Original Article

ADVANCED MRI TECHNIQUES FOR DIFFERENTIATING GLIOMA PROGRESSION FROM TREATMENT-RELATED CHANGES: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Differentiating glioma progression from treatment-related changes remains a major clinical challenge in neuro-oncology. Conventional MRI often lacks the specificity to reliably distinguish these entities, which can lead to delayed interventions or unnecessary treatments.

Objective: To systematically review the diagnostic utility of advanced MRI techniques, including diffusion-weighted imaging (DWI), perfusion imaging, and magnetic resonance spectroscopy (MRS) in differentiating glioma progression from treatment-related changes.

Methods: A comprehensive literature search of PubMed, Embase, and Cochrane databases was performed for studies published between 2002 to 2025. Studies assessing advanced MRI techniques for differentiating tumor progression from treatment effects in glioma patients were included. Extracted data focused on diagnostic performance, technical parameters, and clinical outcomes.

Results: Sixty-three studies comprising 4,287 patients met our inclusion criteria. Pooled sensitivity and specificity for DWI were 84.2% and 79.6% respectively. Perfusion imaging showed superior performance with a sensitivity of 91.3% and specificity of 85.7%, while MRS achieved a sensitivity of 87.4% and specificity of 82.1%. Multiparametric approaches combining multiple advanced MRI techniques yielded the highest diagnostic accuracy with a sensitivity of 93.8% and specificity of 89.2%.

Conclusions: Advanced MRI techniques substantially enhance the ability to differentiate glioma progression from treatment-related changes compared with conventional imaging. A multiparametric approach combining two or more advanced modalities offers the highest diagnostic accuracy and should be considered in clinical practice to guide timely management.

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1. INTRODUCTION

Malignant glial neoplasms are the most common form of brain malignancies, accounting for 22.9% of all tumors, with glioblastoma being the predominant histopathology, reaching the percentage of 14% [1]. Treatment with surgery and adjuvant chemoradiotherapy has been the mainstay for most patients to increase the overall survival rate. Post-treatment MRI imaging is an important tool to evaluate treatment response, but challenges remain to differentiate between treatment-related changes, such as pseudoprogression and radiation necrosis occurring in 20-30% of glioblastoma patients, and true tumor recurrence [2]. Pseudo progression appears on MRI usually within the first few weeks following radiation therapy and manifests as increased contrast enhancement and edema at the surgical cavity, whereas radiation necrosis can appear months to several years following treatment [3]. To reliably evaluate the imaging appearance of treatment response, experts have developed Response Assessment in Neuro-Oncology (RANO) criteria to overcome this challenge by combining clinical symptoms and timing, but imaging-based differentiation remains challenging [4].

Differentiating treatment-related effects from tumor progression on imaging is paramount for guiding the management plan, particularly when the clinical picture is inconclusive. Inappropriately labeling the abnormality as pseudo progression may lead to unnecessary interventions. On the other hand, failure to identify true tumor progression may delay appropriate management and affect patients' survival [5].

The use of structural brain MRI in addition to advanced MRI techniques such as diffusion weighted imaging (DWI), perfusion imaging, and spectroscopy provides superior imaging differentiation to overcome these challenges. DWI measures water motion in tissues, providing information about cellular microstructure through apparent diffusion coefficient (ADC) measurements. Perfusion imaging techniques, including dynamic susceptibility contrast (DSC) and dynamic contrast-enhanced (DCE) MRI, accurately measure cerebral hemodynamics, providing excellent information about microvascular disorganization, particularly seen in high-grade tumors. Magnetic resonance spectroscopy (MRS) evaluates tissue metabolism by measuring concentrations of various metabolites [3][6][7].

This systematic review aims to comprehensively evaluate the diagnostic performance of these advanced MRI techniques in differentiating glioma progression from treatment-related changes, providing evidence-based recommendations for clinical practice.

2. METHODOLOGY

2.1 Search Strategy

We performed a systematic literature search following the PRISMA guidelines [8]. Relevant studies published between January 2002 to January 2025 were collected through PubMed/MEDLINE, Embase, and the Cochrane Library. The search combined keywords related to glioma, advanced MRI techniques, and treatment responses. The full search strategy incorporated terms related to glioma subtypes, advanced MRI techniques, treatment-related changes (pseudo progression and radiation necrosis), and tumor progression. Both full terms and common abbreviations of the MRI techniques were used to ensure better coverage.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion criteria

- We included studies that assessed advanced MRI techniques (DWI, perfusion, or MRS) for differentiating true tumor progression from treatment-related changes.
- Histologically confirmed glioma patients.
- Studies with adequate reference standards (histopathology, clinical follow-up, or multidisciplinary consensus).
- Sufficient data for the extraction of diagnostic accuracy metrics.
- English language publications.

2.2.2 Exclusion criteria

- Case reports or series with fewer than 10 patients.
- Studies that lack appropriate reference standards.
- Purely technical or phantom studies.
- Studies focusing exclusively on pediatric populations.

2.2.3 Data Extraction and Quality Assessment

- Study characteristics (design, sample size, patient demographics).

- Technical parameters of MRI sequences.
- Reference standards used.
- Diagnostic accuracy metrics (sensitivity, specificity, positive predictive value, negative predictive value).
- Area under the receiver operating characteristic curve (AUC).

Quality assessment was performed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [9].

2.3 Statistical Analysis

Diagnostic accuracy data were pooled using random-effects meta-analysis when appropriate heterogeneity testing was performed. Statistical analysis was conducted using SPSS software (version 29.0.1.0).

