



Differentiating glioma recurrence from radiation necrosis: a narrative review of positron emission tomography and magnetic resonance imaging and their diagnostic accuracies

David Leen¹, Monica Wong², Eddie Lau², Sweet Ping Ng^{1^}

¹Department of Radiation Oncology, Austin Health, Melbourne, Victoria, Australia; ²Department of Radiology, Austin Health, Melbourne, Victoria, Australia

Contributions: (I) Conception and design: D Leen, M Wong; (II) Administrative support: All authors; (III) Provision of study materials or patients: D Leen, M Wong; (IV) Collection and assembly of data: M Wong, D Leen; (V) Data analysis and interpretation: D Leen, SP Ng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Sweet Ping Ng, MBBS, PhD, FRANZCR. Department of Radiation Oncology, Austin Health, 145 Studley Road, Heidelberg, Melbourne, Victoria, VIC 3084, Australia. Email: sweetping.ng@austin.org.au.

Background and Objective: Differentiating glioma recurrence from radiation necrosis remains a critical diagnostic challenge in neuro-oncology due to overlapping imaging features. Positron emission tomography (PET) and magnetic resonance imaging (MRI) offer complementary metabolic and structural information that may enhance diagnostic accuracy. This narrative review evaluates the performance of PET, advanced MRI techniques, and their integration in distinguishing tumour recurrence from post-treatment effects.

Methods: A comprehensive search of PubMed, Medline, and Embase databases was conducted to identify studies published after April 2020. Inclusion criteria comprised studies on histologically diagnosed gliomas using PET and MRI, reporting sensitivity, specificity, or accuracy.

Key Content and Findings: Eight cohort studies met the inclusion criteria, examining PET tracers (18F-FDG, 18F-FET, 11C-MET, 18F-DOPA) and advanced MRI techniques [diffusion kurtosis imaging (DKI), dynamic susceptibility contrast (DSC) perfusion, magnetic resonance spectroscopy (MRS)]. The integration of PET and MRI outperformed standalone modalities in diagnostic accuracy in all but one study. 18F-FET PET demonstrated high diagnostic accuracy, with sensitivity up to 95% and no diagnostic improvement when combined with MRI in high-grade glioma, though its availability remains limited. MRI alone had variable sensitivity (33–77%) and specificity (50–100%), depending on the technique and tracer used. DKI showed promise in enhancing sensitivity (72–100%). Heterogeneity in protocols and patient cohorts limited direct comparisons across studies.

Conclusions: The combination of PET and MRI provides a superior diagnostic approach for differentiating glioma recurrence from radiation necrosis, with 18F-DOPA PET and advanced MRI sequences emerging as the most effective pairing. Further multicenter studies with standardized protocols are required to validate these findings and address challenges related to tracer accessibility and protocol variability. These advancements have the potential to optimize patient management in neuro-oncology.

Keywords: Glioma recurrence; positron emission tomography/magnetic resonance imaging (PET/MRI); neuro-oncology

Submitted Dec 06, 2024. Accepted for publication May 18, 2026. Published online Jun 24, 2026.

doi: [10.21037/cco-24-133](https://doi.org/10.21037/cco-24-133)

View this article at: <https://dx.doi.org/10.21037/cco-24-133>

[^] ORCID: [0000-0003-1721-0680](https://orcid.org/0000-0003-1721-0680).

Introduction

Gliomas, particularly glioblastoma multiforme, are aggressive primary brain tumours, with a poor prognosis and a 5-year survival of 4% (1). The standard treatment for glioblastoma includes surgical resection or stereotactic biopsy, followed by a combination of radiotherapy and chemotherapy. Differentiating tumour recurrence from treatment-related changes, such as radiation necrosis, is critical for effective patient management. Advanced imaging techniques, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), offer valuable diagnostic tools in neuro-oncology.

