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Systematic Review

Diagnostic and Planning Value of T2-Weighted and Flair MRI for Radiotherapy Target Contouring in Brain Tumors

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ABSTRACT

Introduction: Brain and central nervous system tumors, particularly gliomas, represent a growing global burden with poor prognosis. Radiotherapy post–maximal resection is central to management, yet its success depends on precise target delineation to preserve healthy tissue. MRI, especially T2-weighted and FLAIR sequences, is standard for planning, but the optimal sequence remains unclear.

Material and Methods: A systematic review was conducted according to PRISMA guidelines. Literature searches were performed in PubMed, ScienceDirect, and EuropePMC databases up to 25 May 2025. Observational or comparative studies assessing T2-weighted and/or FLAIR MRI for radiotherapy target contouring were included. Study selection, data extraction, and quality assessment using ROBINS-I were independently performed by two reviewers.

Results: From 246 identified studies, four studies met the inclusion criteria. Overall, FLAIR-based delineation consistently produced larger clinical and planning target volumes compared with T2-weighted imaging, capturing additional regions of peritumoral abnormality. Recurrence pattern analyses suggested that FLAIR-defined volumes may better encompass infiltrative tumor margins. High interobserver agreement was reported for MRI-based target delineation, supporting the feasibility of MRI-only workflows, although selective CT integration remained important for certain organs at risk.

Conclusion: Although the evidence is limited, both T2-weighted and FLAIR MRI sequences play an important role in brain tumor radiotherapy planning. While T2-weighted imaging generates more conservative target volumes, FLAIR sequences better capture infiltrative edema, potentially lowering recurrence risks at the cost of increased healthy tissue irradiation. Careful, consensus-driven sequences selection is required to balance tumor coverage and normal tissue sparing.

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INTRODUCTION

Brain and central nervous system (CNS) tumors represent a significant and growing global health challenge, with 5-year prevalence rate estimated at 10.70 per 100,000 people and will increase each year due to population growth and aging [1,2]. A meta-analysis of 27 studies determined the overall prevalence of glioma to be 42.8% among primary CNS tumors, with glioblastoma as the most common (17.7%) [1]. These predicted will increase 39.30% by 2040 in Asia [1,3]. Despite advances in diagnosis and treatment, brain tumors carry a poor prognosis and represent a substantial burden due to morbidity and mortality with average 5-year survival rate for

all brain and central nervous system (CNS) cancers is approximately 36% [1]. Not only will rehabilitation and hospitalization result in a high economic burden, but the quality of life (QoL) is also significantly decreased because of neurocognitive deficits and other symptoms caused by the disease [4].

The diagnosis of glioma requires a multidisciplinary team that combines clinical evaluation, advanced neuroimaging, surgical tissue sampling, and detailed molecular analysis. Imaging not only plays a role to differentiating from other tumor-like conditions, but can also as surveillance tool, confirming the diagnosis, classifying tumor grading, and planning for further treatment. Magnetic Resonance Imaging (MRI) with gadolinium-based contrast is known as the gold standard for diagnosing brain tumors, with T2-weighted and fluid-attenuated inversion recovery (FLAIR) as one of the standard sequences, accompanied by T1 before and after contrast administration, diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), perfusion, and spectroscopy [5].

Depending on histological types and tumor grade, the treatment of choice for glioma is relatively standard, especially for high-grade gliomas, which includes maximal safe resection followed by adjuvant radiation and chemotherapy [6]. Radiation treatment planning is based on landmark studies to perform accurate delineation of the target volumes to precisely target the tumor while protecting healthy tissue during radiation treatment. However, it is still a major controversy due to uncertainties in tumor outlines through various MRI sequences [7].

Among several MRI sequences, T2-weighted and fluid-attenuated inversion recovery (FLAIR) images are commonly employed to visualize the extent of tumor and surrounding edema, which is helpful to define tumor margin and outline target volume for radiotherapy. T2-weighted sequences provide high sensitivity for water content changes, highlighting tumor and peritumoral edema, whereas FLAIR sequences suppress cerebrospinal fluid signals, enhancing lesion conspicuity in regions adjacent to fluid spaces. Both sequences have complementary strengths; however, institutional preferences and clinical protocols differ regarding which sequence offers better accuracy and reproducibility in radiotherapy target contouring [8,9].