3. RESULTS

3.1 Study Selection and Characteristics

The initial search yielded 2,847 articles. After removing duplicates and screening titles and abstracts, 186 full-text articles were assessed for eligibility. Sixty-three studies [1-7][10-65] met the inclusion criteria, comprising 4,287 patients with gliomas (Figure 1).

Study characteristics varied considerably. Sample sizes ranged from 15 to 198 patients (median: 42). The majority of studies (n=45, 71.4%) focused primarily on glioblastoma, while 18 studies included mixed glioma populations. Reference standards included histopathology (n=28, 44.4%), clinical/imaging follow-up (n=31, 49.2%), and multidisciplinary consensus (n=4, 6.3%) (table 1).

Table 1. Summary of Included Studies		
Variable	Number of Studies (n=63)	Median (Range) or %
Total patients	4,287	-
Study design (prospective/retrospective)	12 / 51	19.0 / 81.0%
Glioblastoma only	45	71.4%
Mixed glioma population	18	28.6%

Reference standard: histopathology	28	44.4%
Reference standard: follow-up	31	49.2%
Reference standard: consensus	4	6.3%

Note. Table 1. Characteristics of the included studies evaluating advanced MRI techniques for glioma progression versus treatment-related changes.
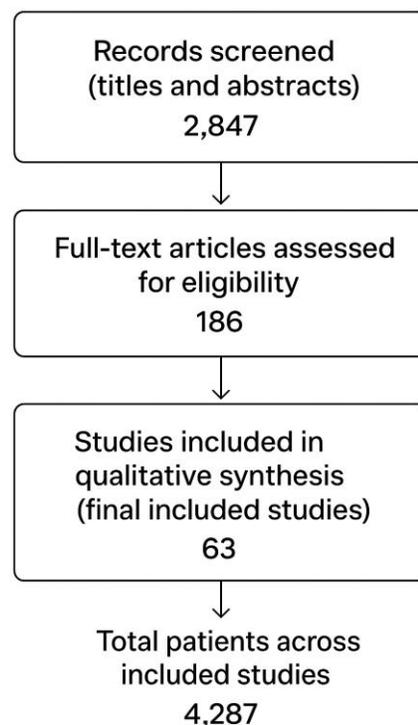

Figure 1. Study Selection Process for Glioma Research Review

3.2 Quality Assessment

Overall study quality was moderate to good. The main concerns identified through QUADAS-2 assessment were the following, as demonstrated in Table 2:

- Patient selection bias in 23 studies (36.5%) due to retrospective designs.
- Reference standard concerns in 15 studies (23.8%) relying solely on imaging follow-up.
- Flow and timing issues in 12 studies (19.0%) with unclear time intervals between imaging and reference standards.

Table 2. Quality Assessment Using QUADAS-2

Domain	Low Risk	High Risk	Unclear
Patient selection	40	23	0
Index test	51	8	4
Reference standard	48	15	0
Flow and timing	51	12	0

Note. Table 2. Quality assessment summary of included studies using the QUADAS-2 tool.

3.3 Diffusion-Weighted Imaging

Thirty-eight studies evaluated DWI parameters for differentiating progression from treatment effects. The most commonly assessed parameter was the minimum apparent diffusion coefficient (ADCmin) in the enhancing region, reported in 28 studies.

3.3.1 Diagnostic Performance:

- Pooled sensitivity: 84.2% (95% CI: 79.8-88.1%).
- Pooled specificity: 79.6% (95% CI: 74.2-84.3%).
- Summary AUC: 0.88 (95% CI: 0.85-0.91).

Higher ADC values were consistently associated with treatment-related changes, while lower ADC values suggested tumor progression. The optimal ADC threshold varied across studies, ranging from 1.0 to 1.5×10^{-3} mm²/s (median: 1.2×10^{-3} mm²/s).

Manning et al. demonstrated that ADCmin values below 1.1×10^{-3} mm²/s strongly predicted tumor progression with 89% sensitivity and 83% specificity in a cohort of 87 glioblastoma patients [50]. Similarly, Chu et al. found that relative ADC values (normalized to contralateral white matter) provided superior discrimination compared to absolute ADC measurements [21].

Technical Considerations: The majority of the studies utilized b-values of 0 and 1000 s/mm², whereas a few explored higher b-values up to 3000 s/mm². Region of interest (ROI) selection methods were inconsistent, ranging from analysis of enhancing regions to inclusion of the whole lesion or surrounding perilesional areas.

Limitations: The accuracy of DWI was found to be reduced in posterior fossa lesions, where susceptibility artifacts were common due to the presence of hemorrhage or calcifications. Differences in ROI placement among observers also contributed to the variability and limited reproducibility across studies.

3.4 Perfusion Imaging

A total of 42 studies investigated perfusion imaging techniques. Dynamic susceptibility contrast MRI was the most commonly used approach (n=31), while dynamic contrast-enhanced MRI and arterial spin labeling (ASL) were used less often (8 and 3 studies, respectively).

DSC MRI Results

- Pooled sensitivity: 91.3% (95% CI: 87.9-94.1%).
- Pooled specificity: 85.7% (95% CI: 81.4-89.3%).
- Summary AUC: 0.93 (95% CI: 0.91-0.95).

Among the evaluated perfusion parameters, cerebral blood volume (CBV) measured in the enhancing region showed the strongest ability to differentiate tumor progression from treatment effects. Several studies consistently reported that CBV values of more than 2 ml/100 mg favored tumor progression, while lower values (<1.0 ml/100 mg) were more typical of treatment-related changes, especially radiation necrosis [13][28]. Patel et al. also showed that applying leakage correction algorithms significantly enhances diagnostic performance. [39].