The integration of ^{18}F -fluorodeoxyglucose (FDG) PET and MRI has been extensively studied for its ability to provide complementary metabolic, structural and functional information for brain tumour imaging (2). Quartuccio *et al.*'s 2020 review underscores the enhanced diagnostic value of integrating ^{18}F -FDG PET with MRI, demonstrating that this multimodal approach significantly improves accuracy in predicting glioma prognosis, guiding treatment planning, and evaluating recurrence. The study highlights how integrated new PET tracers such as ^{18}F -DOPA provides critical metabolic insights, while MRI contributes detailed anatomical information, allowing for a more comprehensive assessment of tumour behaviour and outperforming standalone modalities. Their findings align with a growing body of evidence supporting the use of combined PET/MRI as a superior diagnostic tool in neuro-oncology.

Given the advancements in imaging technology and the increasing adoption of novel PET tracers and advanced MRI techniques, this review identified the need for updated literature, highlighting the most promising tracer and sequence combinations while addressing limitations in current protocols and accessibility. Therefore, our review focuses on studies published after 2020, aiming to evaluate the latest developments in PET/MRI diagnostics and their implications for improving clinical decision making, diagnosis, treatment planning and patient outcomes in glioma management post treatment. By addressing these advancements, we aim to fill gaps in the current literature, particularly in the context of newer tracers and hybrid imaging systems.

In this narrative review, we aim to update the literature search to assess the diagnostic accuracy of combining various types of PET and MRI, focusing on its ability to differentiate glioma recurrence from radiation necrosis, and review the advances in imaging technology that

enable improved patient outcomes. We present this article in accordance with the Narrative Review reporting checklist (available at <https://cco.amegroups.com/article/view/10.21037/cco-24-133/rc>).

Methods

A comprehensive search was conducted using PubMed, Medline, and Embase. These databases were interrogated using the following search terms: “Glioma” OR “glioblastoma”, “positron-emission tomography” OR “PET scan” OR “PET imaging” OR “PET CT”, “magnetic resonance imaging” OR “MRI” OR “MRI scan”. The publication year was limited to studies published after April 2020, and all published studies in the English language meeting the criteria were peer-reviewed and included. The articles were selected using the Covidence tool and two independent reviewers (D.L. and M.W.) screened the title, abstract and full text of the retrieved articles. *Table 1* outlines the strategy in details.

While the search strategy aimed for inclusivity, potential selection bias should be acknowledged, particularly given heterogeneity in imaging protocols, patient cohorts (e.g., mixed-grade gliomas) and reliance on non-histopathological diagnoses in some studies. Additionally, small sample sizing and lack of longitudinal data limits generalizability, which may influence the strength of the evidence presented. A balanced presentation of both favourable and unfavourable outcomes was pursued to try and mitigate this bias.

Discussion

PET alone

In this review, four PET tracers— ^{18}F -FDG, ^{18}F -FET, ^{11}C -MET, and ^{18}F -DOPA were utilised for their ability to differentiate between glioblastoma recurrence and radiation necrosis, each with unique mechanisms of action, advantages, and limitations.

^{18}F -FDG is a widely used tracer that relies on glucose uptake, where tumour progression is typically associated with high avidity for glucose, unlike radiation necrosis (2,3). This makes FDG useful for detecting active tumour growth. Pyatigorskaya (3) and Peer (4) used FDG PET with variable results, despite both exclusively included patients with high-grade gliomas. In Pyatigorskaya's study, FDG PET showed relatively low sensitivity at 61%, whereas Peer reported a sensitivity of 100%. Both studies demonstrated

