

ORIGINAL ARTICLE

MRI-CT Image Fusion in 3D-Conformal Radiotherapy for Glioblastoma: Impact on Target Volume and Eye Dose

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Abstract

Purpose: Accurate target delineation is essential for radiotherapy planning in glioblastoma. While CT provides the electron density information required for dose calculation, MRI offers superior soft-tissue contrast and may improve tumor delineation.

Materials and Methods: Computed Tomography (CT) is routinely used for radiotherapy treatment planning; however, Magnetic Resonance Imaging (MRI) provides superior soft-tissue contrast. This study evaluated the improvement of treatment planning in glioblastoma patients by fusing MRI and CT images, with a focus on changes in Clinical Target Volume (CTV) and radiation dose to the eye region. Thirty patients with histologically confirmed glioblastoma underwent both CT and MRI scans. Two plans were generated per patient: MRI–CT fused (dual-modality) and CT-only (single-modality). Demographics, tumor location, CTV, and eye dosimetry (maximum dose, mean dose, D_{0.03cc}, dose–volume histogram metrics) were collected. CT and MRI protocols, registration, and fusion procedures were performed. Statistical comparisons the Wilcoxon signed-rank test, with significance set at $P \leq 0.05$ and 95% Confidence Intervals (CI).

Results: Image fusion significantly reduced CTV in both phases (initial: 443.45 ± 190.64 vs 200.19 ± 133.67 cm³; mean difference -243.27 cm³ [95% CI -316.82 , -169.71], $P < 0.001$; boost: 265.72 ± 140.72 vs 84.28 ± 57.48 cm³; mean difference -181.44 cm³ [95% CI -232.92 , -129.96], $P < 0.001$). Eye doses were consistently lower with fusion: left eye D_{mean} (initial: -225.06 cGy, $P = 0.006$; boost: -68.05 cGy, $P = 0.007$), left eye D_{max} (initial: -620.44 cGy, $P = 0.010$; boost: -142.14 cGy, $P = 0.015$), right eye D_{mean} (initial: -268.73 cGy, $P = 0.006$; boost: -89.08 cGy, $P = 0.013$), right eye D_{max} (initial: -662.06 cGy, $P = 0.004$; boost: -135.52 cGy, $P = 0.024$). Across endpoints, 70–93% of cases favored CT–MRI plans.

Conclusion: In 3D-CRT for glioblastoma, CT–MRI fusion improves anatomical specificity, enabling smaller CTVs and meaningfully lower ocular doses. These findings support routine MRI fusion for safer, more conformal planning. MRI–CT fusion enhances target delineation in glioblastoma but may increase eye dose; careful organ-at-risk sparing is warranted.

Keywords: Glioblastoma; Magnetic Resonance Imaging–Computed Tomography Fusion; 3D-Conformal Radiation Therapy; Target Volume; Ocular Dose; Dose Volume Histogram; Dose Metrics.

1. Introduction

Accurate target delineation is critical for brain radiotherapy. Computed Tomography (CT) provides geometric accuracy and electron density information necessary for dose calculation, while Magnetic Resonance Imaging (MRI) offers superior soft-tissue contrast, which is essential for identifying tumor extent in glioblastoma [1]. Glioblastoma is the most common and aggressive primary brain tumor in adults [2]. According to the 2021 WHO Classification of Tumors of the Central Nervous System (WHO CNS5), the term “glioblastoma multiform” has been replaced with “glioblastoma” [3]. Accurate imaging is fundamental for treatment planning, as underestimation or overestimation of tumor volume can result in insufficient coverage or unnecessary irradiation of healthy tissue [4, 5]. While MRI is the gold standard for delineating brain tumors, CT is indispensable for radiotherapy dose calculation and patient positioning [6]. CT–MRI image fusion combines the strengths of both modalities, potentially improving target definition and sparing Organs At Risk (OARs) [7]. Previous studies have shown that MRI fusion can reduce target volume and modify dose distribution in Intensity-Modulated Radiotherapy (IMRT) and stereotactic techniques, but limited data exist for its impact in conventional 3D-Conformal Radiotherapy (3D-CRT) for glioblastoma [8]. The purpose of this study was to evaluate the effect of CT–MRI image fusion on target volume delineation and ocular dose metrics (mean and maximum doses) in two phases of 3D-CRT for glioblastoma.

