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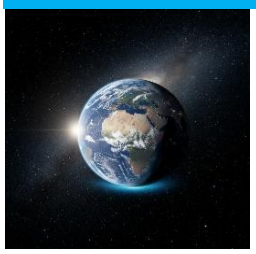

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Integration of Artificial Intelligence in Magnetic Resonance Imaging analysis and Liquid Biopsy in diagnosing and monitoring Glioblastoma Multiforme - A Systematic Review

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Abstract

Glioblastoma multiforme (GBM) is the most aggressive primary brain tumor among adults and is associated with rapid progressions and poor prognosis. Modern diagnostic techniques, including molecular biology, have improved the perception of disease development emphasizing the role of disturbed signaling pathways, genetic mutations and tumor microenvironment.

The following review aims to conclude current comprehension of molecular mechanisms leading to GBM development and contemporary diagnostic and therapeutic approaches. Articles present in PubMed database published from 2022 onwards were researched to perform analysis of tumor biology, subcellular mechanisms and diagnostic possibilities.

Magnetic resonance imaging (MRI) remains the most fundamental diagnostic method which enhanced by modern approaches such as radiomics and artificial intelligence (AI) supports proper diagnosis and enables tumor characteristics analysis. Moreover, combining imaging with modern pathomorphological methods such as liquid biopsy can lead to increased accuracy and personalization in diagnostics.

To conclude, GBM development is a complex process combining genetic alterations and disturbed molecular pathways that can be detected using modern diagnostic techniques. Advanced pathomorphological methods and AI-supported imaging lead to accurate diagnosis, proper therapeutic decisions and better patient outcome.

Keywords

Glioblastoma, Glioblastoma Multiforme, molecular mechanisms, pathogenesis, magnetic resonance, artificial intelligence, radiomics, diagnostics.

1. Introduction

Glioblastoma Multiforme (GBM) is a highly malignant primary brain tumor originating from glial cells that accounts for more than 50% of all gliomas (Makowska et al., 2023). The risk of occurrence is greater in men than women and increases with age with a 5-year survival rate of 7% (Czarnywojtek et al., 2023). It is known for its severe course and poor therapeutic response due to infiltrating growth accompanied by necrosis and ability to prominent vascularization. It is most frequently localized in the supraential part of the cranial cavity and is followed by unspecific symptoms which leads to diagnostic obstacles and late detection.

Specific causes of GBM have not been discovered yet, however, disturbed epigenetic changes, signaling pathways and accumulated genetical mutations play a crucial role in development of this severely aggressive brain tumor. Epigenetics such as DNA methylation, chromatin structure changes and histone modifications are believed to be the most significant factors contributing to tumor regulation and interaction between neoplastic cells and microenvironment by monitoring transcription of cytokines that ensure immunosuppressive character of GBM. Moreover, epigenetic alterations modulate crucial signaling pathways leading to aggressive nature of tumor cells (Królikowska et al., 2025). The main significances are observed in epidermal growth factor receptor (EGFR) pathway, fibroblast growth factor receptor (FGFR) pathway, Wnt/β-catenin signaling event as well as PI3K/AKT/mTOR cascade (Kumari et al., 2023). These pathways enable neuronal differentiation of GBM cells resulting in abrupt progression. The Wnt pathway mediates cellular proliferation and its heightened activity is responsible for chemotherapy resistance, aggressive course and invasive potential of GBM. Increased production of proangiogenic growth factors such as VEGF that stimulates endothelial cell growth leads to substantial tumor vascularization which is a significant proliferation factor and conversely a therapeutic opportunity to use angiogenesis inhibitors such as bevacizumab . Aggressive characteristics of GBM is also mediated by TGF-β that disturbs cell cycle and insufficient tumor suppression (Khabibov et al., 2022).
Epigenetic modifications are also believed to take part in development of GBM with methylation of the O^6-methylguanine-DNA methyltransferase (MGMT) promoter being the most frequent one (Pouyan et al., 2025). MGMT is a DNA repairing enzyme that ensures genomic stability by removing alkyl groups from the O^6 position of guanine. Silencing the MGMT gene results in disturbed DNA repair and improved response to alkylating chemotherapy using temozolomide. Absence of MGMT methylation leads to alkylating agents resistance, therapeutic obstacles and poorer prognosis. It is believed to be one of the most crucial biomarkers in glioblastoma and has got predictive as well as prognostic value (Szylberg et al., 2022). TP53 and PTEN mutations occur frequently in GBM and account for aggressive course and pessimistic prognosis as a result of poorer oncogenesis prevention. Another alteration that might be found in GBM is co-deletion of chromosomes 1p and 19q which contributes to increased chemosensitivity and more positive prognosis (Pouyan et al., 2025).