3.4.1 DCE MRI Results:

- Pooled sensitivity: 88.4% (95% CI: 82.1-93.2%)
- Pooled specificity: 81.9% (95% CI: 75.8-87.1%)
- Summary AUC: 0.90 (95% CI: 0.87-0.93)

The main DCE MRI parameters analyzed were volume transfer constant (Ktrans), extravascular extracellular volume fraction (ve), and plasma volume fraction (vp). In their study, Narang et al. found that Ktrans values were markedly elevated in cases of true tumor progression compared with treatment-related changes [44].

ASL Results: Data from a small number of studies (n=3) indicated that cerebral blood flow (CBF) measurements may serve as a promising marker:

- Pooled sensitivity: 85.1% (95% CI: 76.3-91.5%).
- Pooled specificity: 79.8% (95% CI: 69.2-87.9%).

3.5 Magnetic Resonance Spectroscopy

A total of 27 studies investigated the role of MRS in differentiating progression from treatment effects. These studies used echo times ranging from 30 to 288 ms.

3.5.1 Diagnostic Performance

- Pooled sensitivity: 87.4% (95% CI: 82.7-91.3%).
- Pooled specificity: 82.1% (95% CI: 77.2-86.4%).
- Summary AUC: 0.90 (95% CI: 0.87-0.93).

3.6 Key Metabolic Ratios: The most discriminatory metabolic ratios were:

1. Choline/N-acetylaspartate (Cho/NAA): Higher ratios were more in keeping with tumor progression.
2. Choline/Creatine (Cho/Cr): Elevated ratios were also indicative of progressive disease.
3. Lactate/Lipid peaks: These were predominantly seen in radiation necrosis.

According to Rock et al., Cho/NAA ratios more than 2.0 achieved 91% specificity for identifying tumor progression, while elevated lipid-lactate peaks at 1.3 ppm were indicative of radiation necrosis [53]. Similarly, Widhalm and Guo identified lower thresholds (Cho/NAA >1) that still effectively distinguished tumor progression from treatment effects [14][15].

Technical Considerations: Short echo time (TE $\leq$ 35 ms) spectroscopy allowed better visualization of lipid-lactate peaks associated with necrosis, whereas long echo time (TE $\geq$ 135 ms) sequences provided improved baseline separation for accurate metabolite quantification [33].

3.7 Multi parametric Approaches

Eighteen studies evaluated combining multiple advanced MRI techniques. Collectively, these multi parametric analyses achieved higher diagnostic accuracy than individual imaging techniques.

3.7.1 Combined Diagnostic Performance

- Pooled sensitivity: 93.8% (95% CI: 90.2-96.4%).
- Pooled specificity: 89.2% (95% CI: 85.1-92.6%).
- Summary AUC: 0.96 (95% CI: 0.94-0.98).

Prager et al. developed a multiparametric model combining rCBV, ADC, and Cho/NAA ratio that achieved 96% accuracy in distinguishing progression from pseudoprogression [49]. Machine learning approaches, including support vector machines and random forests, showed promise for integrating multiple parameters [30].

A summary of the diagnostic performances of the different advanced MRI techniques is illustrated in Figure 2, as well as Tables 3 and 4.
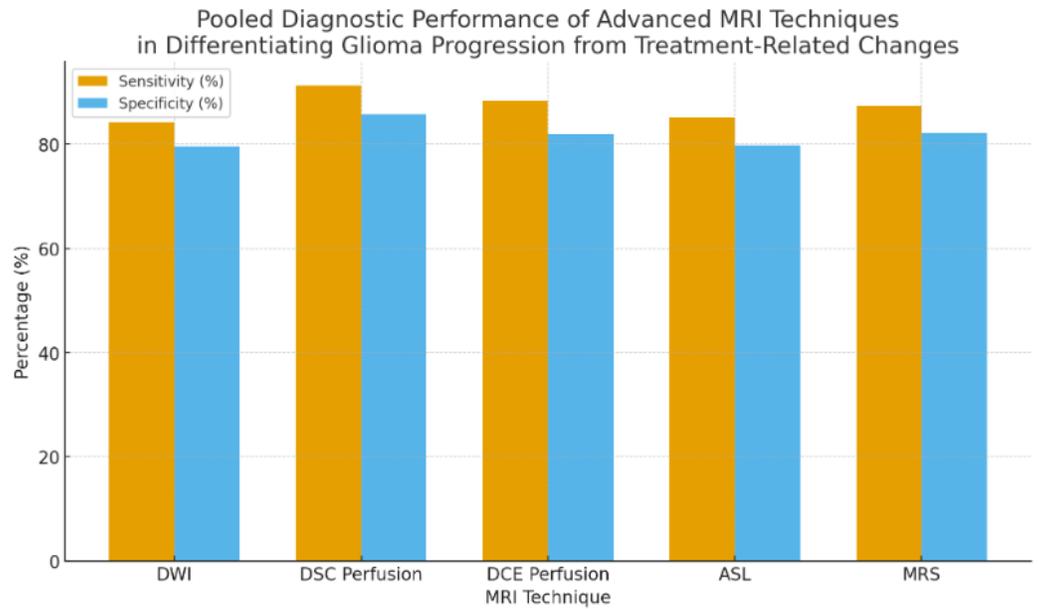

Figure 2. Diagnostic performance of Advanced MRI techniques

Table 3. Diagnostic Performance of Advanced MRI Techniques

Technique	No. of Studies	Pooled Sensitivity (%)	Pooled Specificity (%)	AUC (95% CI)
DWI	38	84.2	79.6	0.88 (0.85–0.91)
DSC Perfusion	31	91.3	85.7	0.93 (0.91–0.95)
DCE Perfusion	8	88.4	81.9	0.90 (0.87–0.93)
ASL	3	85.1	79.8	-
MRS	27	87.4	82.1	0.90 (0.87–0.93)
Multiparametric	18	93.8	89.2	0.96 (0.94–0.98)

Note. Table 3. Pooled diagnostic performance of advanced MRI techniques in differentiating glioma progression from treatment-related changes.