2. Materials and Methods

We conducted a retrospective case–control analysis of 30 patients with histologically confirmed glioblastoma treated between January 2021 and December 2022. Patients were eligible if they were between 18 and 75 years of age, had available pre-treatment CT and MRI scans, and had no history of prior cranial radiotherapy. Patients younger than 18 years were excluded to avoid pediatric variability. Additional exclusion criteria included contraindications for MRI (such as claustrophobia or the presence of metallic implants incompatible with magnetic fields), poor image quality precluding

fusion, abnormal cranial or facial anatomy, and a history of prior neurosurgical interventions other than tumor resection. To minimize confounding variables, only patients with two anatomically normal eyes, without any history of ocular injury, visual impairment, or ophthalmic pathology, were included. Demographic data included a mean age of 55.2 ± 9.1 years (range 34–72), with 18 males (60%) and 12 females (40%). Tumor locations were frontal (40%), temporal (33%), parietal (17%), and occipital (10%). CT scans were acquired on a Siemens SOMATOM Definition AS scanner (120 kVp, 300 mAs, 1 mm slices) with immobilization using a thermoplastic mask. MRI was performed on a Philips Ingenia 1.5T scanner, including T1-weighted pre- and post-contrast, T2-weighted, and FLAIR sequences with 1 mm slice thickness. Patient positioning and immobilization matched the CT setup to ensure accuracy. Rigid registration of MRI to CT was performed within the treatment planning system (LinaTech TPS v1.08.545) using anatomical landmarks and a mutual-information-based algorithm. Co-registration accuracy was verified in axial, sagittal, and coronal planes. All treatment plans were generated using three-Dimensional Conformal Radiotherapy (3DCRT). The Gross Tumor Volume (GTV) was defined on fused images, and a 2–3 cm margin was applied to obtain the Clinical Target Volume (CTV) according to departmental protocol. Radiotherapy was delivered in two distinct phases:

- Phase I (23 fractions): A total dose of 46 Gy was prescribed to the peritumoral edema region, with a 1.5 cm margin around the edema delineated as CTV and an additional 1 cm margin added to define the planning target volume (PTV).
- Phase II (7 fractions, 14 Gy): An additional boost dose was delivered to the tumor bed and resection cavity, with a 1.5 cm margin applied to define the CTV and 1 cm added for PTV expansion.

This stepwise approach accounts for the highly infiltrative nature of glioblastoma, which is typically associated with extensive peritumoral edema. Organs at risk included the optic nerves, optic chiasm, eyes, and lenses. Eye dosimetry metrics included maximum dose ($D_{\max}$), mean dose (D_{mean}), and dose to 0.03 cc ($D_{0.03\text{cc}}$). Dose–volume histograms (DVHs) were computed for all structures. All data were imported into SPSS software for analysis. Normality of

distributions was assessed using the Kolmogorov–Smirnov test. Data are presented as mean, median, minimum, maximum, and standard deviation. Since not all variables followed a normal distribution, paired comparisons between single- and dual-modality plans were performed using the Wilcoxon signed-rank test. A P-value of <0.05 was considered statistically significant, and results were presented with 95% Confidence Intervals (CI). The workflow of CT–MRI rigid fusion and contour transfer is shown in Figure 1.