There is still a lack of consensus regarding the optimal imaging sequence for radiotherapy planning, and the clinical impact of imaging sequence choice on treatment outcomes remains uncertain. However, the use of T2 and FLAIR MRI sequences to delineate target volume remains widespread in clinical practice and warrants further investigation. Therefore, this systematic review aims to evaluate the diagnostic and planning value of T2-weighted and FLAIR MRI in brain tumor radiotherapy target delineation based on the latest evidence.

MATERIAL AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This study involved the collection and study of existing data and documents that were publicly available and were recorded by the investigator in a way that did not identify patients directly or using a patient-related identifier. Therefore, this study was not subject to institutional review board approval and did not require informed consent.

A systematic search was conducted using relevant keywords around the title referring to Medical Subject Headings (MeSH) and free words combined with Boolean terms in the PubMed, ScienceDirect, and EuropePMC databases up to May 25, 2025. This search aimed to focus on studies of brain tumors undergoing radiotherapy, with outcomes focused on radiotherapy planning results, dosimetric outcomes (e.g., target volume coverage, doses to OARs), or clinical outcomes (e.g., local tumor control, overall survival, incidence of radiation necrosis or neurotoxicity).

The inclusion and exclusion criteria were established before to the conducted search to ensure homogeneity among the included studies. The inclusion criteria included 1) published in English and 2) observational or comparison studies (e.g. cohort, case-control) that used T2 sequences or FLAIR in head MRI examination. The exclusion criteria for studies were as follows: 1) non-human studies; 2) the study had been

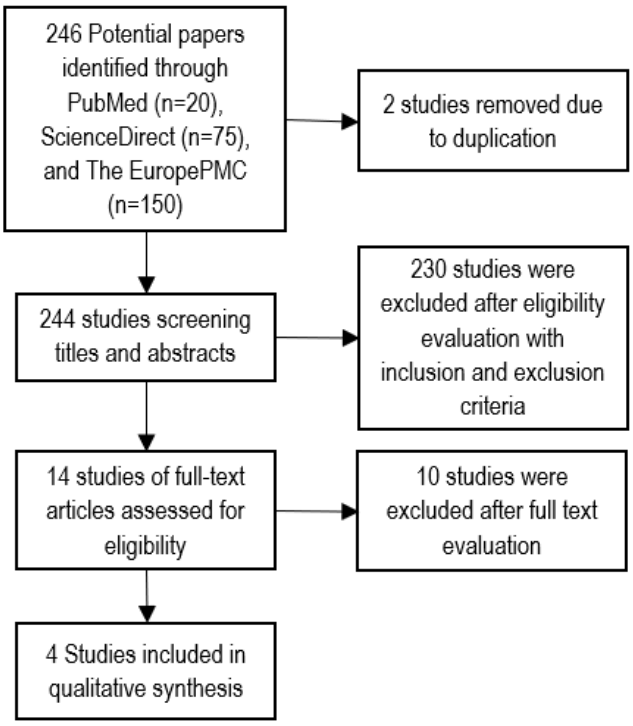


Figure 1. Flow Diagram of Study Selection.

published repeatedly; 3) the study data were incomplete; 4) or the study was a case report, meta-analysis, review, or a letter.

Two researchers with similar levels of experience conducted screening and data extraction, respectively. Discrepancies between the two researchers were resolved by consensus. The main information extracted from each study included the author's name, publication year, country of the study, average patient age, study type, clinical tumor volume (CTV), and planning tumor volume (PTV). The methodological quality and risk of bias of included studies were evaluated using an appropriate and study design-specific tool (ROBINS-I), which allows a more structured assessment of the reliability and validity of the evidence before further reporting according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

RESULTS

The initial database search using the above strategy produced a total of 246 potentially relevant studies identified from PubMed (n=20), ScienceDirect (n=75), and EuropePMC (n=150). Following the removal of 2 duplicate studies, the remaining 244 studies proceeded to a preliminary screening of titles and abstracts. This screening led to the exclusion of 230 studies based on established inclusion and exclusion criteria, leaving 14 studies for a more detailed full-text eligibility assessment. This second evaluation phase resulted in the exclusion of an additional 10 studies. A detailed flowchart of study selection is shown in Figure 1.