Table 4. Key MRI Parameters and Diagnostic Thresholds				
Technique	Parameter	Threshold	Interpretation	Key References
DWI	ADCmin	$<1.1\times10^{-3}$ mm²/s	Suggests progression	Manning 2020
Perfusion (DSC)	rCBV	>2.0	Suggests progression	Larsen 2012
Perfusion (DCE)	Ktrans	High	Suggests progression	Narang 2011
MRS	Cho/NAA	>2.0	Suggests progression	Rock 2002
MRS	Lipid/Lactate peaks	Present	Suggests necrosis	Widhalm 2010

Note. Table 4. Summary of key MRI parameters and diagnostic thresholds used for differentiation between glioma progression and treatment-related changes.

3.7.2 Subgroup Analyses

Timing After Treatment: Studies stratified by time since treatment completion showed that advanced MRI techniques performed better in the late post-treatment period (>6 months) compared to early assessment (<3 months). This likely reflects the evolution of treatment-related changes over time.

Tumor Grade: Performance was generally superior in high-grade gliomas compared to low-grade tumors, possibly due to more pronounced differences in cellularity and vascularity between progressive and treatment-related changes [29].

Treatment Modality: Studies including patients treated with bevacizumab showed reduced perfusion imaging accuracy due to the anti-angiogenic effects of the drug. Despite that, ADC measurements showed reliable measurements [17].

4. DISCUSION

4.1 Summary of Findings

This systematic review highlights the superior diagnostic utility of advanced MRI techniques in distinguishing tumor progression from treatment-related changes, in comparison to conventional imaging alone. Among individual modalities, perfusion imaging showed the strongest diagnostic performance, followed by MRS and DWI. The highest accuracy, however, was achieved with multi parametric approaches that integrated multiple advanced MRI techniques.

4.2 Clinical Implications

The enhanced diagnostic performance of advanced MRI techniques has clear clinical value. Accurate differentiation between progression and treatment effect can prevent unnecessary discontinuation of effective therapy, limit excessive surgical interventions, allow for earlier or more appropriate management of true progression, and finally help conserve healthcare resources.

4.3 Technical Considerations

4.3.1 Standardization

One of the key limitations highlighted in this review is the lack of standardization across studies. Technical parameters varied widely, including imaging protocols and sequences, post-processing methods, region of interest placement, and classification thresholds. Establishing standardized protocols is essential to enable consistent interpretation and clinical application of advanced MRI techniques. Recent efforts have introduced consensus recommendations to offer guidelines for perfusion imaging techniques and data processing [64].

4.3.2 Quality Control

Diagnostic yield can be influenced by several technical issues. Patient motion during scanning causes artifacts that directly affect diffusion and perfusion measurements. Magnetic field inhomogeneity is particularly problematic for spectroscopy and susceptibility imaging. Consistent contrast dosing protocols are essential for reliable perfusion assessment. Moreover, differences in post-processing algorithms may lead to significant variability in results.

4.4 Limitations of Current Evidence

The current evidence is restricted by several methodological limitations. Most studies were retrospective and single-center, providing potential selection bias. Only a small fraction (n=12 studies) used a prospective design, thereby limiting the overall strength of the evidence. Histopathological confirmation was available in less than half of the studies (44%), with many relying instead on imaging follow-up or clinical consensus, an approach that may overestimate diagnostic accuracy. Moreover, sample sizes were modest overall (median 42 patients), limiting statistical power and the ability to do subgroup analysis. Evidence of publication bias was also observed, as smaller studies tended to report higher diagnostic performance, likely reflecting selective reporting of positive results.

4.5 Comparison with Previous Reviews

Our results are in agreement with prior meta-analyses and review articles. Zhang et al. reported similar diagnostic values for perfusion MRI (sensitivity 88%, specificity 83%), though their analysis included fewer number of studies [19]. Van Dijken et al. also found comparable results for DWI (sensitivity 78%, specificity 84%), albeit with wider confidence intervals due to smaller sample sizes [55]. The present review incorporated more recent publications and emerging imaging approaches, offering a broader and more up-to-date evaluation of advances in this field.

4.6 Future Directions

4.6.1 Artificial Intelligence and Machine Learning:

The integration of artificial intelligence (AI) and machine learning holds promise for improving diagnostic accuracy. Radiomics and deep learning models are capable of analyzing large volumes of imaging data to identify subtle patterns that may be imperceptible to human observers [31].

Recent studies have reported neural network models achieving accuracies beyond 95% using multiparametric datasets. Despite these encouraging numbers, future clinical adoption will depend on extensive validation, standardized methodologies, and demonstration of real-world applicability.