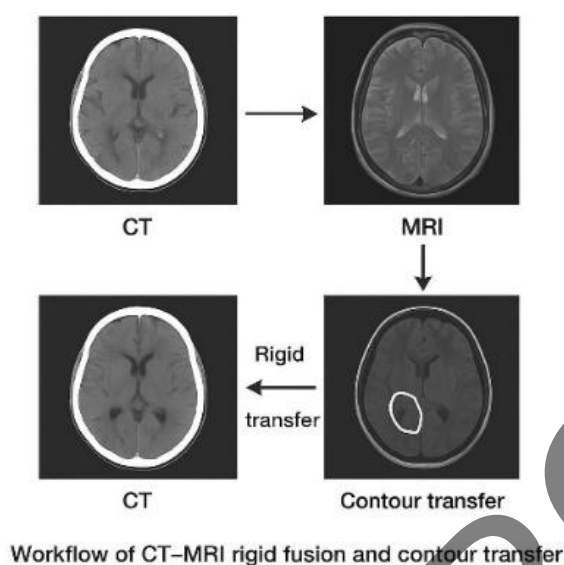


Figure 1. Workflow of CT–MRI rigid fusion and contour transfer

3. Results

3.1. Clinical Target Volume (CTV)

Dual-modality (MRI–CT) planning yielded larger CTVs in 27/30 (90%; 95% CI: 73–98%) patients in the initial phase and 28/30 (93.3%; 95% CI: 77–99%) in the boost phase. Comparison of CTV measurements in the boost and initial phase for single and dual modality RTP is shown in Tables 1 and 2.

3.2. Eye Dose

From DVHs, the following were extracted for each phase: CTV volume (cm^3) left and right eye mean dose (D_{mean}) and maximum dose (D_{max}) (cGy). In the majority of patients, D_{max} and D_{mean} to both eyes were higher with dual-modality planning. Data are

presented as mean $\pm$ standard deviation (SD). Paired t-tests and Wilcoxon signed-rank tests were used to compare CT-only and CT–MRI fused plans. Statistical significance was defined as $P \leq 0.05$. Mean differences with 95% confidence intervals (CIs) were calculated. For all ocular dose metrics except one, CT–MRI fusion resulted in statistically significant reductions. Dose reductions were observed for both D_{mean} and D_{max} in left and right eyes, in both phases. First treatment phase and the local (boost) treatment phase. Data are presented as individual patient values. As demonstrated in Figures 2–4 and detailed in Tables 2–4, CT–MRI fusion consistently reduced both mean and maximum ocular doses. In the initial phase (Table 3), fused plans achieved lower doses to both eyes compared with CT-only plans, with significant differences observed. In the boost phase (Table 4), although absolute dose levels decreased overall, the relative advantage of fusion remained evident, with statistically significant reductions in both mean and

Table 1. Comparison of CTV measurements (cm^3) between CT-only and MRI–CT fusion plans in the initial phase

Metric	CTV-Boost
N	30
CT-only(mean $\pm$ SD)	265.72 $\pm$ 140.72
CT-MRI fused(mean $\pm$ SD)	84.28 $\pm$ 57.48
Mean diff [95% CI]	–181.44 [–232.92, –129.96]
P	<0.0001
Wilcoxon P	<0.0001
CT < Fused(n,%)	2 (6.7%)
CT > Fused(n,%)	28 (93.3%)

Table 2. Comparison of CTV measurements (cm^3) between CT-only and MRI–CT fusion plans in the initial phase

Metric	CTV-initial
N	30
CT-only(mean $\pm$ SD)	443.45 $\pm$ 190.64
CT-MRI fused(mean $\pm$ SD)	200.19 $\pm$ 3.67
Mean diff [95% CI]	–243.27 [–316.82, –169.71]
P	<0.0001
Wilcoxon P	<0.0001
CT < Fused(n,%)	3 (10.0%)
CT > Fused(n,%)	27 (900%)

