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MR-Linac-Guided Adaptive Radiotherapy for HGG: Retrospective Analysis of Therapeutic Outcomes with Concurrent Chemoradiotherapy Integrated

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Abstract

Background: Tumor Treating Fields (TTFields) may potentiate radiotherapy (RT) efficacy in high-grade glioma (HGG) through dual mechanisms: enhancing tumor membrane permeability for chemotherapeutic agents, and exerting synergistic anti-glioma activity with ionizing radiation via DNA damage suppression. This study applied MR-Linac technology to quantify temporal gross tumor volume (GTV) dynamics during chemoradiotherapy (CRT) with or without TTFields, explore correlations between volumetric patterns and clinical features, and evaluate TTFields' impact on survival and recurrence.

Methods: We retrospectively analyzed 15 HGG patients receiving concurrent TTFields plus CRT and 15 control patients treated with CRT alone. On-treatment MR-guided GTV contours were delineated by a senior radiation oncologist per

RTOG guidelines. GTV changes were assessed using Dice similarity coefficient (DSC) and relative volumetric change (ΔV). Between-group comparisons focused on treatment response, survival endpoints and recurrence patterns.

Results: As of February 20, 2025, the TTFields group had significantly longer median overall survival (not reached vs. 19.0 months; p=0.0091) and improved progression-free survival (13.11 vs. 8.0 months) versus controls. Recurrence patterns differed markedly: controls showed 40% in-field, 20% marginal, and 20% distant recurrences, while TTFields patients had 6% in-field, 27% marginal, and 40% distant recurrences. Both groups exhibited declining GTV ΔV and DSC during RT, with more pronounced reductions in the TTFields cohort.

Conclusion: Concurrent TTFields is associated with improved survival and accelerated GTV regression in HGG. The shift from predominant in-field failure in controls to higher distant progression in TTFields patients indicates enhanced local control, supporting closer systemic surveillance in clinical practice.

Keywords: High-grade glioma; Tumor Treating Fields; MR-Linac

Introduction

High-grade gliomas (HGGs), comprising WHO grade 3 and 4 diffuse gliomas according to the 2021 WHO Classification of Tumors of the Central Nervous System,(1)are among the most aggressive primary malignant CNS tumors. Among adult gliomas, glioblastoma (GBM) represents the most common and lethal subtype. The median overall survival (OS) for grades III and IV gliomas is 37.6 and 14.4 months, respectively.(2)

Since 2005, maximal safe resection followed by radiotherapy with concomitant and adjuvant temozolomide (TMZ) has been the standard treatment for GBM.(3)With medical advancements, the clinical understanding of HGG has deepened, leading to the development of targeted therapies and immunotherapies. Among these, Tumor Treating Fields (TTFields) therapy, which is non-invasive and utilizes low-intensity, intermediate-frequency alternating electric fields, represents the first treatment to significantly improve outcomes for GBM patients. When combined with the standard regimen, emerging evidence suggests that TTFields may potentiate radiotherapy (RT) through modulation of tumor cell membrane permeability and potential synergy with ionizing radiation via impaired DNA damage repair.(4, 5)In the EF-14 trial, TTFields plus maintenance TMZ extended median OS to 20.9 months, with a 5-year survival rate of 13%. Although these figures represent significant progress over the baseline standard, the prognosis for HGG patients remains poor.(6)

The MR-Linac, a novel MR-guided radiotherapy device integrating magnetic resonance (MR) imaging with a linear accelerator, addresses several limitations of traditional image-guided radiotherapy. (7)It offers superior image quality compared to CBCT, excellent soft-tissue contrast without radiation exposure (unlike CT or CBCT), real-time imaging capabilities, and online adaptive treatment planning.(8-10)This study aimed to use magnetic resonance-guided linear accelerator (MR-Linac) technology to quantify dynamic changes in gross tumor volume (GTV), including absolute volume and relative volume change, at different treatment fractions.(11)In patients with high-grade glioma undergoing chemoradiotherapy with or without concurrent TTFields, we further explored associations between on-treatment volumetric changes, clinical features, survival outcomes, and recurrence patterns.

Materials and Methods

Participants

We retrospectively reviewed patients with high-grade glioma who received MR-Linac-guided radiotherapy between April 1, 2022 and October 1, 2024 at Sun Yat-sen University Cancer Center. The inclusion criteria were as follows:(1) age ⩾18 years; (2) receipt of MR-Linac-guided radiotherapy; (3) integrated histological and molecular diagnosis of WHO grade 3 or 4 glioma according to the fifth edition of the WHO Classification of Tumors of the Central Nervous System; and (4) completion of standard Stupp-regimen chemoradiotherapy. Patients were categorized according to whether they received concurrent TTFields for ⩾4 weeks.

