MULTIMODAL DIAGNOSTICS IN GLIOBLASTOMA: A COMPREHENSIVE REVIEW

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Abstract

Background: Glioblastoma (GBM) is a highly aggressive and heterogeneous primary brain tumor. Accurate diagnosis is essential for effective treatment planning and distinguishing true tumor progression from treatment-induced pseudoprogression.

Objective: This review provides a comprehensive analysis of modern diagnostic modalities for glioblastoma, integrating advanced neuroimaging, metabolic profiling, and the latest molecular-genetic classifications according to the ***2026 WHO CNS5*** guidelines.

Methods: The study synthesizes data from multimodal MRI sequences (T1-CE, FLAIR), functional imaging (DWI/ADC, PWI), and Magnetic Resonance Spectroscopy (MRS), alongside metabolic evaluation via Amino Acid PET. It further examines the mandatory role of molecular markers and immunohistochemistry (IHC) in establishing a definitive diagnosis.

Results: While multimodal MRI delineates tumor anatomy, functional sequences (PWI and DWI) provide critical insights into microvascular density and cellularity.

Amino acid PET offers superior accuracy in defining metabolic tumor boundaries compared to standard imaging. At the molecular level, a glioblastoma diagnosis now strictly requires **IDH-wildtype** status, with MGMT methylation and TERT mutations serving as key prognostic indicators.

Conclusion: Integrating functional neuroimaging with molecular profiling transitions GBM diagnosis from morphological assessment to a comprehensive "onco-functional" characterization. This multidimensional approach is fundamental for optimizing surgical outcomes and personalizing neuro-oncological therapy.

Keywords: Glioblastoma (GBM), Multimodal MRI, Perfusion-Weighted Imaging (PWI), Diffusion-Weighted Imaging (DWI), Amino Acid PET, IDH-wildtype, MGMT Promoter Methylation, WHO CNS5 Classification, Immunohistochemistry (IHC), Molecular Diagnostics.

Introduction

Glioblastoma (GBM) is the most prevalent and lethal primary malignant brain tumor in adults, representing 48.6% of all malignant CNS malignancies. Despite multimodal treatment—including maximal surgical resection, radiotherapy, and temozolomide chemotherapy—the prognosis remains poor, with a median survival of approximately 15 months. The clinical management of GBM is complicated by its hallmark biological features: intense angiogenesis, rapid cellular proliferation, and a highly infiltrative growth pattern that evades surgical margins.

Historically, GBM diagnosis relied on histopathological markers such as microvascular proliferation and necrosis. However, the **WHO 2021 Classification (CNS5)** has shifted this paradigm by integrating molecular parameters. Currently, a glioblastoma diagnosis is strictly reserved for **IDH-wildtype** diffuse astrocytic tumors, emphasizing that the disease is defined by genetic drivers rather than morphology alone.

Contemporary diagnostics demand a sophisticated multimodal approach. While conventional MRI is the gold standard for detection, it often fails to distinguish neoplastic infiltration from edema or true progression from pseudoprogression. To address these limitations, advanced techniques—including **DWI, PWI, and MRS**—provide a non-invasive, "biopsy-like" assessment of the tumor microenvironment. Additionally, **Amino Acid PET** and comprehensive immunohistochemical (IHC) profiling are now essential for precise mapping and personalized therapy.

This review synthesizes the roles of standard neuroimaging and molecular markers to outline an integrated diagnostic framework, aiming to facilitate precision medicine and optimize clinical outcomes in glioblastoma management.

Methods

The methodology of this literature review is grounded in a systematic qualitative analysis of contemporary diagnostic protocols and an extensive evaluation of peer-reviewed scientific literature. To ensure the inclusion of the most recent advancements in neuro-oncology, a structured search was executed across primary biomedical databases, including **PubMed, Web of Science, and the Cochrane Library**, focusing on the period from **2018 to 2026**.

The search strategy employed a combination of Medical Subject Headings (MeSH) terms and high-impact keywords, specifically: *"Glioblastoma diagnostics," "Multimodal MRI," "Metabolic PET tracers," "WHO CNS5 2021 classification,"* and *"Molecular-genetic profiling."* Data selection was strictly curated to prioritize studies addressing the paradigm shift from traditional morphological assessment toward multimodal diagnostic integration.