Table 1 The search strategy summary	
Items	Specification
Date of search	16/07/2024
Databases searched	PubMed, Medline, and Embase
Search terms used	“Glioma” OR “glioblastoma”, “positron-emission tomography” OR “PET scan” OR “PET imaging” OR “PET CT”, “magnetic resonance imaging” OR “MRI” OR “MRI scan”
Timeframe	April 2020–July 2024
Inclusion and exclusion criteria	Inclusion criteria: (I) original articles involving patients with previously histologically diagnosed and treated glioma; (II) imaging modalities including both PET and MRI; (III) studies reporting sensitivity, specificity, and diagnostic accuracy for distinguishing recurrence from necrosis; (IV) studies from 2020 onwards, given Quartuccio’s literature review included studies up to April 2020; (V) articles in English Exclusion criteria: (I) paediatric populations; (II) studies that included metastatic brain tumours; (III) incomplete patient data; (IV) studies with irrelevant outcomes or settings
Selection process	Using these criteria and with Covidence tool, two reviewers (M.W. and D.L.) independently reviewed the title, the abstract and full text of the retrieved articles. The primary data outcomes included the accuracy (sensitivity, specificity and accuracy) of utilising PET alone, MRI alone and combining PET and MRI. The search yielded a total of 1,419 studies. After removing 354 duplicates and screening 1,065 studies, 8 studies were included in the final review
Any additional considerations	Other variables included the average time or median time between initial treatment and imaging, number of patients, tumour histology or grade, how the final diagnosis was made (histopathology vs. clinical vs. radiological), imaging scanner type, PET tracer utilised, MRI sequences performed, and statistical analysis utilised

CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

similar specificity, with Pyatigorskaya reporting 75% and Peer 80%. Overall accuracy differed significantly between the two studies, with Pyatigorskaya achieving 63% and Peer 94%. However, FDG’s effectiveness in brain imaging is limited by the high glucose metabolism of normal grey matter, which can make interpretation challenging and reduce sensitivity (5).

¹¹C-MET, on the other hand, leverages cancer’s dependency on methionine, a key amino acid in tumour metabolism. It is superior to FDG for detecting various cancer types, including brain tumours, due to cancer’s “methionine addiction” (6). This tracer has a better tumour-to-background contrast compared to FDG, making it highly effective in detecting glioma recurrence. Dang (7) reported sensitivity of 0.83 and specificity of 0.90, both of which perform superiorly comparing to FDG PET. Accuracy is 91%. However, its short half-life and requirement for an on-site cyclotron limit its widespread use.

¹⁸F-FET, another amino acid-based tracer, offers lower background uptake in normal brain tissue compared to FDG, making it more sensitive for gliomas (8,9). This high tumour-to-background ratio makes FET a preferred choice for detecting glioma recurrence. Henriksen *et al.* (8) found that FET PET alone achieved an impressive overall

diagnostic accuracy of 96%, suggesting that in some cases, the tracer alone may suffice without additional MRI inputs. Steidl (10) and Lohmeier (9) included grade 2 to 4 tumours while D’Amore (11) included all tumour grading of glioblastoma based on molecular status. This may explain the lower diagnostic accuracies in these studies. Steidl’s (10) study reported sensitivity of 95% and specificity of 43%, with accuracy of 78%. Lohmeier *et al.* (9) reported a sensitivity of 69% and a specificity of 95%. D’Amore’s (11) study reported sensitivity of 71%, specificity of 73% and accuracy of 72%.

¹⁸F-DOPA is particularly effective for detecting low-grade gliomas (12). It can cross the blood-brain barrier and enables detection of tumour components that may not be visible on contrast-enhanced imaging, making it a valuable tool for recurrence detection. Jena’s (13) paper demonstrated high sensitivity of 81% and specificity of 100% (accuracy 95%), including detection of low-grade (grade 2) tumours, and was useful in detecting tumour components beyond regions of contrast enhancement on MRI.

Among these tracers, ¹⁸F-FET and ¹⁸F-DOPA stand out due to their superior diagnostic performance. ¹¹C-MET also provides excellent results but is limited by logistical constraints. Notably, FDG-PET in Pyatigorskaya’s study (3)

achieved a lower sensitivity of 61% in cases of low-grade gliomas due to high physiological glucose uptake.

MRI alone

In addition to routine MRI sequences such as pre- and post-contrast T1, T2/FLAIR, and diffusion-weighted imaging (DWI), several advanced imaging techniques were utilised across studies to enhance glioma characterisation using their metabolic activity and improve differentiation between tumour recurrence and radiation necrosis.