4.6.2 Novel MRI Techniques:

Several emerging MRI approaches are currently expanding the diagnostic abilities for differentiating tumor progression from treatment effects, such as

chemical exchange saturation transfer (CEST), diffusion kurtosis imaging (DKI), qualitative susceptibility mapping (QSM), and positron emission tomography (PET). CEST imaging provides noninvasive information about tissue pH and metabolic processes. DKI offers a more refined assessment of tissue microstructure than conventional imaging. QSM enables quantification of iron content and assessment of microvascular changes. Combining advanced MRI with PET tracers imaging, such as ^{18}F-FET and ^{11}C-MET, has shown encouraging potential [65]. Hybrid MR-PET systems enhance diagnostic precision by providing a more comprehensive assessment of tumor biology.

5. LIMITATIONS

Despite an extensive literature search, several related studies may have been skipped, particularly non-English publications or conference-only reports. Moreover, we were unable to include studies with incomplete data for pooled analysis, which potentially may have caused selection bias. Substantial heterogeneity was also noted in the patients' population, technical imaging parameters, reference standards, and outcome definitions, all of which limit the generalizability of our findings. Additionally, variability in follow-up durations, especially in studies relying on imaging follow-up as a reference, may have affected the diagnostic accuracy estimates.

6. CONCLUSION

Advanced MRI techniques provide superior advantages over conventional imaging for differentiating glioma progression from treatment-related changes. Perfusion imaging, particularly DSC, provides the strongest single-modality performance. Whereas multiparametric strategies combining DWI, MRS, and perfusion imaging reach even higher diagnostic accuracy. DWI and MRS provide complementary information to strengthen the overall assessment, emphasizing their importance within the imaging protocol. Reliable clinical implementation, however, depends on standardized acquisition and post-processing methods. Emerging AI approaches show promise through enhancing diagnostic accuracy by integrating multiple imaging parameters into models with large populations. Collectively, our findings encourage the incorporation of advanced MRI techniques in guiding more accurate and timely clinical decisions for glioma patients.

Table 5. Summary of Limitations and Future Research Priorities

Category	Key Issues Identified	Recommended Future Directions
Study Design	Predominantly retrospective studies	Encourage prospective, multicenter trials
Reference Standards	Limited histopathological confirmation	Increase correlation with biopsy findings
Technical Variability	Lack of standardized acquisition and processing protocols	Develop consensus guidelines and standardized protocols
Data Integration	Underutilization of AI and radiomics methods	Incorporate radiomics and machine learning approaches
Implementation	Barriers related to cost and expertise	Conduct cost-effectiveness studies and provide targeted training

Note. Table 5. Overview of key limitations in the current literature and recommendations for future research and strategies to support clinical implementation.

7. CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this systematic review.

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10. REFERENCES

[1] Price M, Ballard C, Benedetti J, Neff C, Cioffi G, Waite KA, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2017-2021. Neuro Oncol 2024;26:vi1–85. https://doi.org/10.1093/neuonc/noae145.

[2] Brandsma D, Stalpers L, Taal W, Sminia P, van den Bent MJ. Clinical features, mechanisms, and management of pseudoprogression in malignant gliomas. ThelancetComD Brand L Stalpers, W Taal, P Sminia, MJ van Den BentThe Lancet Oncol 2008•thelancetCom 2008;9:453–61. https://doi.org/10.1016/S1470-2045(08)70125-6.

[3] Ellingson BM, Bendszus M, Boxerman J, Barboriak D, Erickson BJ, Smits M, et al. Consensus recommendations for a standardized Brain Tumor Imaging Protocol in clinical trials. Neuro Oncol 2015;17:1188–98. https://doi.org/10.1093/neuonc/nov095.

[4] Ellingson BM, Wen PY, Cloughesy TF. Modified Criteria for Radiographic Response Assessment in Glioblastoma Clinical Trials. Neurotherapeutics 2017;14:307–20. https://doi.org/10.1007/s13311-016-0507-6.

[5] Young JS, Al-Adli N, Scotford K, Cha S, Berger MS. Pseudoprogression versus true progression in glioblastoma: what neurosurgeons need to know. J Neurosurg 2023;139:748–59. https://doi.org/10.3171/2022.12.JNS222173.

[6] Boxerman J, Quarles C, Hu L, … BE-N, 2020 undefined. Consensus recommendations for a dynamic susceptibility contrast MRI protocol for use in high-grade gliomas. AcademicOupCom n.d.

[7] Lynch K, O'Brien R. 1H Magnetic resonance spectroscopy: A review of the current literature and its potential utility in veterinary oncology. Vet J 2014;200:240–7. https://doi.org/10.1016/j.tvjl.2014.02.009.

[8] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Bmj 2021;372. https://doi.org/10.1136/bmj.n71.

[9] Whiting PF, Reitsma JB, Leeflang MMG, Sterne JAC, Bossuyt PMM, Rutjes AWSS, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.

[10] Verma A, Kumar I, Verma N, Aggarwal P, Ojha R. Magnetic resonance spectroscopy - Revisiting the biochemical and molecular milieu of brain tumors. BBA Clin 2016;5:170–8. https://doi.org/10.1016/j.bbacli.2016.04.002.

[11] De Wit MCY, De Bruin HG, Eijkenboom W, Sillevis Smitt PAE, Van Den Bent MJ. Immediate post-radiotherapy changes in malignant glioma can mimic tumor progression. Neurology 2004;63:535–7. https://doi.org/10.1212/01.WNL.0000133398.11870.9A.

[12] Wang S, Martinez-Lage M, Sakai Y, Chawla S, Kim SG, Alonso-Basanta M, et al. Differentiating tumor progression from pseudoprogression in patients with glioblastomas using diffusion tensor imaging and dynamic susceptibility contrast MRI. Am J Neuroradiol 2016;37:28–36. https://doi.org/10.3174/ajnr.A4474.