Data collection

Electronic medical records were queried for relevant clinical factors, including age, sex, extent of resection, WHO grade, IDH status, pathological type, radiotherapy, chemotherapy, survival outcomes (median progression-free survival [mPFS] and median overall survival [mOS]), and receipt of concurrent TTFields. Patients were classified into two groups: those who received concurrent TTFields (TTF group) and those who did not (non-TTF group).PFS was defined as the time from diagnosis to the first documented disease progression or recurrence, while OS was defined as the time from diagnosis to death or last follow-up. Disease progression was assessed according to the Response Assessment in Neuro-Oncology (RANO) criteria.(12)Dice similarity coefficient (DSC) was used to evaluate the overlap between target contours and ranges from 0 to 1, with higher values indicating greater overlap.Hausdorff distance (HD) was defined as the maximum distance between any point on the fractional GTV contour and the closest point on the reference GTV contour, reflecting target displacement. A smaller HD indicates less displacement.Relative volume change (Δ V) was calculated as (GTVx - GTV1) / GTV1 and was used to assess the degree of target volume change. A smaller absolute value indicates less GTV volume variation.Patients with incomplete medical records were excluded.

Statistical analysis

For the target-dynamics analysis, 15 HGG patients receiving concurrent TTFields (TTF group) and 15 patients without concurrent TTFields (non-TTF group) were included. Baseline and on-treatment GTV contours, delineated by a senior radiation oncologist according to RTOG guidelines, were compared using the Dice similarity coefficient (DSC), Hausdorff distance (HD), and relative volumetric change (Δ V). Comparative analyses between the TTF and non-TTF groups focused on recurrence patterns and survival outcomes. Continuous variables were described as median and range, whereas categorical variables were presented as numbers and percentages. Progression-free survival (PFS) and overall survival (OS) were analyzed using the nonparametric Kaplan-Meier method. All statistical analyses were performed with SPSS 17.0, and $P<0.05$ was considered statistically significant.

$$\Delta V = \frac{|GTV_x| - |GTV_0|}{|GTV_0|} \tag{1}$$

$$DSC = 2 \times \frac{GTV_x \cap GTV_0}{GTV_x \cup GTV_0} \tag{2}$$

$$HD = \max_{a \in GTV_x} \left\{ \min_{b \in GTV_0} \{d(a,b)\} \right\} \quad (3)$$

Radiomics model

For the radiomics analysis, 15 HGG patients receiving concurrent TTFields (TTF group) and 42 HGG patients without concurrent TTFields (non-TTF group) were included to explore radiomics-based prediction of recurrence outcomes. Multimodal radiomic features were extracted from the 1st, 10th, 20th, and 30th treatment fractions obtained from the MR-Linac, specifically including clinical features, CT radiomic features, fraction-specific MRI radiomic features, and fraction-specific dose radiomic features. All extracted features were normalized, and Pearson correlation analysis and LASSO regression models were used to further screen the features, thereby identifying the multimodal features most strongly associated with recurrence patterns. Multiple recurrence prediction models were constructed using various machine learning algorithms, including logistic regression (LR), support vector machines (SVM), and ensemble learning, and model performance was evaluated using metrics such as accuracy and the area under the receiver operating characteristic curve (AUC).

Results

From April 2022 to October 2024, 15 patients received the Stupp regimen plus concurrent TTFields, while another 15 patients received the Stupp regimen alone. Among them, 8 were male (26.7%) and 22 were female (73.3%). The median age was 45 years. Patient characteristics are detailed in Table 1. Two patients (6.7%) had recurrent glioblastoma. 26 patients (86.6%) had newly diagnosed glioblastoma, and 2 patients (6.7%) had grade III glioma.Seven patients (23.3%) had no recurrence, while 23 patients (76.7%) experienced tumor progression/recurrence, including 7 patients (30.4%) with in-field recurrence, 7 patients (30.4%) with marginal recurrence, and 9 patients (39.2%) with distant progression.The clinical characteristics of the two groups were generally comparable, reducing but not eliminating potential statistical imbalance attributable to baseline characteristics.

Table1 Patient Characteristics

		non-TTF (n=15)	TTF (n=15)	P
Age (years)				1
	Median	45.87	45.87	
Sex				0.6513
	Female	12(80)	10(66.67)	
	male	3(20)	5(33.33)	
Extent of resection				1
	GTR	10(66.67)	9(60)	
	STR	5(33.33)	6(40)	
WHO Grade				0.7318
	WHO Grade 4 (Newly diagnosed)	14(93.33)	12(80)	
	WHO Grade 4 (Recurrent)	1(6.67)	1(6.67)	
	WHO Grade 3	0(0)	2(13.33)	
IDH Status				1
	Wild-type	13(86.67)	12(80)	
	Mutation	2(13.33)	3(20)	
MGMT Promoter methylation				1
	Methylated	11(73.33)	11(73.33)	
	Unmethylated	4(26.67)	4(26.67)	
1p/19q Codeletion				
	Non-codeleted	13(86.67)	14(93.33)	1
	Unknown	2(13.33)	1(6.67)	
TERT Promoter Mutation Status				0.6051
	Wild-type	3(20)	6(40)	
	Mutation	10(66.67)	7(46.67)	
	Unknown	2(13.33)	2(13.33)	
BRAF V600E				1
	Wild-type	13(86.67)	13(86.67)	
	Unknown	2(13.33)	2(13.33)	
Recurrence pattern				0.2357
	no recurrence	3(20)	4(26.67)	
	in-field	6(40)	1(6.67)	
	marigina1	3(20)	4(26.67)	
	distant	3(20)	6(40)	