Imaging methods such as MRI, functional MRI, diffusion tensor imaging (DTI) and positron emission tomography (PET) remain a standard in diagnostics of GBM assuring accurate detection and treatment (Ahangari et al., 2025). MRI provides essential information about the localization of the tumor and important characteristics such as necrosis presence and contrast enhancement. Histopathological and molecular biology techniques enable precise classification and diagnosis as well as adequate therapeutic choices. Traditional histopathology focuses on certain changes in the tissue's shape and structure such as necrosis and vascular proliferation. However, these signs alone do not give a complete picture of the tumor's complexity. These days, the approaches that are used are more advanced and include enhancing the tumor's genetic features. This involves identifying specific biomarkers, such as presence of the MGMT promoter methylation and the EGFR amplification. These biomarkers provide crucial information about the tumor's prognosis and its response to treatment. By combining the traditional tissue analysis with the genetic information, a more accurate understanding of the tumor can be acquired. The new WHO guidelines propose that some of the lower-grade tumors may be classified as more aggressive than they are currently through their genetic profiles (Ahangari et al., 2025). The use of AI to evaluate tissue samples and genomics will also aid in developing improved diagnoses and personalized therapy options. When combining various evaluation tools, such as evaluating the physical characteristics of a tumor with the genetic information about it, it enhances the ability to provide high quality medical care by enabling a better understanding of different treatment options.

The incorporation of artificial intelligence and radiomics represents a major advancement in glioblastoma diagnostics.. Radiomics enables the extraction of high-dimensional quantitative features from standard imaging methods capturing tumor characteristics that are not detectable to the human eye. It is an advanced way to get precise and consistent measurements of tumor features like shape, intensity and their various combinations. It works by taking images, identifying the most essential parts, detecting

important details and then using machine learning to analyze them. The information mentioned above will enable researchers to build predictive models that help to understand how tumors grow and develop, assess the overall outcome of a cancer patient's condition and relate clinical or imaging information directly to molecular alterations. This means radiomics can help understand tumor biology more effectively and make more personalized treatment plans (Kwiatkowska-Miernik et al., 2023).

AI algorithms, particularly deep learning models, can analyze complex datasets to improve tumor detection, classification, and segmentation enhancing diagnostic accuracy (Ahangari et al., 2025), AI-based approaches have proved to be comparable or even more satisfying than traditional manual methods while being less subjective. Furthermore, AI facilitates the combination of different data types resulting in more comprehensive evaluation of tumor heterogeneity and truthful prediction of clinical outcomes (Zhu et al., 2022). By utilizing AI on biopsy samples and genomic information, clinicians are able to enhance their ability to diagnose cancer more accurately and assist in the development of individualized therapy options. The integration of the aforementioned approaches allows to make more informed decisions about the patients' treatment and ultimately provide them with a higher quality of care.

Ultimately, the best way to understand a complex tumor is through an interdisciplinary model which considers both the physical attributes of a tumor and its genetic makeup. Through this combined methodology, healthcare providers can develop more effective therapeutic protocols which will lead to improved health status for cancer patients. Despite its promising potential, the clinical implementation of AI and radiomics remains limited by the need for standardization, large-scale validation, and integration into routine workflows.