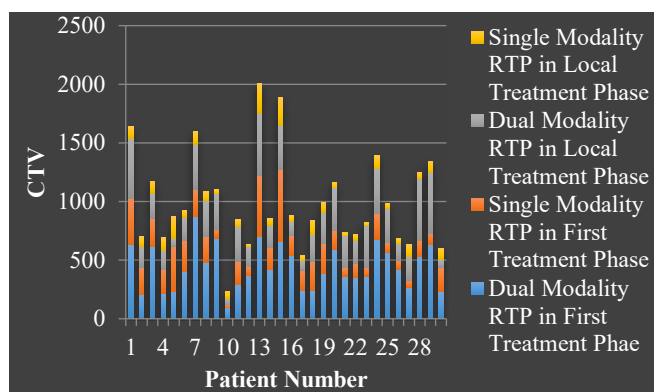


Figure 2. Clinical target volume (CTV) for each patient in single-modality and dual-modality radiotherapy treatment plans, shown separately for the first treatment phase and the local (boost) treatment phase. Data are presented as individual patient values

maximum doses. The patient-specific dose distributions illustrated in the figures further confirm these patterns, underscoring the robustness of the fusion approach. Collectively, these findings highlight the dual advantage of fusion in sparing ocular structures while ensuring adequate target coverage.

4. Discussion

This study demonstrates that adding MRI to CT via rigid fusion for 3D-CRT planning in glioblastoma significantly reduces target volume and ocular doses. These findings are consistent with prior reports showing that MRI provides superior delineation of tumor extent compared with CT alone [9, 10]. Previous studies in advanced techniques such as IMRT and stereotactic radiotherapy have also reported reductions in target volume and improved organ-at-risk sparing with MRI fusion [11, 12]. However, evidence in the context of conventional 3D-CRT has been limited [13, 14]. Our results add to this body of knowledge, showing that even in 3D-CRT, rigid CT–MRI fusion can yield clinically meaningful benefits across both treatment phases and all ocular dose metrics. The integration of MRI into CT-based planning significantly improved visualization of tumor extent and altered target delineation in most

Table 3. Eye dose metrics (D_{max} and D_{mean}) for left eye during initial and boost phases

Metric	$D_{mean-initial}$	$D_{max-initial}$	$D_{mean-Boost}$	$D_{max-Boost}$
N	30	30	30	30
CT-only(mean±SD)	549.62 ± 524.33	1339.26 ± 1299.68	163.52 ± 209.80	348.79 ± 385.60
CT-MRI fused(mean±SD)	324.56 ± 395.00	718.82 ± 827.92	95.47 ± 153.49	206.64 ± 255.07
Mean diff[95% CI]	−225.06 [−375.67, −74.45]	−620.44 [−1087.28, −153.60]	−68.05 [−115.79, −20.31]	−142.14 [−254.95, −29.34]
P	0.0059	0.0098	0.0068	0.0153
Wilcoxon P	0.0073	0.0098	0.0028	0.0077
CT < Fused(n,%)	7 (23.3%)	9 (30.0%)	8 (26.7%)	9 (30.0%)
CT > Fused(n,%)	23 (76.7%)	21 (70.0%)	22 (73.3%)	21 (70.0%)

Table 4. Eye dose metrics (D_{max} and D_{mean}) for right eye during initial and boost phases

Metric	$D_{mean-initial}$	$D_{max-initial}$	$D_{mean-Boost}$	$D_{max-Boost}$
N	30	30	30	30
CT-only(mean±SD)	837.45 ± 563.81	1763.72 ± 1326.34	286.56 ± 383.92	447.61 ± 348.27
CT-MRI fused(mean±SD)	568.72 ± 551.97	1101.66 ± 1099.36	197.48 ± 250.08	312.10 ± 292.43
Mean diff[95% CI]	−268.73 [−454.57, −82.89]	−662.06 [−1099.07, −225.05]	−89.08 [−157.86, −20.30]	−135.52 [−252.83, −18.21]
P	0.0061	0.0043	0.0130	0.0240
Wilcoxon P	0.0005	0.0010	0.0023	0.0243
CT < Fused(n,%)	5 (16.7%)	6 (20.0%)	8 (26.7%)	10 (33.3%)
CT > Fused(n,%)	25 (83.3%)	24 (80.0%)	22 (73.3%)	20 (66.7%)