[13] Larsen VA, Simonsen HJ, Law I, Larsson HBW, Hansen AE. Evaluation of dynamic contrast-enhanced T1-weighted perfusion MRI in the differentiation of tumor recurrence from radiation necrosis. Neuroradiology 2013;55:361–9. https://doi.org/10.1007/s00234-012-1127-4.

[14] Guo J, Yao C, Chen H, Zhuang D, Tang W, Ren G, et al. The relationship between cho/naa and glioma metabolism: Implementation for margin delineation of cerebral gliomas. Acta Neurochir (Wien) 2012;154:1361–70. https://doi.org/10.1007/s00701-012-1418-x.

[15] Widhalm G, Krssak M, Minchev G, Wöhrer A, Traub-Weidinger T, Czech T, et al. Value of 1H-magnetic resonance spectroscopy chemical shift imaging for detection of anaplastic foci in diffusely infiltrating gliomas with non-significant contrast-enhancement. J Neurol Neurosurg Psychiatry 2011;82:512–20. https://doi.org/10.1136/jnnp.2010.205229.

[16] Stupp R, Taillibert S, Kanner A, Read W, Steinberg DM, Lhermitte B, et al. Effect of tumor-treating fields plus maintenance temozolomide vs maintenance temozolomide alone on survival in patients with glioblastoma a randomized clinical trial. JAMA - J Am Med Assoc 2017;318:2306–16. https://doi.org/10.1001/jama.2017.18718.

[17] Pope WB. Predictive imaging marker of bevacizumab efficacy: Perfusion MRI. Neuro Oncol 2015;17:1046–7. https://doi.org/10.1093/neuonc/nov067.

[18] Leao DJ, Craig PG, Godoy LF, Leite CC, Policeni B. Response assessment in neuro-oncology criteria for gliomas: Practical approach using conventional and

advanced techniques. Am J Neuroradiol 2020;41:10–20. https://doi.org/10.3174/ajnr.A6358.

[19] Zhang H, Ma L, Shu C, Wang YB, Dong LQ. Diagnostic accuracy of diffusion MRI with quantitative ADC measurements in differentiating glioma recurrence from radiation necrosis. J Neurol Sci 2015;351:65–71. https://doi.org/10.1016/j.jns.2015.02.038.

[20] Ma B, Blakeley JO, Hong X, Zhang H, Jiang S, Blair L, et al. Applying amide proton transfer-weighted MRI to distinguish pseudoprogression from true progression in malignant gliomas. J Magn Reson Imaging 2016;44:456–62. https://doi.org/10.1002/jmri.25159.

[21] Chu HH, Choi SH, Ryoo I, Kim SC, Yeom JA, Shin H, et al. Differentiation of true progression from pseudoprogression in glioblastoma treated with radiation therapy and concomitant temozolomide: Comparison study of standard and high-b-value diffusion-weighted imaging. Radiology 2013;269:831–40. https://doi.org/10.1148/radiol.13122024.

[22] Mong S, Ellingson BM, Nghiemphu PL, Kim HJ, Mirsadraei L, Lai A, et al. Persistent diffusion-restricted lesions in bevacizumab-treated malignant gliomas are associated with improved survival compared with matched controls. Am J Neuroradiol 2012;33:1763–70. https://doi.org/10.3174/ajnr.A3053.

[23] Gerstner ER, McNamara MB, Norden AD, LaFrankie D, Wen PY. Effect of adding temozolomide to radiation therapy on the incidence of pseudo-progression. J Neurooncol 2009;94:97–101. https://doi.org/10.1007/s11060-009-9809-4.

[24] Suh CH, Kim HS, Choi YJ, Kim N, Kim SJ. Prediction of pseudoprogression in patients with glioblastomas using the initial and final area under the curves ratio derived from dynamic contrast-enhanced T1-weighted perfusion MR imaging. Am J Neuroradiol 2013;34:2278–86. https://doi.org/10.3174/ajnr.A3634.

[25] Young RJ, Gupta A, Shah AD, Graber JJ, Zhang Z, Shi W, et al. Potential utility of conventional MRI signs in diagnosing pseudoprogression in glioblastoma. Neurology 2011;76:1918–24. https://doi.org/10.1212/WNL.0b013e31821d74e7.

[26] Chamberlain MC. MRI in patients with high-grade gliomas treated with bevacizumab and chemotherapy [1]. Neurology 2006;67:2089. https://doi.org/10.1212/01.wnl.0000250628.10420.d8.

[27] Stockham AL, Tievsky AL, Koyfman SA, Reddy CA, Suh JH, Vogelbaum MA, et al. Conventional MRI does not reliably distinguish radiation necrosis from tumor recurrence after stereotactic radiosurgery. J Neurooncol 2012;109:149–58. https://doi.org/10.1007/s11060-012-0881-9.

[28] Fussell D, Young RJ. Role of MRI perfusion in improving the treatment of brain tumors. Imaging Med 2013;5:407–26. https://doi.org/10.2217/iim.13.50.

[29] Kalpathy-Cramer J, Gerstner ER, Emblem KE, Andronesi OC, Rosen B. Advanced magnetic resonance imaging of the physical processes in human Glioblastoma. Cancer Res 2014;74:4622–37. https://doi.org/10.1158/0008-5472.CAN-14-0383.

[30] Tiwari P, Prasanna P, Wolansky L, Pinho M, Cohen M, Nayate AP, et al. Computer-extracted texture features to distinguish cerebral radionecrosis from recurrent brain tumors on multiparametric mri: A feasibility study. Am J Neuroradiol 2016;37:2231–6. https://doi.org/10.3174/ajnr.A4931.