The four included studies provide complementary insights into the diagnostic and planning relevance of T2-weighted and FLAIR MRI sequences in radiotherapy target contouring for brain tumors. Tseng et al. demonstrated that MRI-only workflows offer high interobserver agreement in target delineation, supporting the clinical feasibility of MRI-based radiotherapy planning [10]. Stall et al. reported that FLAIR-based targets were consistently larger than those derived from T2 imaging, capturing additional regions of infiltrative abnormality [6]. Yilmaz et al. further showed that recurrence patterns frequently overlapped with FLAIR-defined abnormalities, suggesting a potential role for FLAIR in reducing

Table 1. Study Characteristics

Study	Year	Study Design	Population / Tumor Type	MRI Sequences / Workflow Compared	Primary Objective	Key RT Relevance
Stall et al.	2010	Prospective comparative study	High-grade glioma patients (RT candidates)	T2-weighted vs FLAIR for CTV delineation	To assess differences in CTV volumes obtained using T2 vs FLAIR sequences	FLAIR-based CTVs were larger than T2-based CTVs, suggesting better capture of infiltrative regions
Regnery et al.	2020	Retrospective cohort analysis	Glioblastoma multiforme (GBM) patients	T2 vs FLAIR-based target volume definition	To evaluate impact of MRI sequence choice on target volume and recurrence patterns	FLAIR-derived volumes showed greater coverage of regions that later recurred, implying improved inclusion of microscopic spread
Yılmaz et al.	2020	Retrospective dosimetric evaluation	Brain tumor patients undergoing RT	T2 vs FLAIR CTV delineation with dosimetric impact	To compare dosimetric outcomes based on T2 vs FLAIR-derived CTVs	FLAIR-based targets led to higher normal brain dose exposure, highlighting trade-off between coverage and toxicity
Tseng et al.	2020	Observer variability and workflow study	Brain tumor cases reviewed by multiple observers	MRI-only vs CT-MRI fusion workflows	To assess interobserver consistency in GTV/CTV delineation across workflows	MRI-only target delineation showed comparable reproducibility to CT-MRI fusion after consensus, supporting potential MR-only RT planning

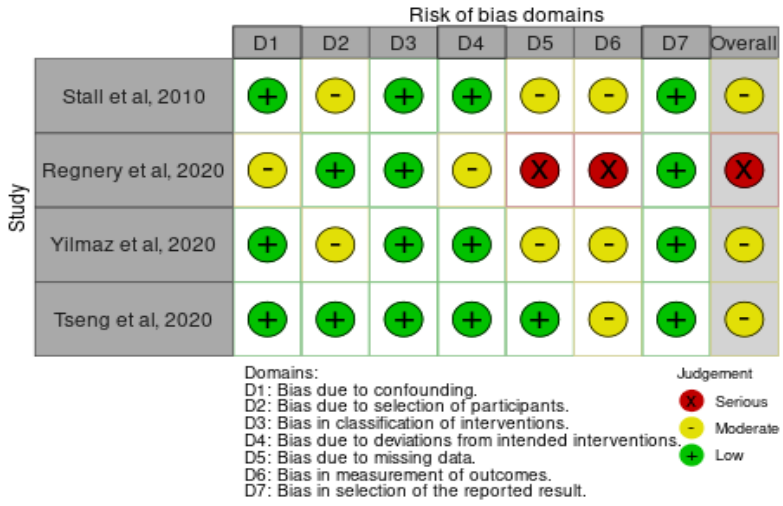


Figure 2. Risk Bias Assessment

demonstrated that high-resolution 7T FLAIR imaging may refine GTV contours and improve visualization of tumor infiltration and surrounding anatomy compared with standard 3T imaging [12]. Collectively, these findings indicate that FLAIR may offer improved detection of infiltrative disease compared with T2, while emerging high-field and MRI-only planning workflows could further enhance target precision in radiotherapy.