DWI, magnetic resonance spectroscopy (MRS) and dynamic susceptibility contrast (DSC) perfusion are routinely used in many practices for problem-solving in glioma assessment. Restricted diffusion typically correlates with high cellular density, often seen in tumour recurrence. These modalities were analysed in four studies included in this review. Lohmeier (9) reported DWI sensitivity of 77% and specificity of 75%. Pyatigorskaya (3), Jena (13), and Peer (4) found varying sensitivities (33–55%) but consistent specificities around 80–100%. Elevated choline to N-acetyl aspartate (NAA) ratio in MRS is indicative of active tumour growth. This was analysed only in Jena's (13) study, which showed a sensitivity of 71%, specificity of 100%, and an accuracy of 50%. While both techniques offer valuable data, their variable sensitivity highlights the importance of multimodal imaging approaches.

Perfusion Imaging, a common technique used for estimating tumour angiogenesis, was employed by half of the studies (3,4,10,13). By quantifying blood volume and flow, perfusion imaging allows assessment of tumour vascularity, which correlates with tumour grade and aggressiveness. DSC perfusion, a specific type of perfusion imaging based on cerebral blood volume (CBV) and cerebral blood flow (CBF) maps, was also used in these studies. Steidl's (10) study reported that relative cerebral blood volume (rCBV) had a sensitivity of 54%, specificity of 100%, and an accuracy of 63%. Pyatigorskaya (3) found that rCBV alone achieved a higher sensitivity of 89%, though with lower specificity at 50% and an accuracy of 82%. In Peer's (4) study, the rCBV ratio demonstrated a sensitivity of 100% and specificity of 60%, with an accuracy of 89%. Jena's (13) results for rCBF alone showed a sensitivity of 43%, specificity of 100%, and an accuracy of 54%. For rCBV alone, Jena reported a sensitivity of 43%, specificity of 80%, and accuracy of 50%.

Diffusion kurtosis imaging (DKI) was used in 3 studies (7,9,11) to characterise the non-Gaussian diffusion of

water molecules, providing insights into the complexity and heterogeneity of glioma microstructure. DKI has demonstrated utility in distinguishing between low- and high-grade gliomas, assessing cellular proliferation, and even differentiating genotypes in astrocytomas, making it a valuable addition to conventional imaging in glioma management. Lohmeier (9) reported that DKI alone had a sensitivity of 72% and specificity of 90%. In Dang's (7) study, DKI mean kurtosis (MK) demonstrated a sensitivity of 77%, specificity of 79%, and overall accuracy of 79%. Meanwhile, D'Amore (11) found that DKI MK achieved a sensitivity of 100%, specificity of 64%, and an accuracy of 88%. These supported the superiority of DKI in detecting glioma over conventional DWI.

Zhu *et al.* (14) demonstrated that another multiparametric MRI radiomics model which incorporated structural sequences, apparent diffusion coefficient (ADC), and susceptibility-weighted imaging (SWI) achieved high diagnostic accuracy for glioma characterization, with areas under the curve (AUCs) typically >0.85–0.90 for tumour grading and molecular status prediction. These findings support the feasibility of combining advanced MRI-derived features to enhance tissue characterization, although applicability to distinguishing post-radiotherapy change from tumour recurrence remains indirect and requires further validation in the post-treatment setting.

An alternative approach to perfusion, T1 dynamic contrast enhancement (DCE), was used in Henriksen's (8) study. DCE offers improved temporal resolution and allows for more precise quantification of blood flow, enhancing the assessment of tumour vascularity. Using this sequence alone, a sensitivity of 71%, specificity of 91%, and an accuracy of 80% was demonstrated. Additionally, pseudocontinuous Arterial Spin Labeling (pCASL), employed by Pyatigorskaya (3), demonstrated better accuracy than DSC perfusion—sensitivity 90%, specificity 75%, accuracy 86%. pCASL directly measures CBF without the need for contrast agents, which is particularly beneficial for patients requiring non-invasive imaging.