Survival Analysis

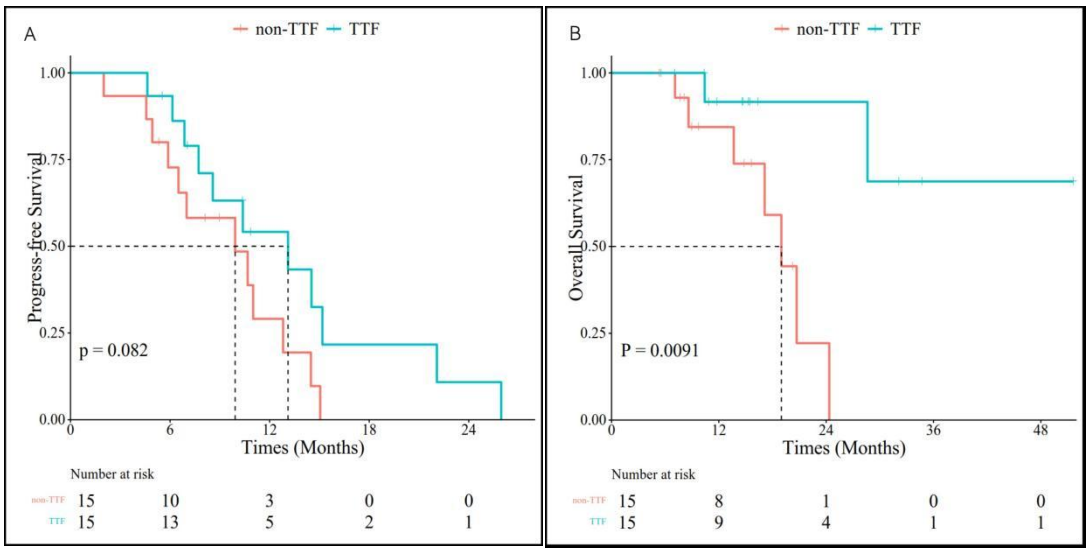
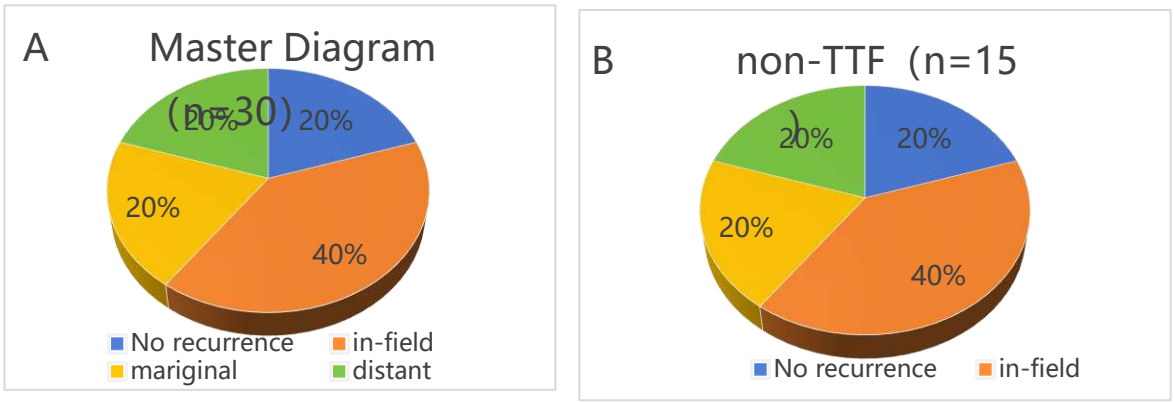


Fig. 1 Kaplan-Meier curves for progression-free(A)and overall survival(B) since glioma diagnosis. A general Kaplan-Meier curves for progression-free； B general Kaplan-Meier curves for overall survival.

Our analysis of survival outcomes between the two groups showed that the 2-year PFS rates for the TTF group and non-TTF group were 6.7% and 0%, respectively. The 2-year overall survival rates for both groups were 26.7% and 6.7%, respectively. The TTF group demonstrated significantly better median overall survival (19.0 months vs. 13.11 months; p=0.0091) and numerically superior progression-free survival (13.11 vs. 9.92 months; p=0.082) compared to the non-TTF group.As shown in Fig. 1.

Recurrence Pattern

Recurrence patterns differed substantially: non-TTF group exhibited 40% in-field, 20% marginal, and 20% distant recurrences, while TTF reversed predominance with 40% distant, 27% marginal, and 6% in-field recurrences.As shown in Fig. 2.