Based on the Risk Bias Assessment (Figure 2), no studies were classified with low overall risk, and even 25% showed serious risk. Stall et al. (2010) and Yilmaz et al. (2020) had identical methodological risk profiles with moderate risk in participant selection, missing data, and outcome measurement. However, Regnery et al. (2020) present significant methodological concerns. Meta-analysis was not possible due to data heterogeneity and was not performed in this study.

DISCUSSION

Comparative Volumetric Effects of T2-Weighted vs FLAIR Imaging in Target Delineation

Accurate volumetric delineation of gross and clinical target volumes is pivotal in radiotherapy for brain tumors, as inadequate coverage of microscopic disease may increase the risk of marginal recurrence, while excessive expansion may unnecessarily irradiate surrounding normal brain tissue [13]. MRI-based sequences, particularly T2-weighted and FLAIR imaging, are frequently used to define the extent of peritumoral infiltration; however, these sequences may capture different regions of abnormal signal intensity, potentially leading to variability in target volume definition [14]. However, several studies indicate that FLAIR typically outlines larger areas than T2. In the comparative study by Stall et al., clinical target volumes (CTVs) based on FLAIR imaging were significantly larger than those based on T2 sequences.

FLAIR contributed 25.7% unique portion to the union volume compared with 12.9% uniquely contributed by T2 imaging, suggesting that FLAIR encompasses additional regions of peritumoral abnormality, potentially indicative of microscopic infiltration. Similarly, Yilmaz et al. reported that FLAIR-based GTV defines wider non-enhancing tumor extensions and dominates final GTV contours when compared with T2, especially in high-grade gliomas where peritumoral infiltration is more pronounced. Overall, FLAIR appears to be more sensitive to low-level parenchymal changes adjacent to the tumor compared to T2-weighted imaging.

The extended volume captured by FLAIR has potential implications for microscopic disease coverage, particularly in poorly demarcated infiltrative tumors such as glioblastoma. With the limitations of existing data, Regnery et al. were able to demonstrate higher-field 7T FLAIR imaging to improve the detection of subtle infiltrative abnormalities. However, increases in target volume must be balanced against the potential for unnecessary irradiation of normal brain tissue, particularly in eloquent regions. While Stall et al. observed that FLAIR-based contours sometimes overlap with organs at risk such as the brainstem and optic chiasm, these differences did not consistently meet, raising questions about whether the additional FLAIR-only volume always translates to clinically meaningful. It remains a challenge to distinguish genuine tumor infiltration from edema-related changes when expanding target volumes based on FLAIR alone.

Dosimetric and Normal Tissue Implications

Differences in the target volume delineation between FLAIR-based and T2-weighted MRI contours have direct dosimetric consequences, from tumor coverage as well as radiation exposure to surrounding normal tissues. According to Stall et al., FLAIR-derived PTVs and CTVs were significantly larger than T2-based volumes ($p < 0.0001$). FLAIR contributed roughly 25.7% of the composite CTV, whereas T2 only contributed 12.9% [6]. Although larger volumes are associated with increased radiation dose burden on normal brain parenchyma, this may have clinical benefits by reducing the risk of marginal underdosage. Another study further demonstrated that FLAIR-based target volumes improved conformity indices and coverage metrics relative to T2-weighted delineation, albeit at the cost of higher mean doses to adjacent organs-at-risk depending on tumor proximity [12].

Guideline recommendations have also emphasized the dosimetric impact of expanded MRI-based CTVs. The latest ESTRO-EANO consensus mention the significance of carefully balancing tumor control probability (TCP) against normal tissue complication probability (NTCP), while acknowledging that abnormal T2/FLAIR signal intensities may represent non-enhancing tumor infiltration and should be incorporated into target definition [15]. It is also important to avoid indiscriminate expansion of MRI-based contours when imaging abnormalities are non-specific, as evidenced by comparative imaging studies using metabolic modalities like amino acid PET, which show that biologically refined target volumes may reduce unnecessary radiation exposure to normal brain structures [16]. In this case, when FLAIR hyperintensity represents non-infiltrative edema rather than a true tumor expansion, smaller T2-based volumes may reduce neurotoxicity.