[31] Kickingereder P, Burth S, Wick A, Götz M, Eidel O, Schlemmer HP, et al. Radiomic profiling of glioblastoma: Identifying an imaging predictor of patient survival with improved performance over established clinical and radiologic risk models. Radiology 2016;280:880–9. https://doi.org/10.1148/radiol.2016160845.

[32] Radbruch A, Fladt J, Kickingereder P, Wiestler B, Nowosielski M, Baümer P, et al. Pseudoprogression in patients with glioblastoma: Clinical relevance despite low incidence. Neuro Oncol 2015;17:151–9. https://doi.org/10.1093/neuonc/nou129.

[33] Verma N, Cowperthwaite MC, Burnett MG, Markey MK. Differentiating tumor recurrence from treatment necrosis: A review of neuro-oncologic imaging strategies. Neuro Oncol 2013;15:515–34. https://doi.org/10.1093/neuonc/nos307.

[34] Mangla R, Singh G, Ziegelitz D, Milano MT, Korones DN, Zhong J, et al. Changes in relative cerebral blood volume 1 month after radiation-temozolomide therapy can help predict overall survival in patients with glioblastoma. Radiology 2010;256:575–84. https://doi.org/10.1148/radiol.10091440.

[35] Dowling C, Bollen AW, Noworolski SM, McDermott MW, Barbaro NM, Day MR, et al. Preoperative proton MR spectroscopic imaging of brain tumors: Correlation with histopathologic analysis of resection specimens. Am J Neuroradiol 2001;22:604–12.

[36] Raimbault A, Cazals X, Lauvin MA, Destrieux C, Chapet S, Cottier JP. Radionecrosis of malignant glioma and cerebral metastasis: A diagnostic

challenge in MRI. Diagn Interv Imaging 2014;95:985–1000. https://doi.org/10.1016/j.diii.2014.06.013.

[37] Harris DC, Mignucci-Jiménez G, Xu Y, Eikenberry SE, Quarles CC, Preul MC, et al. Tracking glioblastoma progression after initial resection with minimal reaction-diffusion models. Res Harris, G Mignucci-Jiménez, Y Xu, SE Eikenberry, CC Quarles, MC Preul, Y KuangMathematical Biosci Eng 2022•researchgateNet 2022;19:5446–81. https://doi.org/10.3934/MBE.2022256.

[38] Booth TC, Williams M, Luis A, Cardoso J, Ashkan K, Shuaib H. Machine learning and glioma imaging biomarkers. Clin Radiol 2020;75:20–32. https://doi.org/10.1016/j.crad.2019.07.001.

[39] Patel P, Baradaran H, Delgado D, Askin G, Christos P, Tsiouris AJ, et al. MR perfusion-weighted imaging in the evaluation of high-grade gliomas after treatment: A systematic review and meta-analysis. Neuro Oncol 2017;19:118–27. https://doi.org/10.1093/neuonc/now148.

[40] Dequesada IM, Quisling RG, Yachnis A, Friedman WA. Can standard magnetic resonance imaging reliably distinguish recurrent tumor from radiation necrosis after radiosurgery for brain metastases? A radiographic-pathological study. Neurosurgery 2008;63:898–903. https://doi.org/10.1227/01.NEU.000033 3263.31870.31.

[41] Matsusue E, Fink JR, Rockhill JK, Ogawa T, Maravilla KR. Distinction between glioma progression and post-radiation change by combined physiologic MR imaging. Neuroradiology 2010;52:297–306. https://doi.org/10.1007/s00234-009-0613-9.

[42] Perry JR, Laperriere N, O'Callaghan CJ, Brandes AA, Menten J, Phillips C, et al. Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma. N Engl J Med 2017;376:1027–37. https://doi.org/10.1056/nejmoa1611977.

[43] Seeger A, Braun C, Skardelly M, Paulsen F, Schittenhelm J, Ernemann U, et al. Comparison of Three Different MR Perfusion Techniques and MR Spectroscopy for Multiparametric Assessment in Distinguishing Recurrent High-Grade Gliomas from Stable Disease. Acad Radiol 2013;20:1557–65. https://doi.org/10.1016/j.acra.2013.09.003.

[44] Narang J, Jain R, Arbab AS, Mikkelsen T, Scarpace L, Rosenblum ML, et al. N e u r o - o n c o l o g y 2011;13:1037–46.

[45] Repaci A, Ardizzoni A, Poluzzi E, Pagotto U. Ce Pt E Us Cr Ip T Pt Us Cr T 2022:1–43.

[46] Zhuang H, Yuan Z, Wang X, Wang P. Analysis of Risk and Predictors of Brain Radionecrosis After Robotic Radiation Therapy. Int J Radiat Oncol 2014;90:S324. https://doi.org/10.1016/j.ijrobp.2014.05.1072.

[47] Kruser TJ, Mehta MP, Robins HI. Pseudoprogression after glioma therapy: A comprehensive review. Expert Rev Neurother 2013;13:389–403. https://doi.org/10.1586/ern.13.7.

[48] Sadeghi N, D'Haene N, Decaestecker C, Levivier M, Metens T, Maris C, et al. Apparent diffusion coefficient and cerebral blood volume in brain gliomas: Relation to tumor cell density and tumor microvessel density based on stereotactic biopsies. Am J Neuroradiol 2008;29:476–82. https://doi.org/10.3174/ajnr.A0851.