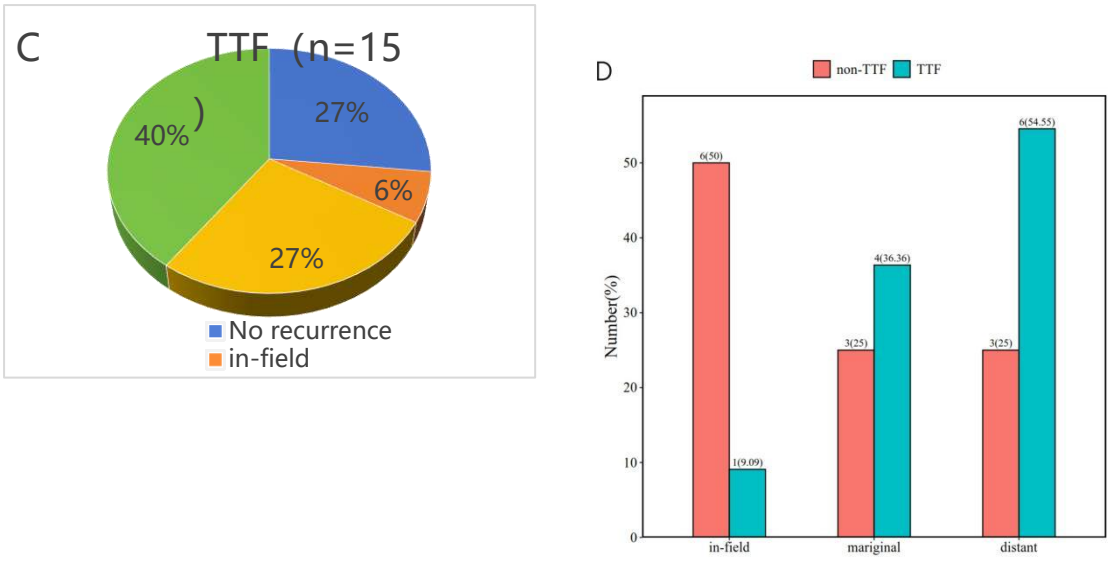
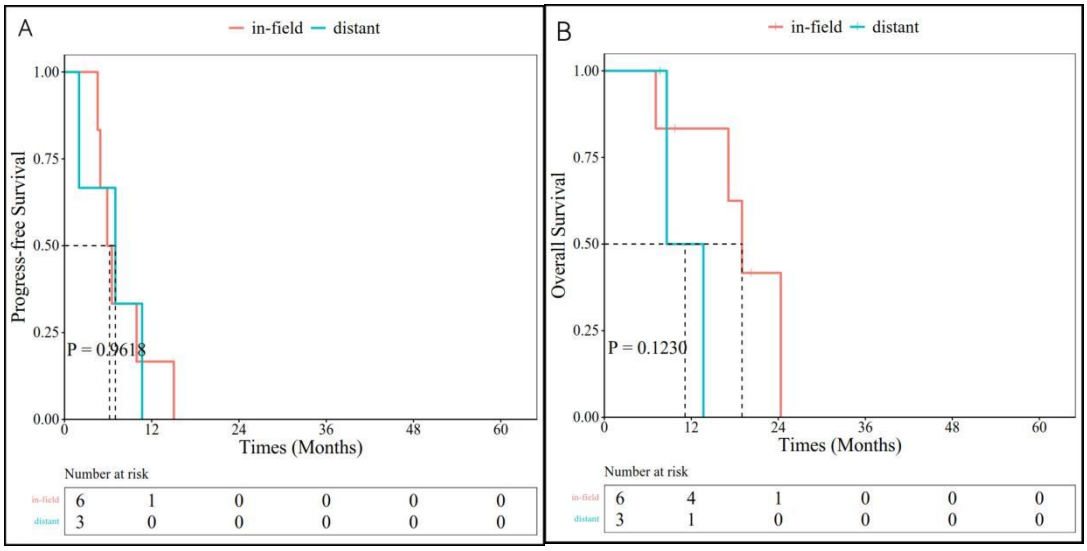


Fig.2 Distribution of recurrence patterns. A Overall distribution of recurrence patterns in 30 patients; B Distribution of recurrence patterns in the non-TTF group; C Distribution of recurrence patterns in the TTF group; D Data comparison between the two groups under different recurrence patterns

Recurrence Pattern

In the non-TTF group, there was no statistically significant difference in progression-free survival (PFS) or overall survival (OS) between patients with distant progression and those with in-field recurrence. In the concurrent TTFields (TTF) group, the PFS for the distant progression group was 9.48 months and was significantly longer than that of the in-field recurrence group. This finding is consistent with previous reports suggesting that patients receiving TTFields may be more likely to experience distant rather than in-field progression, and that distant progression may be associated with longer PFS. However, there was no significant difference in OS between the two groups.As shown in Fig. 3.