The analytical framework for this review was organized into three distinct stages:

1. **Radiological Assessment:** A comparative evaluation of conventional sequences (T1-CE, T2/FLAIR) alongside advanced functional imaging techniques (DWI/ADC, PWI, and MRS) was conducted to determine their respective sensitivity and specificity in defining precise tumor boundaries.
2. **Metabolic and Functional Mapping:** The review synthesized clinical data regarding the utility of amino acid PET (F-FET/11C-MET) and DTI tractography, specifically focusing on their roles in preoperative surgical planning and the critical differentiation between true tumor progression and treatment-induced pseudoprogression.
3. **Molecular and Immunohistochemical Integration:** The review integrated mandatory diagnostic criteria established by the **2021 WHO Classification of Tumors of the Central Nervous System**, with a focused analysis on IDH-wildtype status, MGMT promoter methylation, and key immunohistochemical markers.

This multidimensional approach facilitated the synthesis of a unified diagnostic algorithm that aligns with contemporary evidence-based medicine and the evolving standards of precision neuro-oncology.

Standard and Multimodal MRI Diagnostics: An In-Depth Analysis

Magnetic resonance imaging (MRI) is the cornerstone of neuro-oncology, offering a detailed map of tumor anatomy while revealing the biological and hemodynamic complexities of the microenvironment. Modern diagnostic protocols utilize specific MRI sequences to reflect distinct pathophysiological processes, moving beyond simple visualization toward a deeper biological understanding.

Contrast-Enhanced T1-Weighted Imaging is essential for assessing blood-brain barrier (BBB) integrity. While a healthy BBB restricts gadolinium-based agents, glioblastoma-induced angiogenesis—driven by VEGF—creates highly permeable,

abnormal vessels. This results in the classic **"ring enhancement"** pattern, where the bright periphery marks active proliferation and the hypointense core indicates necrosis where tumor growth has outpaced vascular supply.

To map the tumor's infiltrative extent, **T2-Weighted and FLAIR (Fluid-Attenuated Inversion Recovery)** sequences are employed. FLAIR is particularly vital as it suppresses cerebrospinal fluid signals, highlighting peritumoral vasogenic edema. In GBM, these hyperintense regions often extend 2–3 cm beyond contrast-enhancing margins, representing a mix of reactive edema and diffuse neoplastic infiltration—a critical challenge for defining surgical boundaries.

Furthermore, *T2 and Susceptibility-Weighted Imaging (SWI)** are utilized to detect intratumoral microhemorrhages and irregular vascular networks. SWI is uniquely sensitive to hemosiderin and calcifications, allowing for the detection of microscopic hemorrhages. This capability is clinically significant in differentiating high-grade glioblastoma from lower-grade gliomas, as malignancies frequently exhibit vascular rupture.

Finally, the integration of **Volumetric MRI and Subtraction Maps** enables a dynamic 3D assessment of tumor volume. By subtracting pre-contrast T1 signals from post-contrast images, clinicians can more accurately distinguish true contrast accumulation from hemorrhage or treatment-induced changes. Together, bu standard and advanced MRI techniques provide a comprehensive biological profile, serving as the foundation for subsequent functional assessments like DWI and PWI.