Current treatment strategies for glioblastoma are based on a combination of surgery, radiation, and medication. The usual approach is maximal surgical resection of the tumor followed by radiotherapy with concurrent and adjuvant temozolomide chemotherapy. This strategy is known as the Stupp protocol and it has been shown to increase survival comparing to radiation alone (Sadowski et al., 2024). However, the outlook is still not positive because the tumor is able to spread easily and does not respond well to traditional treatments. New therapeutic options are being developed with an attempt to try overcoming these barriers, including targeted therapies, angiogenesis inhibitors and innovative approaches like immunotherapy and special devices that treat the tumor. Modern approaches include creating personalized treatment plans based on the genetic profile of each person's tumor. While current treatments provide some benefits, alternative and advanced methods are being researched in order to treat glioblastoma by combining different strategies and using the latest technology aiming to improve the chances of survival for those suffering from GBM. Some of the new treatments being explored include immunotherapy which supports the immune system in fighting the tumor and special devices to disrupt the growth of the tumor. Nanotechnology-based drug delivery systems are also being developed which can help get medication directly to the tumor (Angom et al., 2023). Additionally, advances in our understanding of the genetics of glioblastoma are allowing the development of targeted therapies that are tailored to each patient's specific tumor biology. The newest of these methods are now undergoing study but have the potential to lead to better treatment outcomes for patients suffering from Glioblastoma. Current therapies may not be sufficient; however, studies continue to evaluate the use of multiple modalities combined with advanced technologies in an attempt to increase both the survival rate and overall clinical outcome.

2. Methodology

A literature review was performed using the PubMed database in order to identify the most applicable articles on pathogenesis, modern diagnostic approaches and therapeutic strategies of Glioblastoma Multiforme. The research included publications from January 2022 to March 2026.

The search strategy has been refined by using specific keywords and combinations such as “glioblastoma’, ‘Glioblastoma Multiforme”, “molecular mechanisms”, “pathogenesis”, “magnetic resonance”, “artificial intelligence”, “radiomics” and “diagnostics”.
The study comprises original articles and review papers published in English associated with glioblastoma biology, signaling pathways and diagnostic strategies focusing on artificial intelligence supported imaging and modern histopathology methods. Only PubMed-indexed articles were taken into consideration.
Studies published prior to 2022 or that were not directly related to glioblastoma pathogenesis or diagnostic techniques were excluded.
Titles and abstracts were checked for constructive alignment and chosen articles were fully analyzed. 29 of 67 articles met the inclusion criteria and were included in the final study.
The analysis of gathered data was performed with an emphasis on glioblastoma pathogenesis and recent improvements in diagnostic methods.

3. Results

3.1 Conventional diagnostic methods

Conventional diagnostic methods in glioblastoma primarily combine neuroimaging and histopathological evaluation, with MRI remaining the standard for prime assessment allowing precise tumor visualization. Pathologies that might be detected include irregular contrast enhancement, central necrosis, and surrounding vasogenic edema that suggest a greater level of malignancy (Królikowska et al., 2025). MRI enhances better contrast resolution than CT and can be also used to detect other abnormalities such as vascular malformation or demyelinating disease. The most frequently used sequences are T1-weighted (T1), T1-contrast-enhanced, T2-weighted (T2), and fluid-attenuated inversion recovery (FLAIR) because they enable proper differentiation of brain tissues. Increased cellularity in GBM can be detected by diffusion-weighted imaging (DWI) that is able to identify the restriction of water molecules’ movements. Tumor metabolism and biochemical changes can be enhanced by magnetic resonance spectroscopy (MRS) while functional MRI detects brain areas that are related to the tumor allowing precise therapeutic plans. Positron emission tomography (PET) enables more accurate differentiation of brain tissues using radioactive substances that combine with tumor cells (Zhu et al., 2022). Although modern MRI functions can provide a variety of information, conventional imaging alone is not sufficient for a concluding diagnosis and differentiation from other intercranial findings (Hooper et al., 2023). Thus, biopsy or surgical resection followed by a histopathological examination of acquired tissues is essential in the diagnostic process providing characteristic features such as cellular pleomorphism, high mitotic activity, microvascular proliferation, and necrosis (Królikowska et al., 2025). If combined, these traditional approaches remain a fundamental part of glioblastoma diagnosis that, these days, can be complemented by molecular and AI-supported imaging methods resulting in higher diagnostic accuracy and guided treatment.