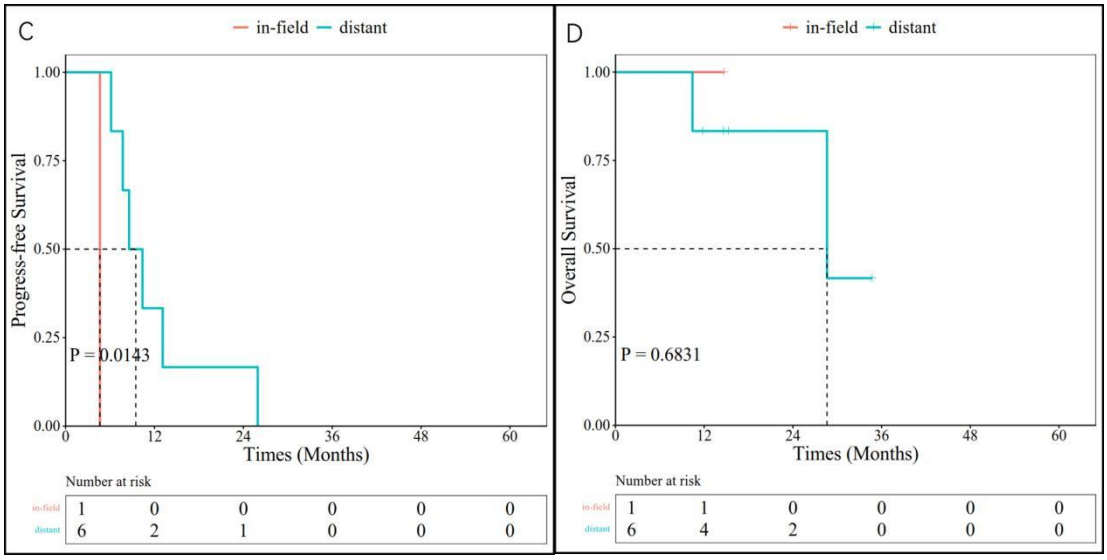


Fig. 3 Kaplan-Meier curves for two groups with different recurrence patterns .A Kaplan-Meier curves for progression-free from without concurrent TTFields(non-TTF) group;B Kaplan-Meier curves for overall survival from without concurrent TTFields(non-TTF) group;C Kaplan-Meier curves for progression-free from concurrent TTFields (TTF) group;D Kaplan-Meier curves for overall survival from concurrent TTFields (TTF) group.

Changes in GTV during RT

As treatment progressed, the average DSC of the GTV gradually decreased in both groups, and the GTV displacement increased progressively.The DSC in the TTF group was lower than that in the non-TTF group, and the GTV displacement changes were more pronounced in the TTF group at the same treatment fraction.With increasing fractions, the average HD of GTV in both groups gradually increased, indicating greater displacement.The HD in the TTF group was higher than in the non-TTF group, and GTV displacement changes were more pronounced in the TTF group at the same fraction.Both groups exhibited a progressive decrease in average GTV volume across fractions 1-30.The TTF group demonstrated greater Δ V compared to non-TTF, with more pronounced GTV volume changes at matched fractions.

Dice similarity coefficient(DSC)

The proportion of target volume overlap (DSC) between the GTVs at 10th, 20th, and 30th fractions and the GTV at 1th fractions was calculated for patients in the TTF group and the non-TTF group, as shown in Fig. 4 and Table 2. As treatment progresses, the DSC values gradually decrease, indicating that the overlap between the fractional GTV and the GTV at the start of treatment gradually shrinks. The comparison between the TTF group and the non-TTF group showed that the average DSC in the TTF group was lower than that in the non-TTF group, indicating that tumor location changes were more pronounced in the TTF group for the same number of fractions.

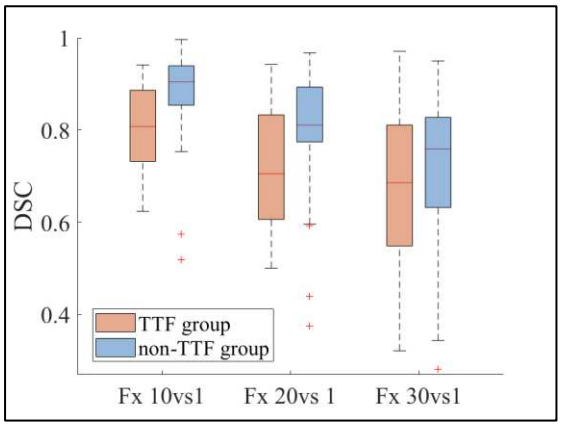


Fig. 4 The DSC values and displacements of the two groups of GTV were compared across different treatment fractions.

Table 2. The average DSC values for the TTF group and the non-TTF group.

Avg DSC	Frac 10vs1	Frac 20vs1	Frac 30vs1
TTF	0.81±0.09	0.73±0.15	0.68±0.18
non-TTF	0.88±0.10	0.80±0.13	0.73±0.15
p	0.003	0.093	0.275

Hausdorff Distance(HD)

The target displacement (HD) between the GTVs at the 10th, 20th, and 30th fractions and the GTV at the 1st fraction was calculated for patients in the TTF group and the non-TTF group, as shown in Fig. 5 and Table 3. As treatment progresses, the HD values gradually increase, indicating that the displacement between the fractional GTV and the GTV at the start of treatment gradually increased. The comparison between the TTF group and the non-TTF group showed that the average HD in the TTF group was higher than that in the non-TTF group, indicating that tumor position shifted more significantly in the TTF group compared to the non-TTF group under the same number of fractions.