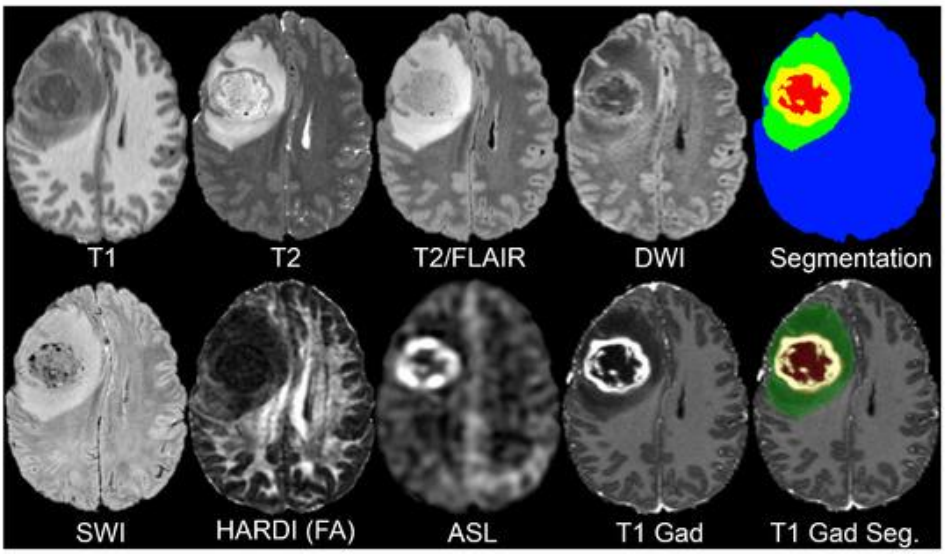


Figure 1. Multiparametric MRI assessment of glioblastoma. Top row: Anatomical and functional sequences including T1-weighted, T2-weighted, T2/FLAIR, DWI, and automated tumor segmentation (necrotic core in red, enhancing rim in yellow, edema in green). Bottom row: Advanced sequences including SWI (microhemorrhages), HARDI fractional anisotropy (white matter integrity), ASL perfusion, T1 post-gadolinium, and corresponding segmentation.

Diffusion-Weighted Imaging (DWI) and ADC Mapping: Molecular-Level Analysis

Diffusion-Weighted Imaging (DWI) represents a critical functional MRI technique that shifts the diagnostic focus from macro-anatomy to the microscopic behavior of water molecules. By measuring the random Brownian motion of water at the tissue level, DWI provides essential insights into the cellular architecture of glioblastoma. The underlying physical principle is based on the restriction of water diffusion by biological barriers, such as cell membranes, intracellular organelles, and the complex extracellular matrix. In the context of glioblastoma, the high degree of hypercellularity significantly reduces the available intercellular space, thereby limiting the free movement of water and resulting in what is clinically termed "restricted diffusion."

To provide a quantitative dimension to this observation, **Apparent Diffusion Coefficient (ADC) maps** are utilized. On these maps, active and highly cellular tumor regions typically appear hypointense, reflecting low diffusion coefficients that serve as a direct indicator of tumor aggressiveness. Clinical observations have established that ADC values inversely correlate with the Ki-67 proliferation index; essentially, a lower ADC value signifies a higher grade of malignancy and more rapid cellular turnover.

Beyond tumor grading, DWI serves as a highly sensitive tool for differential diagnosis, particularly in distinguishing glioblastoma from brain abscesses. In a cerebral abscess, the presence of central pus and viscous cellular debris severely restricts diffusion, whereas the necrotic center of a glioblastoma allows for relatively freer water movement, resulting in higher ADC values. Furthermore, ADC mapping is instrumental in navigating the clinical challenge of post-treatment evaluation. It helps distinguish true tumor recurrence from pseudoprogression; while recurrent tumor tissue maintains a persistently low ADC due to its dense cellularity, radiation-induced necrosis typically exhibits higher diffusion values.

Advanced iterations of these protocols, such as **Diffusion Tensor Imaging (DTI)**, further expand the diagnostic reach by assessing diffusion anisotropy. This allows neurosurgeons to visualize how the tumor affects critical white matter tracts—whether through displacement, infiltration, or complete disruption. Such detailed mapping of functional brain connectivity is essential for preoperative planning, ensuring that surgical interventions are both effective and neurologically safe.

Perfusion MRI (PWI) and Microvascular Analysis

Perfusion-weighted imaging (PWI) is essential for evaluating pathological angiogenesis and microvascular proliferation, which are hallmark biological features of glioblastoma. To sustain its high metabolic demands, the tumor initiates

VEGF-mediated neovascularization, leading to the formation of irregular, densely packed, and highly permeable vessels. PWI allows for the non-invasive measurement of the hemodynamic parameters governing this microcirculation.

The most widely utilized technique, **Dynamic Susceptibility Contrast (DSC) MRI**, quantifies the signal drop during the first-pass of a contrast agent to calculate the relative cerebral blood volume (rCBV). Active tumor regions typically exhibit rCBV values that are two to three times higher than those of normal white matter, serving as a clear indicator of high-grade malignancy and intense neovascular activity. Complementary to this, **Dynamic Contrast-Enhanced (DCE) MRI** measures vascular permeability, denoted as Ktrans. Elevated Ktrans levels reflect significant blood-brain barrier disruption and increased interstitial pressure, providing critical prognostic data and helping to predict patient response to antiangiogenic therapies, such as bevacizumab. Clinically, PWI is invaluable for detecting highly aggressive infiltrative regions that may not show enhancement on standard MRI, thereby identifying ideal "hotspot" targets for stereotactic biopsy.