- Average dose to the left eye in the secondary treatment phase in the single-modality treatment plan
- Average dose to the left eye in the secondary treatment phase in the dual-modality treatment plan
- Average dose to the left eye in the initial treatment phase with a single-modality treatment plan
- Average dose to the left eye in the initial treatment phase with a dual-modality treatment plan
- Maximum dose to the left eye in the secondary treatment phase in a single-modality treatment plan
- Maximum dose to the left eye in the secondary treatment phase in the dual-modality treatment plan
- Maximum dose to the left eye in the initial treatment phase in the single-modality Dorakan plan
- Maximum dose to the left eye in the initial treatment phase in a dual-modality treatment plan

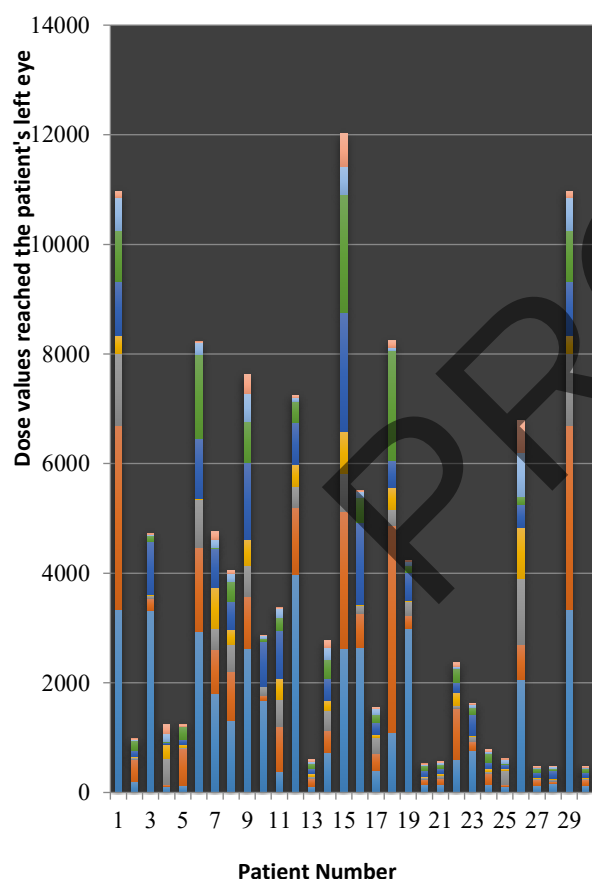


Figure 3. Average and maximum doses to the left eye in initial and boost phases for single- and dual-modality plans

patients, resulting in larger CTVs with dual-modality planning. However, this expansion frequently increased $D_{\max}$ and D_{mean} to the eyes and surrounding anterior structures. These findings are consistent with

- Average dose received by the patient's right eye in the secondary treatment phase with a single-modality treatment plan
- Average dose to the patient's right eye in the secondary treatment phase with a dual-modality treatment plan
- Average dose to the patient's right eye in the initial treatment phase with a single-modality treatment plan
- Average dose to the patient's right eye in the initial treatment phase with a dual-modality treatment plan
- Maximum dose reached to the right eye of the patient undergoing secondary phase therapy with a single-modality treatment plan
- Maximum dose delivered to the patient's right eye in the secondary treatment phase in the dual-modality treatment plan
- Maximum distance reached in the patient's right eye in the initial treatment phase with a single-modality treatment plan
- Maximum dose reached to the right eye in the initial treatment phase with a dual-modality treatment plan