3.2 AI supported MRI combined with liquid biopsy in modern diagnostics

Artificial intelligence has been incorporated into the diagnostic process of glioblastoma significantly improving non-invasive evaluation using imaging data. Deep learning technologies automatically acquire features and patterns and profoundly increase the efficacy of important diagnostic steps such as identifying specific subtypes of tumors, their stage and differentiation with other intracranial pathologies (Wang et al., 2025). The models utilize data from MRI scans to make more precise diagnosis and improve efficiency of the whole process. AI-supported methods achieved accuracy of 97% in distinguishing glioblastoma from conditions such as metastases or primary central nervous system lymphoma. Furthermore, using AI methods enables the prediction of molecular biomarkers, including IDH mutation status and other prognostic features, enabling more personalized treatment strategies. Some models have proved to perform comparably to experienced radiologists while reducing interobserver variability at the same time. Despite positive perspective, challenges such as the need for

external validation, standardized imaging protocols, and integration into clinical workflows remain inevitable barriers in AI-based methods implementation (Contreras et al., 2025).
Artificial intelligence has shown significant potential in glioblastoma prognostic process through MRI-based analysis. Post-radiotherapy MRI scans evaluated by AI tools using data from different centers showed that imaging-based AI models reached higher efficacy of predictive performance with an area under the curve (AUC) of up to 0.93 which exceeds traditional techniques. Incorporating large pre-trained datasets essentially improved model accuracy enhancing the importance of data scale in AI development. AI-supported imaging analysis can become a reliable prognostic biomarker that promotes early identification of patients with poor prognosis and supports more personalized therapeutical approaches (Chelliah et al., 2024).

Radiomics in neuro-oncology aims to enhance the understanding of brain tumor nature and treatment outcomes by gathering quantitative features from medical imaging. Combining radiomics with artificial intelligence, particularly machine learning (ML), is another innovative strategy in glioblastoma diagnostics that transforms standard imaging scans into high-dimensional, quantitative data. Gathering complex imaging features followed by deep learning techniques analysis leads to more objective and accurate tumor characterization comparing to traditional imaging methods. Tumor classification, prediction of treatment response and prognosis has been detectably improved by AI-driven radiomic strategies. ML models are trained on large set of data to identify patterns without straightforward programming and are mainly applied through supervised learning for tasks such as tumor classification and segmentation. The radiomics workflow typically includes data acquisition, preprocessing and augmentation, model training and validation followed by clinical deployment. ML algorithms such as neural networks, support vector machines (SVMs) and decision trees (DTs) are employed to assess high-dimensional imaging information that is then utilized as a data driven process to enhance precision medicine through increased diagnostic efficacy and non-invasive tumor assessment. The aforementioned is not without its own set of issues such as data quality or standardization. Integrating deep learning models into radiomics accounts for increased reproducibility and a lower number of errors comparing to manual segmentation (Zhu et al., 2022). Radiomics has shown essential potential in differentiating pseudoprogression from true tumor progression in glioblastoma after the treatment that used to be a significant diagnostic obstacle. MRI combined with machine learning have demonstrated high diagnostic performance with models incorporating features from T1 contrast-enhanced, FLAIR, Apparent Diffusion Coefficient (ADC) and Cerebral Blood Volume (CBV) sequences achieving an AUC of up to 0.9 and 0.85 in external validation, exceeding approaches that enhanced singular parameters. Even though models based on one source of imaging data, such as T1-weighted contrast-enhanced images, show lower diagnostic accuracy they have still proved higher performance comparing to radiologist assessment in some cases. Multimodal imaging and advanced radiomic analysis are believed to be an outstanding improvement for post-treatment evaluation in glioblastoma (Alizadeh et al., 2023). The differences in the diagnostic process using conventional methods and AI-supported models are gathered in the table below (Table 1). Moreover, the possibility of combining radiomics with genomic data known as radiogenomics enables non-invasive detection of molecular biomarkers which is another step in developing personalized treatment plans (Zhu et al., 2022). It is considered an innovative strategy that may be useful in managing GBM through connecting imaging data (MRI) to biological characteristics of tumors, thus enabling the noninvasive measurement of important indicators like IDH mutations, MGMT promoter methylation, and EGFR status which can assist clinicians to determine the best course of action for a patient based on their prognosis (Corr et al., 2022). The use of AI and Machine Learning allows researchers to obtain numerous radiomic variables using advanced image analysis techniques and increase predictive power of both overall survival and stratify tumors. Radiogenomics also promises to help distinguish between tumor growth and therapy-induced changes and identify those patients most likely to profit from either targeted therapy or immunotherapy strategies. Although research into this field continues to develop rapidly, its application in clinical practice is limited due to lack of established methodology and validated prospective trials to test results (Corr et al., 2022).