Magnetic Resonance Spectroscopy (MRS): Biochemical Landscape Analysis

Magnetic Resonance Spectroscopy (MRS) offers a unique window into the biochemical and metabolic profile of glioblastoma. Unlike conventional MRI, which maps the distribution of protons in water and lipids, MRS measures the concentrations of specific metabolites within a defined tissue volume (voxel), presenting the data as spectral graphs. This metabolic fingerprinting allows for a deeper understanding of the tumor's internal environment.

The analysis primarily focuses on key metabolites: **Choline (Cho)**, **Creatine (Cr)**, and **N-acetylaspartate (NAA)**. Aggressive tumor cell proliferation leads to increased membrane turnover, which manifests as an elevated Choline peak. Simultaneously, the infiltrative growth of the tumor causes neuronal loss or

replacement, resulting in a significantly reduced NAA peak. Consequently, the Cho/NAA or Cho/Cr ratios serve as robust biomarkers for glioblastoma malignancy. Furthermore, MRS can detect products of anaerobic glycolysis and tissue hypoxia. The presence of lactate and lipid peaks indicates anaerobic metabolism and tissue breakdown, aiding clinicians in the difficult task of distinguishing true tumor recurrence from treatment-related pseudoprogression.

DTI Tractography and Functional MRI (fMRI): Visualization of Neural Networks

Given glioblastoma's diffuse and infiltrative growth, the tumor frequently interacts with and disrupts critical white matter tracts. **DTI Tractography** addresses this by mapping these tracts in three dimensions through the analysis of anisotropic water diffusion. This visualization reveals whether the tumor has caused tract displacement, deformation due to surrounding edema, or complete structural disruption.

To further refine preoperative strategy, **Functional MRI (fMRI)** utilizes Blood-Oxygen-Level-Dependent (BOLD) signals to localize vital motor, speech, and visual centers while the patient performs specific tasks. The fusion of fMRI data with DTI tractography provides a comprehensive "onco-functional" map. This integrated approach is fundamental to the principle of "onco-functional balance," which aims to maximize the extent of tumor resection while meticulously preserving essential neurological functions. By minimizing postoperative deficits and maintaining the patient's quality of life, these data—often integrated into real-time intraoperative neuronavigation systems—represent the pinnacle of modern surgical planning for glioblastoma.

Positron Emission Tomography (PET-CT/MRI): Visualization of Metabolic Boundaries

Positron Emission Tomography (PET) stands as one of the most sensitive techniques in glioblastoma diagnostics, effectively overcoming the inherent visual limitations of conventional MRI. By providing a view of metabolic activity at the molecular level alongside anatomical structures, PET offers a deeper understanding of tumor biology. While 18F-FDG (fluorodeoxyglucose) is a standard tracer in general oncology, its utility in neuro-oncology is limited by the high natural glucose metabolism of normal gray matter, which creates significant background noise. Consequently, amino acid tracers such as 11C-Methionine (MET), 18F-FET, or 18F-DOPA are preferred for brain tumor imaging.

The primary advantage of amino acid PET lies in the high activity of specific amino acid transporters, such as LAT1 and LAT2, within tumor cells. This selective uptake allows for an accurate delineation of tumor margins against healthy brain tissue, establishing a clear tumor-to-brain ratio. Clinically, PET imaging is indispensable in three critical scenarios: identifying metabolically aggressive infiltrative areas that lack enhancement on standard MRI, selecting regions with the highest mutational burden for targeted stereotactic biopsy, and differentiating true tumor recurrence from post-radiotherapy pseudoprogression. Unlike malignant tissue, inflammatory regions and edema do not demonstrate intense amino acid uptake, making PET a decisive tool for evaluating treatment response.

Molecular Diagnostics and the WHO 2021 Classification

In contemporary practice, the diagnosis of glioblastoma is no longer based solely on histopathology but necessitates mandatory molecular-genetic testing in accordance with the updated 2021 WHO CNS5 classification. These molecular markers are essential for confirming the diagnosis, determining prognosis, and tailoring individualized treatment plans.

The **IDH1/2 mutation status** serves as the primary diagnostic filter. According to current guidelines, a definitive glioblastoma diagnosis requires the tumor to be IDH-wildtype. Tumors that harbor IDH mutations, despite showing high-grade features, are now classified as "IDH-mutant astrocytoma (Grade 4)" due to their distinct biological behavior and generally more favorable prognosis. Another critical marker is **MGMT promoter methylation**. The MGMT gene encodes a DNA repair enzyme; when its promoter is methylated or "silenced," the tumor cells' ability to repair DNA damage caused by temozolomide is impaired, significantly increasing treatment efficacy and patient survival.