All these results show that there is a dosimetric trade-off when choosing an MRI sequence: While T2-based contours may lessen exposure to normal tissue but carry the risk of marginal recurrence, FLAIR-guided delineation may increase the volume of irradiated normal brain while improving microscopic changes. To achieve optimal radiotherapy planning, dosimetric evaluation must be used in conjunction with sequence-based contour selection. This process should ideally be backed by consensus guidelines.

Interobserver Variability and Reproducibility

Interobserver variability is a crucial factor in determining the clinical feasibility of MRI-based or MR-only radiotherapy planning workflows. Tseng et al. demonstrated high reproducibility in gross tumor volume (GTV) and clinical target volume (CTV) delineations, reporting excellent interobserver agreement with kappa values of approximately 0.88–0.89 and Dice Similarity Coefficients (DSC) of 0.86–0.88 across both MRI-only and CT-MRI fusion workflows [10]. These findings indicate that MRI-only planning is feasible for brain tumor radiotherapy, providing target definition consistency comparable to conventional workflows. However, the study also identified notable exceptions in the contouring of certain organs-at-risk (OARs), such as the cochlea, where agreement was poorer in MRI-only settings and significantly improved with CT integration, emphasizing the continued importance of CT for bony and calcified structures [10,15]. This suggests that while MRI offers superior soft tissue contrast for tumor target delineation, specific OARs may still require CT support to ensure reproducibility and planning safety.

These findings demonstrate that GTV/CTV definition may be reliably conducted using MRI alone when supported by standardized protocols and experienced observers to carefully considerate of OAR visibility and increase interobserver consistency. This will optimize treatment coverage and minimize the risk of recurrence or toxicity. This consideration leads directly into the next discussion on how imaging-based target uncertainties may translate into differences in clinical outcomes and recurrence patterns.

Clinical Feasibility and Implications: Tumor Coverage, Risk of Recurrence, and Challenges

Variability in MRI target definition substantially impacts local control and recurrence risk. Inadequate capture of microscopic tumor extensions can lead to marginal recurrences if a selected sequence is unable to sufficiently capture infiltrative tumor regions. In this regard, several studies have assessed whether variations in recurrence localization with respect to the treatment field result from differences between T2-weighted and FLAIR-based target delineation. By mapping the recurrence patterns, Yılmaz et al discovered that failures occurred outside the defined target volumes, caused by under-delineation [11].

On the other hand, FLAIR-derived clinical target volumes also tended to include regions with higher rates of later recurrence than T2-weighted volumes, suggesting that FLAIR may offer greater sensitivity to infiltrative edema associated with tumor spread. Studies also report frequent recurrences outside the T2-based margins also demonstrate the need to expand these limits, which happens to be a feature of the FLAIR sequence to show peritumoral edema [6]. However, further research is needed before making a clinical judgment to obtain appropriate coverage and avoid unnecessary expansion and radiation-induced toxicity, and whether this possibility can be achieved using FLAIR-based margin.

MRI is beginning to be used in radiotherapy planning, both as an MRI-based workflow and as an MRI-only approach. Its use is supported by evidence demonstrating high feasibility and reproducibility when suitable structures are available. Tseng et al. showed that MRI-only target delineation achieved interobserver agreement comparable to CT-MRI fusion workflows, with notable improvements following observer calibration and training sessions [10]. These observations align with broader findings in radiotherapy planning, where standardized contouring workshops and consensus meetings significantly reduce interobserver variability [17]. MRI-only radiotherapy has also been reported as technically feasible in brain tumor workflows, provided that robust geometric calibration and distortion correction protocols are implemented [18]. Furthermore, the integration of MR-simulation and MR-guided linear accelerators (MR-Linacs) enables adaptive radiotherapy, allowing dynamic updates to tumor and edema characteristics during treatment [19].