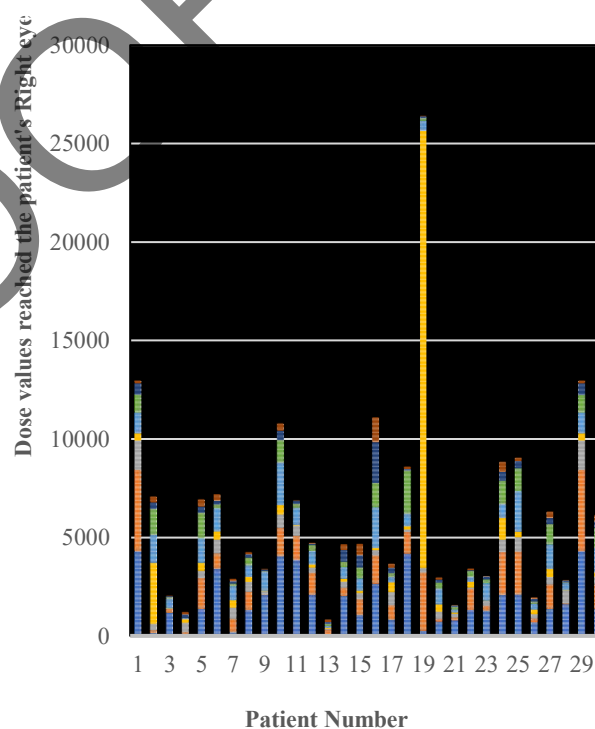


Figure 4. Average and maximum doses to the right eye in initial and boost phases for single- and dual-modality plans

prior studies reporting that MRI-CT fusion refines target definition but must be balanced against OAR sparing (Thornton *et al.*, 1992; Weber *et al.*, 2008; Torresin *et al.*, 2015). In glioblastoma, peritumoral edema is a common and infiltrative feature. Our protocol of treating edema with an extended margin in the initial 23 fractions, followed by a boost to the resection cavity and residual tumor, aligns with contemporary practice and reflects the biological

aggressiveness of this tumor. The increased eye dose observed in dual-modality plans likely reflects the anterior extension of edema margins in tumors located near the frontal lobes.

Based on our clinical experience, the applied margins (1.5 cm for CTV expansion and 1 cm for PTV) provided acceptable local control in routine practice while maintaining tolerable toxicity. Future prospective trials should evaluate advanced MRI sequences (diffusion-weighted, perfusion, spectroscopy) and deformable registration techniques to further refine target delineation. Artificial intelligence-based fusion algorithms also hold promise for optimizing multimodality treatment planning.

4.1. Limitation

Limitations of this work include the relatively small sample size, single-center retrospective design, and absence of correlation with long-term clinical outcomes (local control, survival, toxicity). Nonetheless, our findings highlight the dual benefit and challenge of MRI-CT fusion in glioblastoma radiotherapy planning [15]. Nonetheless, the paired analysis design minimizes inter-patient variability [16].

5. Conclusion

For glioblastoma patients treated with 3D-CRT, CT-MRI fusion yields smaller target volumes and lower ocular doses compared with CT-only planning [17]. This supports routine use of MRI fusion in clinical practice. In summary, CT-MRI fusion in glioblastoma radiotherapy planning not only improves target delineation but also significantly reduces ocular doses compared to CT-only planning, as confirmed by both tabulated data and patient-specific dose distributions. These results emphasize the clinical value of MRI integration in enhancing treatment precision while minimizing toxicity. MRI-CT image fusion meaningfully impacts radiotherapy planning in glioblastoma by improving target delineation, though it may increase radiation doses to the eyes. Careful optimization of dose constraints for organs at risk is essential. Patients with glioblastoma often undergo MRI for diagnostic purposes, making it a readily

available modality for treatment planning. Future research should investigate advanced MRI techniques and AI-based fusion models, combined with prospective evaluation of clinical outcomes, to optimize patient care.

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