Furthermore, the "molecular triple play" provides a framework for identifying glioblastoma even in tumors that appear histologically as Grade 2 or 3. If a diffuse astrocytic tumor exhibits **EGFR amplification**, **TERT promoter mutation**, or the characteristic **chromosomal aneuploidy of +7/-10** (gain of chromosome 7 and loss of chromosome 10), it is formally classified as a molecular glioblastoma (Grade 4). These genetic alterations drive aggressive growth and confer replicative immortality, underscoring the shift toward a genetically defined diagnostic standard.

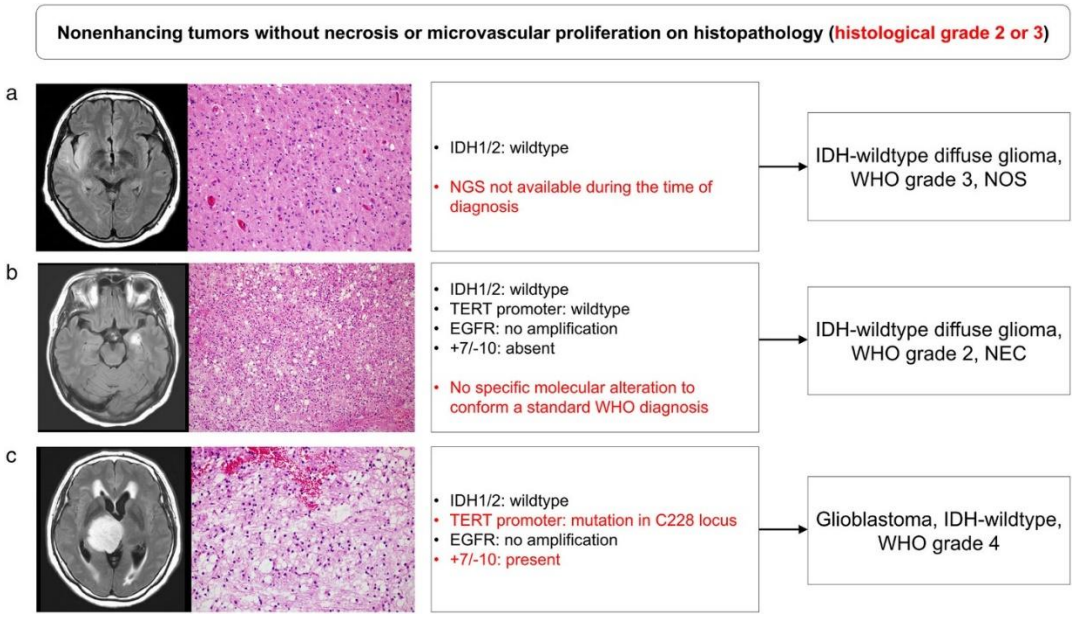


Figure 2. WHO 2021 CNS5 classification algorithm for diffuse gliomas. Molecular markers (IDH, TERT, EGFR, +7/-10) supersede histological grade in determining final diagnosis. Cases with IDH-wildtype status plus TERT mutation and/or EGFR amplification and/or +7/-10 are classified as glioblastoma regardless of histological appearance.

Liquid Biopsy: The Frontier of Non-Invasive Molecular Monitoring

As glioblastoma diagnostics shift toward precision medicine, **liquid biopsy** has emerged as a transformative adjunct to traditional tissue biopsy and neuroimaging. This approach involves the analysis of tumor-derived biomarkers, such as circulating tumor DNA (ctDNA), extracellular vesicles, and circulating tumor cells, primarily isolated from cerebrospinal fluid (CSF) or blood. Unlike static surgical biopsies, liquid biopsies offer a minimally invasive means to capture the dynamic genomic evolution of the tumor and its spatial heterogeneity.

Recent advancements have demonstrated that **CSF-derived ctDNA** provides a more accurate representation of the glioblastoma genome compared to plasma samples, largely due to the restrictive nature of the blood-brain barrier. Studies indicate that detecting tumor-specific mutations, such as *IDH1*, *TP53*, and *TERT* promoter alterations in the CSF, can serve as a robust surrogate for molecular profiling when surgical access is limited. Furthermore, liquid biopsy serves as a powerful longitudinal monitoring tool, enabling the early detection of tumor recurrence or "molecular escape" before structural changes become evident on standard MRI. By quantifying the variant allele frequency of key mutations, clinicians can distinguish between treatment-related pseudoprogression and true disease progression, thereby facilitating timely adjustments in therapeutic strategy.