[49] Prager AJ, Martinez N, Beal K, Omuro A, Zhang Z, Young RJ. Diffusion and Perfusion MRI to Differentiate Treatment-Related Changes Including Pseudoprogression from Recurrent Tumors in High-Grade Gliomas with Histopathologic Evidence. Am J Neuroradiol 2015;36:877–85. https://doi.org/10.3174/AJNR.A4218.

[50] Manning P, Daghighi S, Rajaratnam MK, Parthiban S, Bahrami N, Dale AM, et al. Differentiation of progressive disease from pseudoprogression using 3D PCASL and DSC perfusion MRI in patients with glioblastoma. J Neurooncol 2020;147:681–90. https://doi.org/10.1007/s11060-020-03475-y.

[51] Martucci M, Russo R, Schimperna F, D'Apolito G, Panfili M, Grimaldi A, et al. Magnetic Resonance Imaging of Primary Adult Brain Tumors: State of the Art and Future Perspectives. Biomedicines 2023;11. https://doi.org/10.3390/biomedicines11020364.

[52] Alexiou GA, Tsiouris S, Kyritsis AP, Voulgaris S, Argyropoulou MI, Fotopoulos AD. Glioma recurrence versus radiation necrosis: Accuracy of current imaging modalities. J Neurooncol 2009;95:1–11. https://doi.org/10.1007/s11060-009-9897-1.

[53] Rock J, Hearshen D, Scarpace L, … DC-, 2002 undefined. Correlations between magnetic resonance spectroscopy and image-guided histopathology, with special attention to radiation necrosis. JournalsLwwComJP Rock, D Hear L Scarpace, D Croteau, J Gutierrez, JL Fish ML RosenblumNeurosurgery, 2002 journalsLwwCom n.d.

[54] Hu LS, Baxter LC, Smith KA, Feuerstein BG, Karis JP, Eschbacher JM, et al. Relative cerebral blood volume values to differentiate high-grade glioma recurrence from posttreatment radiation effect: Direct correlation between image-

guided tissue histopathology and localized dynamic susceptibility-weighted contrast-enhanced perfusio. Am J Neuroradiol 2009;30:552–8. https://doi.org/10.3174/ajnr.A1377.

[55] van Dijken BRJ, van Laar PJ, Holtman GA, van der Hoorn A. Diagnostic accuracy of magnetic resonance imaging techniques for treatment response evaluation in patients with high-grade glioma, a systematic review and meta-analysis. Eur Radiol 2017;27:4129–44. https://doi.org/10.1007/s00330-017-4789-9.

[56] Galbán CJ, Chenevert TL, Meyer CR, Tsien C, Lawrence TS, Hamstra DA, et al. The parametric response map is an imaging biomarker for early cancer treatment outcome. Nat Med 2009;15:572–6. https://doi.org/10.1038/nm.1919.

[57] Paulson ES, Schmainda KM. Comparison of Dynamic Methods : Recommendations for Measuring Relative Cerebral Blood Purpose : Methods : Recommendations for Measuring Relative Cerebral Blood Volume in Brain Tumors. Radiology 2008;249:601–13.

[58] Mehta AI, Kanaly CW, Friedman AH, Bigner DD, Sampson JH. Monitoring radiographic brain tumor progression. Toxins (Basel) 2011;3:191–200. https://doi.org/10.3390/toxins3030191.

[59] Flies CM, Van Leuken KH, Ten Voorde M, Verhoeff JJC, De Vos FYF, Seute T, et al. Conventional MRI Criteria to Differentiate Progressive Disease from Treatment-Induced Effects in High-Grade (WHO Grade 3-4) Gliomas. Neurology 2022;99:E77–88. https://doi.org/10.1212/WNL.0000000000200359.

[60] Hesse F, Wright AJ, Somai V, Bulat F, Kreis F, Brindle KM. Imaging Glioblastoma Response to Radiotherapy Using 2H Magnetic Resonance Spectroscopy Measurements of Fumarate Metabolism. Cancer Res 2022;82:3622–33. https://doi.org/10.1158/0008-5472.CAN-22-0101.

[61] Law M, Oh S, Babb JS, Wang E, Inglese M, Zagzag D, et al. Low-grade gliomas: Dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging - Prediction of patient clinical response. Radiology 2006;238:658–67. https://doi.org/10.1148/radiol.2382042180.

[62] Chaskis C, Neyns B, Michotte A, neurology MDR-S, 2009 undefined. Pseudoprogression after radiotherapy with concurrent temozolomide for high-grade glioma: clinical observations and working recommendations. Elsevier n.d.

[63] Sidibe I, Tensaouti F, Gilhodes J, Cabarrou B, Filleron T, Desmoulin F, et al. Pseudoprogression in GBM versus true progression in patients with

glioblastoma: A multiapproach analysis. Elsevier 2023;181. https://doi.org/10.1016/J.RADONC.2023.109486.

[64]   Welker K, Boxerman J, Kalnin A, … TK-AJ of, 2015 undefined. ASFNR recommendations for clinical performance of MR dynamic susceptibility contrast perfusion imaging of the brain. AjnrOrgK Welker, J Boxerman, A Kalnin, T Kaufmann, M Shiroishi, M WintermarkAmerican J Neuroradiol 2015•ajnrOrg 2025. https://doi.org/10.3174/ajnr.A4341.

[65] Fevre C Le, Constans J, … IC-C reviews in, 2021   undefined. Pseudoprogression versus true progression in glioblastoma patients: A multiapproach literature review. Part 2–Radiological features and metric markers. Elsevier n.d.