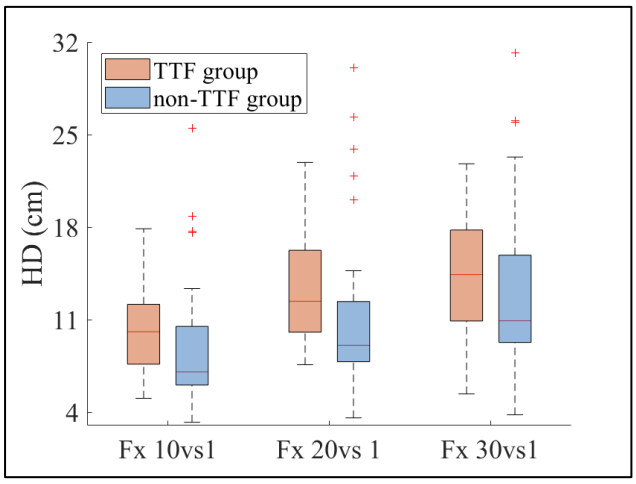
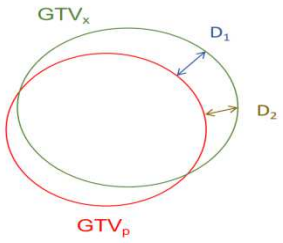


Fig. 5 The HD values and displacement amplitudes of GTV in both groups were measured across different treatment fractions.

Table 3. The average HD values for the TTF group and the non-TTF group.

Avg HD (cm)	Frac 10vs1	Frac 20vs1	Frac 30vs1
TTF	10.46±3.20	13.25±4.04	14.47±4.69
non-TTF	9.40±6.50	11.04±5.68	12.79±5.83
p	0.025	0.019	0.097





The target volumes for the TTF group and the non-TTF group were compared across four treatment fractions, as displayed in Fig. 6. As treatment progressed, the average target volume gradually decreased in both the TTF group and the non-TTF group. The changes in target volume at the 10th, 20th, and 30th fractions compared to the 1st fraction were calculated, as summarized in Table 4 and Table 5. For the same number of treatment fractions, the change in target volume was greater in the TTF group than in the non-TTF group.

A Average GTV volume B Volume Change △V

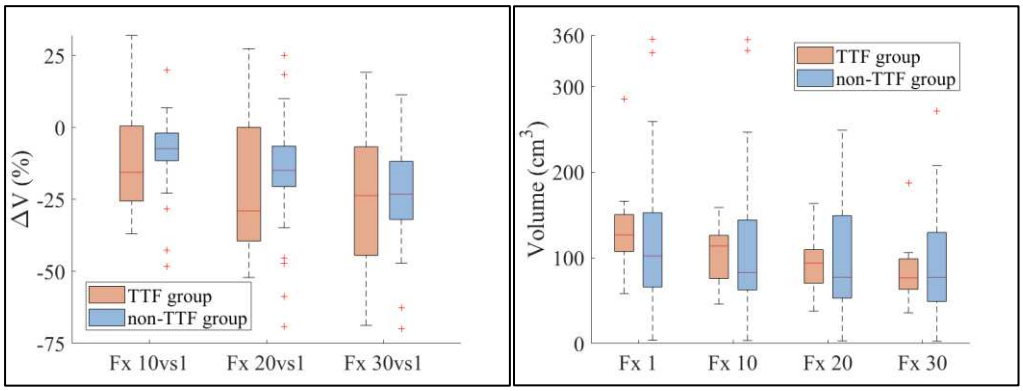


Fig. 6 The average GTV volume and volume change △V of the two groups across different treatment fractions.A. The average GTV volume for the two groups at different doses; B. Changes in GTV volume in the two groups at different doses.

Table 4. The average GTV volume for the TTF group and the non-TTF group.

Avg Volume (cm3)	Frac 1	Frac 10	Frac 20	Frac 30
TTF	130.96±53.63	119.48±77.12	105.39±68.01	99.26±68.32
non-TTF	117.85±78.74	111.03±79.16	103.71±77.20	93.58±70.37
p	0.174	0.564	0.664	0.564

Table 5. The average volume change values for the TTF group and the non-TTF group.