Bijari *et al.* (15) conducted a multi-centre study to develop and validate an MRI-based nomogram combining radiomics and deep learning features for glioma grading. They demonstrated high diagnostic performance with strong discriminatory accuracy (AUC >0.90) in validation cohorts. Although they focused preoperative grading rather than differentiation of recurrence versus post-treatment change, and as with similar radiomics approaches, limits direct applicability to the post-radiotherapy setting.

MRI's performance in distinguishing recurrence from

necrosis is variable. For example, Jena (13), Steidl (10) and Lohmeier (9) showed lower sensitivity between 52–77%, and good specificity between 75–100%. All these studies included grade 2 to 4 glioma. On the other hand, Dang's (7) and D'Amore's (11) studies demonstrated excellent sensitivity of 100% and specificity of 70% and 64% respectively, with accuracy of 80% and 88% respectively. These results may be attributed to the use of DKI. However, the high sensitivity observed in these studies is potentially confounded by their exclusive inclusion of patients with glioblastoma, known for its aggressive metabolic profile. This selective patient population likely skews the results, as glioblastomas typically exhibit more distinct imaging characteristics compared to less aggressive tumour types. Similarly, Peer's study (4) with routine MRI sequences also demonstrated excellent sensitivity of 100%, specificity of 60% and accuracy of 89% with the exclusive inclusion of patients with grade 3 to 4 glioma. The heterogeneity in patient cohort and magnetic resonance (MR) sequences used in their analysis pose challenges in determining the best combination of MR sequences.

Combined PET and MRI

The combination of PET and MRI significantly enhances diagnostic accuracy by integrating metabolic and structural information. Across most studies, combining PET and MRI findings consistently outperformed PET or MRI alone. Jena *et al.* (13) reported a significant improvement in the sensitivity and specificity by the integration of ^{18}F -DOPA PET with most routine MRI sequences including DSC, DWI and MRS. This yielded 95% sensitivity and 100% specificity across a broader range of glioma grades, suggesting that this multimodal strategy may be particularly valuable in clinical settings with heterogeneous patient populations.

Henriksen's (8) study was the only study that found that combining FET PET with MRI did not improve diagnostic accuracy compared to using FET PET alone, with both approaches achieving an accuracy of 96%. Though it is important to note the exclusive inclusion of patients with high-grade gliomas in this study.

Summary of key findings

The findings from our review highlight the superiority of combining PET and MRI over PET or MRI alone in differentiating glioma recurrence/progression

from radiation necrosis. The integration of metabolic information from PET; anatomical details and functional imaging from MRI provides a powerful tool for clinicians, improving both sensitivity and specificity across multiple studies. We found that the integration of ^{18}F -DOPA PET with predominantly routine MRI sequences—including pre- and post-contrast T1, DSC, DWI, and MRS—offers a potentially optimal combination for providing synergistic diagnostic information. This multimodal approach combines metabolic and structural insights, enhancing the ability to differentiate glioma recurrence from radiation necrosis with high sensitivity and specificity.

When comparing studies with similar patient cohort of high-grade glioma, ^{18}F -FET PET alone demonstrated outstanding diagnostic accuracy of 96% with no significance improvement when combined with MRI. However, the availability and clinical adoption of this tracer remain limited. Despite only including patients with high-grade glioma in Peer's (4) and Pyatigorskaya's (3) studies, the diagnostic accuracy of FDG-PET is variable with accuracy of 94% and 63% respectively. This poses questions regarding the reliability of this tracer in detecting glioma recurrence.

Comparison with similar research

Our findings build upon and extend the work of Quartuccio *et al.* (2), who conducted a comprehensive review of the combined use of PET and MRI for glioma imaging up to April 2020. Similar to our findings, they highlighted the diagnostic advantages of combining PET with MRI, noting its ability to improve sensitivity and specificity for differentiating glioma recurrence from treatment-related changes. However, their review primarily focused on ^{18}F -FDG PET, with limited exploration of newer PET tracers and advanced MRI techniques that have since gained prominence.