Table 1. The differences in the diagnostic process using conventional methods and AI-supported models.

Parameter	Conventional MRI (± radiologist)	AI-supported / Radiomics-based methods
Diagnostic accuracy (AUC)	0.59 – 0.92 depending on reader experience	Typically 0.80 – 0.99 depending on task and model
Glioma grading	Moderate accuracy limited by subjective interpretation	AUC 0.825 – 0.946 in ML/DL models
Differentiation (GBM vs metastasis)	Often difficult due to similar imaging features	Accuracy up to 0.98 – 0.99 with radiomics models
Prediction of molecular markers (IDH, MGMT, etc.)	Not possible with imaging alone	AUC 0.72 – 0.99 depending on biomarker
Sensitivity / specificity	Variable, operator-dependent	0.83 / 0.84 (pooled ML radiomics data)
Interobserver variability	High - depends on radiologist experience	Low – automated, reproducible analysis
Feature detection	Limited to visible morphological changes	Detects hidden quantitative features (texture, heterogeneity)
Post-treatment evaluation	Limited reliability	High performance (AUC 0.85 – 0.90 in studies you cited earlier)
Invasiveness	Requires biopsy for molecular diagnosis	Enables non-invasive molecular prediction
Clinical availability	Widely available, standard practice	Emerging, limited by validation and standardization

Based on data gathered in: Zhang H, Zhang B, Pan W, Dong X, Li X, Chen J, Wang D, Ji W, Preoperative Contrast-Enhanced MRI in Differentiating Glioblastoma From Low-Grade Gliomas in The Cancer Imaging Archive Database: A Proof-of-Concept Study; Agosti E, Mapelli K, Grimod G, Piazza A, Fontanella MM, Panciani PP, MRI-Based Radiomics for Non-Invasive Prediction of Molecular Biomarkers in Gliomas; Tan R, Sui Ch, Wang Ch, Zhu T, MRI-based intratumoral and peritumoral radiomics for preoperative prediction of glioma grade: a multicenter study; Bijari S, Jahanbakhshi A, Hajishafiezahramini P, Abdolmaleki P, Differentiating Glioblastoma Multiforme from Brain Metastases Using Multidimensional Radiomics Features Derived from MRI and Multiple Machine Learning Models