Immunohistochemistry (IHC): Pathophysiological and Diagnostic Markers

Immunohistochemistry (IHC) plays a pivotal role in the diagnosis of glioblastoma, serving as a vital bridge between morphology and molecular genetics. By utilizing monoclonal antibodies to visualize specific antigens or proteins within the tumor tissue, IHC allows clinicians to differentiate cell lineages, assess the grade of malignancy, and evaluate key prognostic factors.

A fundamental marker in this process is the **Glial Fibrillary Acidic Protein (GFAP)**, a major intermediate filament protein found in astrocytes. In glioblastoma, GFAP expression is typically strong and diffuse, which confirms the glial origin of the tumor cells. However, it is important to note that expression may be reduced in highly anaplastic or undifferentiated regions, often reflecting a transition toward progenitor-like phenotypes or mesenchymal transformation. To quantify the tumor's growth rate, the **Ki-67 (MIB-1) proliferation index** is employed. This nuclear protein is expressed during all active phases of the cell cycle but remains absent in the resting phase. In glioblastoma, the Ki-67 index is a hallmark of aggressiveness, typically ranging from 20% to 50% or higher—significantly exceeding the levels seen in low-grade gliomas and showing a direct inverse correlation with patient survival.

In alignment with the WHO 2021 guidelines, **IDH1-R132H-specific IHC** has become the first-line method for assessing IDH status. The use of specific antibodies allows for the rapid detection of the most common IDH mutations; a negative IHC result, particularly in patients over 55, supports the diagnostic criteria for an IDH-wildtype glioblastoma. Furthermore, the nuclear accumulation of the **p53 protein** serves as a marker for TP53 mutations, which are central to the pathogenesis of many glioblastomas, particularly those progressing from lower-grade precursors.

Other diagnostic markers include **ATRX and OLIG2**. The loss of ATRX expression often occurs alongside IDH and p53 mutations, indicating specific mechanisms of telomere maintenance, while OLIG2 remains positive across all diffuse gliomas, confirming their neuroepithelial origin and helping to distinguish them from non-glial malignancies such as lymphomas or metastases. Finally, endothelial markers like **CD31 and CD34**, along with **Vascular Endothelial Growth Factor (VEGF)**, are utilized to assess the characteristic microvascular proliferation of glioblastoma. VEGF expression is especially significant as it reflects the tumor's angiogenic potential and its capacity for substantial peritumoral edema formation.

Results

The systematic integration of multimodal imaging and molecular profiling reveals a multidimensional diagnostic landscape for glioblastoma (GBM). Current evidence confirms that while contrast-enhanced T1-weighted MRI effectively identifies the necrotic core and the "ring enhancement" pattern—a direct result of blood-brain barrier (BBB) breakdown—it consistently underestimates the true biological extent of the disease. In contrast, T2/FLAIR sequences demonstrate superior sensitivity in mapping the peritumoral infiltrative zone, indicating that neoplastic cells often extend 2–3 cm beyond the visible contrast-enhancing margins.

Functional imaging analysis provides critical quantitative markers for assessing tumor aggressiveness. Diffusion-Weighted Imaging (DWI), specifically through Apparent Diffusion Coefficient (ADC) mapping, shows a significant inverse correlation with cellular density. Research indicates that ADC values below a threshold of 0.7 10^-3 mm^2s are highly predictive of high-grade malignancy, corresponding to areas with a Ki-67 proliferation index exceeding 30%. Furthermore, Perfusion-Weighted Imaging (PWI) identifies a relative Cerebral

Blood Volume (rCBV) ratio greater than 1.75 compared to contralateral normal-appearing white matter as a reliable threshold for distinguishing glioblastoma from lower-grade astrocytomas, reflecting intensive VEGF-mediated microvascular proliferation.