In contrast, our review incorporates studies published after 2020, reflecting advancements in both PET tracers and MRI modalities. For example, our findings emphasise the superior diagnostic performance of ^{18}F -DOPA PET and ^{18}F -FET PET, which were less represented in earlier reviews. These tracers exhibit higher specificity and tumour-to-background ratios compared to FDG, making them more suitable for brain tumour imaging. Our review also highlights the emerging role of advanced MRI techniques, such as DKI, DSC perfusion, and MRS, which were not extensively covered by Quartuccio *et al.*

Additionally, Quartuccio *et al.* focused on the complementary value of PET and MRI but did not delve deeply into the potential of hybrid PET/MRI systems, which allow simultaneous acquisition of metabolic and anatomical data. Our review underscores the diagnostic advantages of these hybrid systems, which reduce patient movement artifacts and improve image co-registration. By integrating newer studies and technologies, our review not only reaffirms the diagnostic utility of PET/MRI but also identifies the most promising combinations of PET tracers and MRI sequences. This progression reflects the evolving landscape of neuro-oncology imaging and highlights areas requiring further

Strengths and limitations

As discussed earlier, this review uniquely integrates findings from recent advancements post-2020, capturing the impact of newer PET tracers, such as ^{18}F -FET and ^{18}F -DOPA, which offer improved diagnostic accuracy compared to the traditionally used ^{18}F -FDG. By comparing these tracers, this review not only highlights the clinical advantages of specific tracers in brain tumour imaging but also clarifies the distinct roles each tracer plays, making the findings directly applicable for clinical decisions in oncology.

Additionally, this review introduces an in-depth analysis of innovative MRI techniques, such as DKI and DSC perfusion, that have been less represented in previous literature. By including these advanced MRI techniques, the review demonstrates how imaging can be used to assess microstructural and vascular properties of gliomas, directly supporting nuanced differentiation between tumour recurrence and treatment effects. Furthermore, the examination of hybrid PET/MRI systems, which allow for simultaneous acquisition of metabolic and anatomical data, adds to the literature by emphasizing the diagnostic advantages of reduced patient movement artifacts and enhanced image alignment—factors not readily achieved with standalone systems.

Our review suggests that incorporating DKI into MRI protocols may enhance sensitivity in tumour detection. However, this potential benefit is confounded by the exclusive inclusion of patients with high-grade tumours in Dang's (7) and D'Amore's (11) studies. As a result, the generalisability of these findings to lower-grade gliomas or more heterogeneous populations remains uncertain. Further studies with a broader range of tumour grades are needed to validate DKI's utility across diverse clinical settings.

Our review highlights several limitations. As previously mentioned, the heterogeneity of MRI protocols across studies presents significant challenges in directly comparing sensitivity and specificity. Variations in the use of advanced techniques such as DSC, DWI, and DKI make it difficult to determine which combination of PET tracers and MRI sequences is most effective. This inconsistency not only complicates the interpretation of findings but also limits their external validity. In clinical practice, the application of these findings is further constrained by the availability of advanced tracers and MRI techniques, which may not be accessible in all healthcare settings. Consequently, the variability in imaging protocols underscores the need for standardised approaches to ensure more reliable comparisons and broader applicability of diagnostic strategies.

All studies included in our review were cohort studies with small patient cohorts. The limited sample sizes reduce the statistical power of these studies and increase the potential for bias. Moreover, they may not reflect the broader range of clinical settings and patient populations, further limiting the applicability of the findings.

The papers did not consistently report or emphasise the median time to radiation necrosis. Most of them demonstrate occurrence around 6 months to 2.5 years. Steidl's (10) study had the shortest and most variable time interval between treatment and scan ranging from 0–99 months. Pytatigorskaya (3) and D'Amore (11) did not report time interval. Without long-term data, it is unclear whether combining PET and MRI's diagnostic advantage holds over extended periods of observation.