Liquid biopsy is another advancement in GBM diagnostics enabling minimally invasive assessment along with addressing the limitations of conventional imaging and histopathological methods. Traditional evaluation of glioblastoma relies on neuroimaging and molecular analysis that enable accurate diagnosis and personalized therapeutic approach, however, they are still limited by invasiveness and difficulties in repeated assessments. On the other hand, liquid biopsy enables identification of tumor components such as circulating tumor DNA (ctDNA), ribonucleic acid (RNA), circulating tumor cells and extracellular vesicles in body fluids including blood and cerebrospinal fluid then undergo precise analysis using advanced molecular techniques such as next-generation sequencing (NGS), droplet digital polymerase chain reaction (ddPCR), and methylation-specific PCR. This method ensures a better understanding of tumor biology that is highly variable. As it is challenging to get a complete picture with traditional tissue sampling, liquid biopsy is helpful in early diagnosis, treatment accuracy assessment and differentiating the real tumor growth and pseudoprogression which resembles tumor progression while only picturing swollen tissues. This approach is also safer than performing multiple surgeries to get tissue samples (Eibl et al., 2023). Among gathered data. ctDNA analysis allows identification of most crucial genetic alterations such as mutations in TP53, EGFR, MET, and PIK3CA with detection rates reaching approximately 27–55% depending on methodology and cohort (Seyhan, 2024). Importantly, specific alterations such as TERT promoter mutations identified through ddPCR have shown predictive value correlating with glioblastoma progression and enabling earlier detection of recurrence compared to MRI. It is possible to detect important epigenetic biomarkers, especially MGMT promoter methylation in serum and cerebrospinal fluid which leads to advanced diagnostic and prognostic assessment. Extracellular vesicles represent a highly promising component of liquid biopsy due to their stability and protection of molecular cargo. They carry tumor-specific DNA, RNA and proteins, including EGFR mutations and microRNAs such as miR-320 and miR-574-3p, as well as noncoding RNA RNU6-1, which has emerged as an independent predictor of glioblastoma diagnosis. Additionally, elevated levels of extracellular vesicles (EV)-associated markers such as EGFRvIII and podoplanin have been associated with poor response to chemoradiotherapy, while increases in EV concentration may indicate tumor recurrence. Collectively, these techniques and biomarkers highlight the potential of liquid biopsy not only for non-invasive diagnosis but also for real-time monitoring, prognostication, and personalized therapeutic decision-making in glioblastoma (Seyhan, 2024). Liquid biopsy has the potential to revolutionize monitoring GBM but there are many obstacles that will need to be overcome in order for liquid biopsy to become an everyday part of the diagnostic process. For example, liquid biopsies require standardization in terms of collecting and processing samples from cancer patients. Additionally, current detection technology is very limited and therefore requires significant advancements so that it can detect small amounts of genetic material with greater accuracy. Moreover, in order to accurately analyze the large amount of biological information generated by liquid biopsy tests, new analytical and bioinformatics tools (including AI/ML) will likely need to be developed or modified. Currently, only a few clinical trials are using liquid biopsy to monitor patients with GBM. Therefore, most efforts related to liquid biopsy in GBM are investigational and are not a part of the current standard-of-care for diagnosing this specific brain tumor despite its promising value (Seyhan, 2024).

4. Discussion

4.1 Modern approach to treatment

The current state-of-the-art in treating GBM has evolved from the standard three-pronged approach of surgery, radiation, and chemotherapy. The reason for this is largely because traditional treatments provide patients with very poor survival rates. This is primarily caused by the fact that Blood-Brain Barrier (BBB) prevents mant therapeutic agents form reaching the tumor and there is a great deal of heterogeneity in the genetics and biology of GBM leading to a pessimistic course.

Although there are numerous challenges in treating glioblastomas, researchers continue to explore and develop new treatment options. As a result of the aforementioned challenges, current strategies for the treatment of GBM are being directed towards using Molecularly Targeted Therapies (MTT) and Immunotherapies. MTT includes drugs designed to target specific pathways that contribute to the development and expansion of tumors. Examples of these include drugs that target EGFR mutations, drugs that inhibit angiogenesis, and drugs that inhibit the PI3K/AKT/mTOR pathway etc. Immunotherapies include Immune Checkpoint Inhibitors, CAR-T Cell Therapy, Cancer Vaccines, and Oncolytic Viruses. Each of these categories of therapies function to identify and destroy tumor cells without affecting normal cells.

In addition to MTTs and other forms of targeted therapies, researchers have developed additional ways of delivering these targeted therapies to the site where the tumor exists. An example of this is the utilization of Nanoparticles (NPs) which allow drugs to cross the Blood Brain Barrier (BBB) and travel to the tumor site. Upon reaching the tumor site, once released from the NPs, the drug can then be released into the tumor environment in a controlled manner over an extended period of time thereby minimizing adverse reactions and maximizing efficiency. This form of delivery is referred to as Local Sustained Delivery (LSD).