Avg △V (%)	Frac 10vs1	Frac 20vs1	Frac 30vs1
TTF	-11.90±17.84	-20.56±24.65	-25.00±25.75
non-TTF	-8.27±11.97	-15.90±17.41	-24.52±18.01
p	0.316	0.370	0.922

Recurrence prediction

The performance of five machine learning (ML) models in predicting recurrence on the independent testing set (18 patients) was evaluated using metrics such as accuracy, area under curve (AUC), precision, recall, and F1-score, as shown in Table 6. Among the five ML models, ensemble learning (EST) performed the best, achieving a prediction accuracy of 0.931 on the testing set. LR and SVM performed well on metrics such as precision, AUC, recall, and F1-score, while RF and XGB achieved higher precision. Four fractions of multimodal data were used separately for recurrence prediction, and the results are shown in Table 7. Among the five machine learning models, the EST model achieved the highest prediction accuracy across all four fractions, followed by LR and SVM. The multimodal data from the 1st fraction revealed lower prediction accuracy across all five models, whereas the multimodal data from the 20th and 30th fractions demonstrated higher prediction accuracy, indicating that multimodal data from the middle-to-late stages of MR-Linac treatment are more suitable for predicting recurrence.

Table 6. Performance of five machine learning models in predicting recurrence.

	LR	SVM	RF	XGB	EST
Accuracy	0.889	0.889	0.764	0.722	0.931
AUC	0.923	0.923	0.575	0.500	0.921
Precision	0.846	0.846	1.000	1.000	0.942
Recall	1.000	1.000	0.754	0.722	0.961
F1-score	0.917	0.917	0.860	0.839	0.952

Table 7. Performance of four fractions data in predicting recurrence.

Accuracy	LR	SVM	RF	XGB	EST
Frac1	0.778	0.778	0.778	0.722	0.833
Frac10	0.889	0.889	0.722	0.722	0.944
Frac20	0.944	0.944	0.778	0.722	1.000
Frac30	0.944	0.944	0.778	0.722	0.944
All	0.889	0.889	0.764	0.722	0.931

Discussion

In our retrospective cohort study of 30 patients with high-grade gliomas who received MR-Linac-guided therapy, with or without concurrent TTFields, we observed that patients treated with TTFields combined with MR-Linac adaptive radiotherapy exhibited longer progression-free survival (PFS) and overall survival (OS). TTFields, as a novel therapeutic approach for glioblastoma, operates by utilizing alternating electric fields of specific frequencies to disrupt cancer cell division and induce cell death. The EF-14 trial established TTFields plus maintenance TMZ as an evidence-based treatment option for newly diagnosed GBM. (6)Current research on gliomas primarily focuses on optimizing treatment timing (13), combining with targeted therapies (14)or immunotherapy (15), oncolytic viruses (16), and antigen vaccines (17). Further data are needed to investigate the therapeutic strategies combining MR-Linac with TTFields.

MR-Linac (magnetic resonance linear accelerator) has emerged as an important platform in modern radiation oncology. By integrating the imaging advantages of MRI with radiotherapy delivery, MR-Linac enables real-time visualization and online adaptive planning, thereby supporting more individualized treatment strategies. (18, 19)MR-Linac-guided radiotherapy has demonstrated the potential to improve treatment precision and reduce toxicity across multiple anatomical sites, including pancreatic cancer, thoracic tumors,

prostate cancer, liver cancer, and pediatric tumors. (10)

Notably, radiomics—a quantitative imaging analysis application that integrates clinical data to optimize decision-making protocols—has demonstrated potential in predicting tumor response and constructing survival models (20). Future studies will further investigate radiomics analysis to identify correlations between a series of pattern changes in radiotherapy and serial MR-Linac imaging and recurrence patterns, with the potential to support individualized treatment adaptation.

Although the role of radiotherapy in glioblastoma treatment is undisputed, there is currently no consensus on the delineation volume of the target volume (GTV). The commonly used guidelines are the recommendations of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). The EORTC treatment phase is a single-phase approach, where the tumor volume (GTV) is defined as the T1-enhanced area plus the surgical residual cavity (excluding T2/FLAIR hyperintense edematous areas). The clinical target volume (CTV) is the geometric expansion of the GTV by 2–3 cm, with a total irradiation dose of 60Gy delivered in 30 fractions. This strategy relies on extensive geometric expansion to cover abnormal signals in potentially overlooked edematous areas on imaging. (21) In contrast, the RTOG adopts a two-phase treatment volume strategy: Phase 1 (GTV1): T1-enhanced area + surgical residual cavity + T2/FLAIR hyperintense areas, with a GTV expansion of 2 cm, and a total irradiation dose of 46Gy delivered in 23 fractions. Phase 2 (GTV2): T1-enhanced area + surgical residual cavity (reduced field and dose), with a GTV expansion of 2 cm, and an additional 7 fractions to supplement the total irradiation dose to 60 Gy.(22)However, these two guidelines adopt fundamentally different strategies for managing T2/FLAIR abnormal signal regions. Based on this, one study implemented a single-phase CTV-HUTF treatment, where the tumor volume (GTV) was defined as the T1-enhanced area + surgical residual cavity + T2/FLAIR high signal area.
The clinical target volume (CTV) was expanded 0.5-1cm beyond the GTV (adjusted for anatomical barriers), with a total of 60 Gy of radiation delivered through 30 fractions. This protocol utilized MRI to assess infiltration.The visualization of the target region, including edema but with reduced delineation of the target area boundaries, reduced the dose to organs at risk (OAR). The median overall survival (OS) was 21 months and the progression-free survival (PFS) was 11 months, both showing improvements compared to previous data, aiming for precise coverage. (23)