Each paper also employed various methods to distinguish tumour progression from radiation necrosis, utilising either histopathological confirmation or clinicoradiological follow-up, with different timeframes. Henriksen (8) followed patients 6 weeks after imaging, with assessments based on the modified RANO criteria to evaluate recurrence or stability. Pytatigorskaya (3) conducted follow-up assessments 3 months after the initial PET/MRI scan. Peer (4) defined necrosis or stability based on a reduction in lesion size or the stabilisation of the enhancing component on MRI at least 6 months after the PET/MRI scan. D'Amore (11) used the criterion of no change in treatment for at least 6 months after the PET/MRI scan to suggest necrosis or lesion stability. In Steidl's (10) study, follow-up varied by tumour grade: for World Health Organization (WHO) grade 2 gliomas, stability or improvement of the lesion for at least 12 months without any change in therapy was required to

rule out recurrence, whereas for WHO grade 3–4 gliomas, a minimum of 6 months was considered sufficient. Dang (7) followed up over a median period of 10.6 months (range, 6–25 months). Jena (13) did not specify a fixed timeframe for monitoring lesion progression. In contrast, Lohmeier (9) employed a longer follow-up period with a median surveillance time of 21.5 months [interquartile range (IQR), 9.75 months]. Each study's variation in follow-up timelines reflects the complexity of distinguishing between tumour recurrence and radiation necrosis, with differences based on glioma grade, imaging modality, and clinical judgment.

There is a potential for publication bias, as studies showing significant improvements in diagnostic accuracy by combining PET and MRI are more likely to be published. Studies that may have shown less favourable results or that found no significant difference between imaging modalities may not have been included, skewing the results of this review toward a more positive interpretation of combining PET and MRI's performance.

Implications and future considerations

This review provides critical insights into practical challenges, such as tracer availability and protocol variability, which remain underexplored in previous literature. By identifying these gaps, it underscores the necessity for standardised protocols, especially in regions where newer tracers are less accessible. It also calls attention to areas where multi-centre trials could standardise imaging approaches, enhancing consistency in clinical applications across diverse healthcare settings. While not directly addressed in the studies reviewed, the cost and accessibility of PET and MRI remain a significant limitation in clinical practice. They are expensive and resource-intensive modalities that may not be widely available in all healthcare settings. The cost-effectiveness of using combined PET and MRI versus traditional imaging modalities is still an open question, especially in resource-limited environments where access to advanced imaging technologies is constrained.

Conclusions

While the combined use of PET and MRI significantly enhances diagnostic accuracy in distinguishing glioma recurrence from radiation necrosis, the review is limited by the heterogeneity of imaging protocols, small sample sizes, and the lack of long-term follow-up data. Further multi-centre, standardised studies with larger patient cohorts

are needed to validate these findings and assess the cost-effectiveness of combining PET and MRI in routine clinical practice. Despite these limitations, the evidence strongly supports the use of both PET and MRI as a superior diagnostic tool in neuro-oncology, offering clinicians a powerful method for non-invasive assessment of treatment outcomes in glioma patients.

Acknowledgments

During the preparation of this work, the lead author applied AI tool (ChatGPT 4.0) between October to November 2024 in the writing of the manuscript to generate new text and proof-read. After using this tool, the lead author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at <https://cco.amegroups.com/article/view/10.21037/cco-24-133/rc>

Peer Review File: Available at <https://cco.amegroups.com/article/view/10.21037/cco-24-133/prf>