Liquid Biopsy represents a minimally invasive method of testing that involves the examination of Circulating Tumor DNA (ctDNA) and Extracellular Vesicles (EVs) in either the cerebrospinal fluid (CSF) or blood from individuals who have received a diagnosis of GBM. Liquid Biopsy provides healthcare professionals with a mechanism to track tumor progression, anticipate recurrence early, and evaluate molecular-level heterogeneity throughout the tumor. Heterogeneity describes variations in the genetic expression levels of different parts of the tumor. Conventional diagnostic tools such as MRI scans and/or tissue biopsies do not always provide accurate representations of these variations. Researchers are making tremendous strides in employing Artificial Intelligence (AI) to further enhance image interpretation capabilities within neuro-oncology, enhance histopathologic assessments and integrate multiple types of molecular data to facilitate treatments based on the unique features of each patient.

As diagnostics and therapeutics evolve, we are experiencing a significant transformation in the direction of developing more effective, multi-modal, individually tailored GBM therapies through the application of recent advances in scientific research to address one of the most aggressive primary brain cancers identified as Glioblastoma Multiforme.

Traditional treatment modalities employed for GBM have evolved beyond the initial treatment strategy that included surgical removal of tumor mass, radiation therapy, and chemotherapy. However, due to the complexity of GBM, even when provided with maximum therapy, the general prognosis for GBM has remained pessimistic. Therefore, investigators are aggressively examining alternative approaches for treating GBM effectively. One category of potential alternatives includes immunotherapy-based drugs that are capable of inducing anti-tumor immune responses. These days, four main categories of immunotherapy-based drugs have been studied in GBM: immune checkpoint inhibiting drugs, CAR-T-Cell Therapies, oncolytic viruses and cancer vaccines. Although all four categories have exhibited

considerable promise during pre-clinical studies as well as early phase clinical trials, their clinical efficacy in GBM remains under evaluation. Specifically, the very suppressive nature of the tumor microenvironment associated with GBMs severely hampers its capability to initiate an anti-tumor response.

Additional emerging therapeutic modalities include local sustained delivery systems such as nano-carrier drug-delivery systems that are able to penetrate the BBB to localize large amounts of chemotherapeutic agent near the tumor-site (Angom et al., 2023); combination regimens that employ synergistic interactions between two agents to enhance efficacy while limiting resistance mechanisms (Angom et al., 2023). Other novel paradigms include Tumor Treating Fields (TTFields) which is a non-invasive technology that employs alternating electrical fields applied to restrict cell proliferation in tumors and was recently approved by regulatory agencies for use in newly diagnosed GBM patients and in recurrent GBM patients (Sadowski et al., 2024).

Many of these new approaches to therapy are currently being evaluated in ongoing clinical trials. Therefore, they represent a step forward toward personalized treatments for GBM. Many of these therapeutic modalities have also demonstrated promise in preclinical studies and are anticipated to be utilized in future clinical trials in order to provide better outcomes for patients diagnosed with GBM.

5. Conclusion

Glioblastoma Multiforme is a severely aggressive primary brain tumor associated with rapid progression, essential heterogeneity and poor prognosis. The understanding of its pathogenesis has been deepened due to advances in molecular biology followed by embracement of genetic alterations, dysregulated signaling pathways and tumor microenvironment fluctuations in the role of disease development and therapeutic resistance. Modern diagnostic strategies include the impact of biological mechanisms and influence treatment choices.

MRI and histopathological evaluation remain the foundation of glioblastoma diagnosis. Nevertheless, recent technologies such as artificial intelligence or radiomics have refined the process of GBM detection by enabling quantitative analysis of imaging data and improving tumor characterization leading to better diagnostic accuracy. Moreover, the identification of epigenetic changes, such as MGMT promoter methylation status, and novel approaches such as radiogenomics and liquid biopsy help to predict therapeutic response and promote personalized and non-invasive treatment strategies.

Technology development does not eliminate diagnostic challenges such as AI-based tools standardization, validation of biological markers and proper understanding of research findings in clinical practice. Future progress in treating glioblastoma will require further integration of various approaches and development of personalized diagnostic and therapeutic pathways. A deeper understanding of tumor growth mechanisms and usage of innovative technologies holds a promising potential for improving patient outcomes in this serious disease.

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