evaluate treatment options. When tumor growth appears on radiographs and then spontaneously diminishes without additional anti-tumor medication, this is known as pseudoprogression, and it is a sign of an effective therapeutic response. Crucially, it appears on imaging to be very similar to a recurrent, progressing tumor. Therefore, it becomes essential to distinguish between those occurrences to manage patients in an appropriate manner [[8], [9], [10], [11]].

The current international standard for the nomenclature and diagnosis of gliomas is the fifth edition of the WHO Classification of Tumors of the Central Nervous System (WHO CNS5) [12]. This edition has brought significant changes to tumor nomenclature and has emphasized the crucial role of molecular diagnostics in classifying and grading tumors, offering improved prognostic predictions compared to the previous 2016 version [13,14].

Within the WHO CNS5 classification, several molecular alterations of clinical significance have been incorporated. These include *IDH* mutation status, codeletion of chromosomal arms 1p and 19q (1p/19q codeletion), *H3F3A* alterations, mutations in the nuclear alpha-thalassemia/mental retardation X-linked syndrome (*ATRX*) gene, O^6-methylguanine-DNA methyltransferase (*MGMT*) promoter methylation status, loss of cyclin-dependent kinase inhibitor 2A (*CDKN2A*), epidermal growth factor receptor (*EGFR*) amplification,

combined gain of chromosome 7 and loss of chromosome 10 (7+/10−), and telomerase reverse transcriptase (*TERT*) promoter mutations. The inclusion of these numerous biomarkers has significant implications for the clinical management of patients with gliomas [1].

Since the genetic profile of a tumor influences its metabolic pathways and can result in specific changes in cell behavior, advanced magnetic resonance imaging (MRI) techniques hold great promise as a noninvasive means to predict the type and behavior of gliomas.

Radiogenomics offers a promising new paradigm for advancing clinical imaging into the molecular and genomics era by establishing connections between molecular markers and imaging characteristics. Subsequently, genetic biomarkers have established a solid reputation for forecasting overall survival until disease progression or therapeutic response [15,16].

By deriving genetic or pathologic features from radiographic data, the science of radiogenomics holds considerable potential for the possibility of low-cost, noninvasive tumor phenotyping for application in personalized patient therapies or treatment plans [17]. Genetic results frequently require an extended period of time to become available; therefore, this pathway would reduce the time between diagnosis and effective treatment.

This article discusses glioma imaging diagnostics, focusing on modern MRI techniques to predict malignancy grade and genetic alterations, which play a pivotal role in shaping personalized treatment approaches. Moreover, we will delve into the application of MRI in the assessment of pseudoprogression and necrosis induced by radiotherapy. By comprehensively exploring these aspects, we aim to provide a holistic understanding of how advanced MRI techniques can inform clinical decisions and enhance the development of tailored therapeutic strategies for glioma patients.

Section snippets

MRI protocol

Neuroimaging continues to be a leading area in medical imaging technology and research. Nevertheless, the absence of standardized benchmark acquisition protocols, along with the fast pace of technological advancements, often hinders the consolidation of data in multicenter studies. Recognizing this challenge, the Brain Tumor Group (BTG) of the European Organization of Research and Treatment of Cancer (EORTC) emphasized the importance of standardizing MR image acquisition specifically for…

Contrast enhancement

Gliomas can exhibit contrast enhancement due to either BBB disruptions or increased permeability of blood vessels. The BBB in glioma patients frequently sustains damage or exhibits aberrant morphology, facilitating the infiltration of GBCA from the bloodstream into the adjacent tumor tissue. Additionally, gliomas induce angiogenesis to facilitate nutrient supply through the formation of new blood vessels. Vessels that are newly developed in frequently exhibit irregularities and heightened…

Assessment of genetic alterations using MRI

Table 3 provides a summary of the clinical applications parameters derived from MRI discussed in this review that pertain to predicting molecular subtypes in gliomas.…

Progression vs pseudoprogression

The exact cause of pseudoprogression is not well understood, although it is believed that the inflammation of epithelial cells and tissue, together with edema and abnormal vascular permeability, may be triggered by the combination of chemotherapy and radiation [173,174]. The clinical definition of pseudoprogression lacks clarity, since some studies suggest that the lesion must exhibit no symptoms of advancement for a minimum of 6months, while others recommend a 2-month delay following the…

Limitations and challenges

Although there have been technical advancements, there are still difficulties related to visualizing gliomas [202]. A significant obstacle is the absence of thorough validation for sophisticated MRI-derived biomarkers. Although there are suggestions for accelerate the progress of imaging biomarkers in brain tumors, there is a lack of regulatory certifications or well-defined protocols that have been implemented into practice. Furthermore, variations existed in the administration of GBCA,…

Future directions

The future directions in glioma diagnostics and treatment are poised to be significantly influenced by the integration of advanced MRI techniques and the expanding field of radiogenomics. As we move forward, a key focus will be on enhancing the precision and accessibility of DWI and PWI. These techniques, when combined with rapidly evolving molecular diagnostics, have the potential to revolutionize personalized medicine in neuro-oncology. Future research should aim at standardizing MRI…

Conclusions

In conclusion, MR scans have revolutionized the management of glioma patients. The integration of advanced MRI techniques, such as DWI and PWI, alongside the advancements in radiogenomics, marks a significant leap forward in the diagnostics and management of gliomas. These technologies offer a deeper understanding of tumor biology and enable more precise and personalized treatment strategies. However, challenges such as the standardization of MRI protocols and the interpretation of complex…

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Paulina Śledzińska-Bebyn: Writing – review & editing, Writing – original draft, Visualization, Resources, Project administration, Conceptualization. **Jacek Furtak:** Writing – review & editing, Funding acquisition. **Marek Bebyn:** Writing – original draft, Visualization. **Zbigniew Serafin:** Writing – review & editing,

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