However, the adoption of MRI-based planning in routine clinical practice presents practical and technical challenges that require structured mitigation strategies. Limitations such as MRI-related geometric distortion, scanner-dependent variability, potential misalignment with treatment positioning, and the difficulty in visualizing calcified or bony structures (e.g., the skull base) require careful observation and an experienced operator, which may need CT integration in specific scenarios [20–22]. Additionally, MRI interpretation for treatment planning may be influenced by variations in edema extent, artifact susceptibility, and lack of standardized windowing presets compared to CT. When embedded within a multidisciplinary framework and supported by standardized imaging and QA protocols, MRI-based planning can be effectively translated into clinical workflows while minimizing uncertainties and optimizing contour consistency.

Evidence Limitations and Future Directions

While this study provides valuable insights into the utility of T2-weighted and FLAIR MRI for radiotherapy target contouring in brain tumors, several limitations must be acknowledged. With only four limited studies, this limits the statistical power of the synthesis and the broad generalizability of the conclusions. Furthermore, the current evidence is limited to retrospective data and based on single-institution cohort with relatively small sample size, further limiting the evidence regarding T2-weighted versus FLAIR-guided target delineation.

Clinical applicability has also been limited because most studies have relied on surrogate endpoints like volume overlap, recurrence pattern mapping, and dose coverage metrics rather than long-term survival or local control outcomes. The stratification of molecular subtypes that play a key role in determining tumor type was also not further explained in these studies, so that investigations in modern neuro-oncology remain unclear.

In addition, there is significant technical heterogeneity among these studies, ranging from clinical findings, imaging acquisition (from MRI field strength (e.g., 3T vs 7T) to machine protocols), and radiotherapy techniques, including different contour protocols and margin expansion strategies often used in comparative analyses, which may affect dosimetric results and volumetric comparisons.

The absence of uniform standards for determining the extent of abnormal signals is another drawback, which could lead to interpretive subjectivity and inter-sequence variability among observers. Additionally, while many findings suggest that FLAIR may better encompass infiltrative edema in high-grade gliomas, sequence performance may vary by tumor subtype, molecular profile, or treatment phase, none of which are consistently addressed in existing literature.

To better ascertain the clinical significance of sequence-based differences, future research should involve prospective multicenter trials that integrate harmonized imaging acquisition protocols, standardized contouring guidelines, and recurrence-matched outcome analysis. Emerging technologies, including AI-driven segmentation and radiomics, with rigorous clinical validation, show considerable promise in refining infiltrative margin detection and reducing inter-observer variability [23]. Biologically informed target definition may be further supported by multi-parametric techniques that combine FLAIR, T2, diffusion, and perfusion imaging, especially in

MR-Linac-enabled adaptive radiotherapy workflows [24,25]. However, until these advanced methodologies demonstrate definitive improvements in tumor control and normal tissue preservation, they should serve as adjuncts to established imaging standards rather than replacements.

CONCLUSION

This review examines the comparative utility of T2-weighted and FLAIR MRI sequences for radiotherapy target delineation in brain tumors, highlighting a critical dosimetric trade-off between comprehensive tumor coverage and normal tissue toxicity. While T2-weighted imaging typically yields more conservative target volumes, FLAIR provides enhanced visualization of infiltrative edema, which may reduce marginal recurrence risk but conversely increase the irradiation of adjacent healthy tissues. Although standardized training and multidisciplinary protocols can ensure high interobserver reproducibility in MRI-based workflows, the current evidence remains too limited and heterogeneous to establish definitive, sequence-specific contouring standards. Consequently, the evidence base regarding the outcomes is still limited for use as routine protocols, consensus, and practices in clinical applications. As radiotherapy progress transitions toward MRI-dominant and adaptive paradigms, future advancements will critically depend on prospective multicenter validation, the incorporation of radiomics and artificial intelligence for precise segmentation, and continued multimodal imaging strategies to optimize the therapeutic ratio between tumor control and normal tissue preservation.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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