The UNITED trial (ClinicalTrials.gov Identifier: NCT04726397. Registered March 29, 2021. Sunnybrook Health Sciences Centre, Toronto, Canada.) is currently the most representative Phase II clinical study in this field, aimed at evaluating the safety and efficacy of adaptive radiotherapy based on Unity MR-linac for glioblastoma multiforme (GBM). (24)It employs the highly challenging 5-mm CTV expansion margin (traditionally 15-20 mm) and combines weekly measurement volumes to regenerate adaptive treatment plans (ATS). Moreover, the adaptive radiotherapy plan, by adapting to the reduced postoperative resection cavity during radiotherapy in GBM patients, can significantly reduce radiation doses to the hippocampus and normal brain tissue, demonstrating potential to mitigate neurocognitive side effects of radiotherapy. (25)The interim analysis of this trial revealed differences in volume changes among different molecular subtypes of GBM. Tumors with unmethylated MGMT promoter showed a tendency to increase in volume during radiotherapy, whereas methylated tumors tended to decrease or remain stable. This finding suggests that future treatment strategies may need to be stratified according to molecular pathology types—unmethylated patients may require more frequent field expansion, while methylated patients may benefit more from field

reduction for protection.

Another ongoing study, UNITED-3 (NCT05720078), aims to evaluate the impact of small-margin adaptive radiotherapy (RT) and a two-stage approach on local control of visible tumors, as well as on neurocognitive function and quality of life, compared to standard non-adaptive RT. This study is expected to achieve more precise personalized cancer treatment regimens.

Our research has shifted from a "broad-spectrum" preventive irradiation approach based on statistical probability to a "precision radiotherapy" targeting based on daily anatomical and biological realities. Guided by daily MRI, we observed the dynamic evolution of residual cavity shrinkage, tumor migration, and edema after GBM surgery. By employing online adaptive techniques, this approach may reduce geographical miss and improve target coverage in conventional radiotherapy. Clinical trials such as UNITED have also validated the safety and efficacy of the minimal-margin (5-mm) approach, enabling treatment to significantly reduce neurocognitive toxicity without compromising efficacy. Future integration of functional imaging techniques like DWI will make dose sculpting based on biological target volumes (BTV) feasible, providing a novel strategy to overcome GBM radiation resistance. (26)

Although we reported favorable survival outcomes and changes in recurrence patterns, this study still has certain limitations. First, due to the retrospective study design, only a small number of treated patients were included, which may result in limited sample size and diversity of the patient population. The results may not be generalizable to the broader glioma population. Second, we lack long-term data on the therapeutic efficacy of magnetic resonance linear accelerator (MR-Linac) for high-grade gliomas, which is another limitation that needs to be addressed. More extensive follow-up studies are required to validate the sustained efficacy and safety of MR-Linac-guided radiotherapy combined with TTFields. Additionally, the implementation of advanced technologies such as TTFields and MR-Linac requires specialized skills and resources, which may limit their widespread application in all medical institutions. Future studies should address these limitations to validate the findings and ensure that the benefits of MR-Linac-guided radiotherapy combined with TTFields can be broadly applied to various high-grade glioma patient populations. Overall, although this study provides valuable insights into the efficacy and challenges of MR-Linac-guided transcranial magnetic field therapy (TTF), the limitations of sample size and the lack of long-term efficacy data highlight the need for further research and improvements in this field.

Conclusion

Patients receiving TTFields combined with MR-Linac adaptive radiotherapy demonstrated longer overall survival (OS) but not longer progression-free survival (PFS), accompanied by target volume change (ΔV) and morphological changes (DSC, HD). MR-Linac monitoring revealed more dynamic target volume changes, suggesting that TTFields may be associated with more pronounced on-treatment target changes; however, this observation requires validation in larger prospective cohorts. The recurrence pattern in the TTFields group underwent significant alterations: reduced local recurrence, while distant recurrence was associated with longer PFS. Although previous studies have suggested the feasibility of combining TTFields with conventional radiotherapy, our findings indicate that MR-Linac-based precision radiotherapy may provide a useful platform for longitudinal response monitoring and hypothesis generation when combined with TTFields.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Sun Yat-sen University Cancer Center (approval number: SL-B2025-632-02).We state that the informed consent was obtained from all subjects and/or their legal guardian(s).All the patients included in this study are above 18 years old.We confirm that all research procedures were performed in accordance with relevant guidelines and regulations.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Mengqi Sun:participation in the whole work;drafting of the manuscript;final approval of the submitted version; Qun He: participation in the whole work; drafting of the manuscript; final approval of the submitted version;Mengke Qi:data analysis; final approval of the submitted version.Xin Jiang:drafting of the manuscript;final approval of the submitted version.Zihuang Li:participation in the whole work;drafting of the manuscript;final approval of the submitted version.Yuanyuan Chen:participation in the whole work;drafting of the manuscript;final approval of the submitted version.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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