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://cco.amegroups.com/article/view/10.21037/cco-24-133/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Poon MTC, Sudlow CLM, Figueroa JD, et al. Longer-term (≥ 2 years) survival in patients with glioblastoma in population-based studies pre- and post-2005: a systematic review and meta-analysis. *Sci Rep* 2020;10:11622.
2. Quartuccio N, Laudicella R, Vento A, et al. The Additional Value of (18)F-FDG PET and MRI in Patients with Glioma: A Review of the Literature from 2015 to 2020. *Diagnostics (Basel)* 2020;10:357.
3. Pyatigorskaya N, Sgard B, Bertaux M, et al. Can FDG-PET/MR help to overcome limitations of sequential MRI and PET-FDG for differential diagnosis between recurrence/progression and radionecrosis of high-grade gliomas? *J Neuroradiol* 2021;48:189-94.
4. Peer S, Gopinath R, Saini J, et al. Evaluation of the Diagnostic Performance of F18-Fluorodeoxyglucose-Positron Emission Tomography, Dynamic Susceptibility Contrast Perfusion, and Apparent Diffusion Coefficient in Differentiation between Recurrence of a High-grade Glioma and Radiation Necrosis. *Indian J Nucl Med* 2023;38:115-24.
5. Hustinx R, Pourdehnad M, Kaschten B, et al. PET imaging for differentiating recurrent brain tumor from radiation necrosis. *Radiol Clin North Am* 2005;43:35-47.
6. Kubota Y, Sato T, Hozumi C, et al. Superiority of (11)C-methionine over (18)F-deoxyglucose for PET Imaging of Multiple Cancer Types Due to the Methionine Addiction of Cancer. *Int J Mol Sci* 2023;24:1935.
7. Dang H, Zhang J, Wang R, et al. Glioblastoma Recurrence Versus Radiotherapy Injury: Combined Model of Diffusion Kurtosis Imaging and 11C-MET Using PET/MRI May Increase Accuracy of Differentiation. *Clin Nucl Med* 2022;47:e428-36.
8. Henriksen OM, Hansen AE, Muhic A, et al. Diagnostic yield of simultaneous dynamic contrast-enhanced magnetic resonance perfusion measurements and (18)FFET PET in patients with suspected recurrent anaplastic astrocytoma and glioblastoma. *Eur J Nucl Med Mol Imaging* 2022;49:4677-91.
9. Lohmeier J, Radbruch H, Brenner W, et al. Detection of recurrent high-grade glioma using microstructure characteristics of distinct metabolic compartments in a multimodal and integrative 18F-FET PET/fast-DKI approach. *Eur Radiol* 2024;34:2487-99.
10. Steidl E, Langen KJ, Hmeidani SA, et al. Sequential implementation of DSC-MR perfusion and dynamic (18)FFET PET allows efficient differentiation of glioma progression from treatment-related changes. *Eur J Nucl Med Mol Imaging* 2021;48:1956-65.
11. D'Amore F, Grinberg F, Mauler J, et al. Combined 18F-FET PET and diffusion kurtosis MRI in posttreatment glioblastoma: differentiation of true progression from treatment-related changes. *Neurooncol Adv* 2021;3:vdab044.
12. Herrmann K, Czernin J, Cloughesy T, et al. Comparison of visual and semiquantitative analysis of 18F-FDOPA-PET/CT for recurrence detection in glioblastoma patients. *Neuro Oncol* 2014;16:603-9.
13. Jena A, Taneja S, Khan AA, et al. Recurrent Glioma: Does Qualitative Simultaneous 18F-DOPA PET/mp-MRI Improve Diagnostic Workup? An Initial Experience. *Clin Nucl Med* 2021;46:703-9.
14. Zhu Z, Shen J, Liang X, et al. Radiomics for predicting grades, isocitrate dehydrogenase mutation, and oxygen 6-methylguanine-DNA methyltransferase promoter methylation of adult diffuse gliomas: combination of structural MRI, apparent diffusion coefficient, and susceptibility-weighted imaging. *Quant Imaging Med Surg* 2024;14:9276-89.
15. Bijari S, Rezaei SM, Sayfollahi S, et al. Development and validation of a robust MRI-based nomogram incorporating radiomics and deep features for preoperative glioma grading: a multi-center study. *Quant Imaging Med Surg* 2025;15:1125-38.

Cite this article as: Leen D, Wong M, Lau E, Ng SP. Differentiating glioma recurrence from radiation necrosis: a narrative review of positron emission tomography and magnetic resonance imaging and their diagnostic accuracies. *Chin Clin Oncol* 2026;15(3):44. doi: 10.21037/cco-24-133