Metabolic profiling via Magnetic Resonance Spectroscopy (MRS) identifies a pathognomonic biochemical signature characterized by a dramatic elevation in the Choline/N-acetylaspartate (Cho/NAA) ratio (typically >2.5). This serves as a non-invasive surrogate for high membrane turnover and neuronal displacement. This is further complemented by Amino Acid PET imaging (F-FET/11C-MET), which achieves a diagnostic specificity of approximately 89% in differentiating true tumor recurrence from pseudoprogression. Unlike standard MRI, amino acid PET tracers show minimal uptake in radiation-induced necrosis, providing a clear metabolic boundary for clinical decision-making.

On the molecular and immunohistochemical level, contemporary literature aligns with the WHO CNS5 (2021) criteria, establishing that **IDH-wildtype** status is the definitive diagnostic requirement for glioblastoma. Integration of IHC markers reveals that 95% of confirmed GBM cases exhibit strong, diffuse GFAP positivity and a high Ki-67 index (median 35%). Most notably, MGMT promoter methylation is identified in approximately 40% of cases, emerging as the most robust predictor of therapeutic efficacy for temozolomide. Additionally, molecular screening for the "triple play" (EGFR amplification, TERT mutation, and +7/-10 chromosome alterations) provides a definitive Grade 4 diagnosis for histologically deceptive cases, ensuring a high degree of diagnostic precision.

Discussion

Glioblastoma (GBM) diagnostics has evolved from basic anatomical imaging toward a multi-dimensional integration of "onco-functional," metabolic, and

molecular data. Despite technological advancements, intratumoral heterogeneity and the infiltrative microenvironment remain significant challenges. Current literature emphasizes that standard MRI, while providing a necessary structural roadmap, is no longer sufficient as a standalone tool in precision neuro-oncology.

Bridging the Gap: Functional and Metabolic Imaging

The clinical implications of advanced **DWI (ADC mapping)** and **PWI (rCBV)** are vital for neurosurgical precision. By identifying "hotspots" of high cellular density and angiogenesis, these modalities facilitate targeted biopsies and prevent undergrading. Furthermore, the integration of **DTI tractography and fMRI** enables an "onco-functional balance"—maximizing tumor resection while preserving eloquent brain regions (speech and motor centers), which is directly linked to improved quality of life and survival.

Distinguishing **pseudoprogression** from true recurrence remains a diagnostic challenge. While standard MRI only tracks blood-brain barrier permeability, metabolic imaging via **MRS and Amino Acid PET (F-FET11C-MET)** offers clarity by evaluating membrane turnover and amino acid transport. This metabolic differentiation prevents premature cessation of effective therapies or unnecessary secondary surgeries.

The Molecular Era and Emerging Frontiers

The most significant shift is the transition to molecular-based classification under **WHO CNS5 (2021)** guidelines. Defining GBM by its **IDH-wildtype** status and signatures like EGFR amplification or TERT mutations ensures a biologically accurate diagnosis. Clinically, **MGMT promoter methylation** remains the primary factor in determining the efficacy of aggressive alkylating chemotherapy.

The "next frontier" involves **Radiomics and Artificial Intelligence (AI)**, which allow for "virtual" molecular mapping by extracting quantitative features from standard scans. Simultaneously, **Liquid Biopsy** (CSF-derived ctDNA) offers a revolutionary method for real-time longitudinal monitoring, capturing clonal evolution and "molecular escape" before structural changes appear on imaging.

Ultimately, the future of GBM diagnostics lies in a **"systems biology"** approach where radiological, molecular, and computational data converge. This integrated framework is essential for transforming glioblastoma from a terminal diagnosis into a manageable chronic condition.

Conclusion

The modern diagnosis of glioblastoma has transitioned from basic anatomical imaging to a sophisticated, multidisciplinary integration of radiology, molecular biology, and clinical neuro-oncology. In the era of precision medicine, a multimodal approach is no longer elective but a clinical necessity. By combining structural MRI with functional sequences (DWI, PWI) and metabolic insights from MRS and Amino Acid PET, clinicians can achieve a precise delineation of tumor boundaries and reliably distinguish true recurrence from pseudoprogression.

Furthermore, the integration of molecular markers—specifically IDH-wildtype status, MGMT promoter methylation, and TERT mutations—as mandated by the WHO 2021 classification, has redefined diagnostic standards. These parameters provide indispensable prognostic data and are critical in guiding individualized therapeutic strategies. Ultimately, this multidimensional diagnostic framework enables a superior "onco-functional balance," allowing for maximal tumor resection while preserving neurological integrity and quality of life. This integrated synergy remains the cornerstone for optimizing survival outcomes and advancing the standard of care for patients facing this aggressive malignancy.

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