Original Article

Efficacy of scalp-sparing volumetric-modulated arc therapy approach in reducing scalp radiation dose for patients with glioblastoma: a cross-sectional study

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Background: Radiation is integral to the treatment of glioblastoma (GBM). However, radiation-induced scalp toxicity can negatively impact patients' quality of life. Volumetric-modulated arc therapy (VMAT) optimizes the dose to organs at risk (OARs). We hypothesize that a scalp-sparing VMAT (SSV) approach can significantly reduce undesirable doses to the scalp without compromising the target dose.

Methods: This is a retrospective cross-sectional study of GBM patients who originally received radiation with non-SSV. We contoured the scalp as a 5 mm rind-like structure beneath the skin above the level of the foramen magnum. We replanned our patients using SSV techniques. We compared dosimetric data for the scalp, planning target volume (PTV), and select critical normal structures between non-SSV and SSV plans.

Results: Nineteen patients with newly diagnosed GBMs were included in our study. All patients received 60 Gy in 30 fractions. 9 patients received it in a single course. The rest received 46 Gy in 23 fractions to an initial volume followed by 14 Gy in 7 fractions to a cone-down volume (split course). New VMAT plans were generated after adding the scalp as an OAR. The median scalp volume was 416 cm^3 (363–468 cm^3). The median reductions in scalp D_{min}, D_{max}, and D_{mean} were 43.5% (–100% to 0%), 2.8% (+13.4% to –24.9%), and 15.7% (+2.1% to –39.9%) respectively. Median reductions in scalp D20cc and D30 cc were 19.5% (–2.7% to –54.5%), and 19.0% (–5.3% to –39.5%) respectively. The median volumes of the scalp receiving 30 Gy, 40 Gy, and 50 Gy were reduced by 42.3% (–70.6% to –12.5%), 72% (–100% to –2.3%), and 92.4% (–100% to +5.4%) respectively. There were no significant differences in the doses delivered to the PTV, brainstem, optic nerves, and optic chiasm between SSV and non-SSV plans.

Conclusions: SSV can significantly reduce scalp radiation dose without compromising target coverage or critical normal structure doses. This may translate into reduced acute and late radiation toxicity to the scalp. A prospective trial evaluating the clinical benefits of SSV is ongoing (NCT03251027).

Keywords: Scalp sparing; skin toxicity; glioblastoma (GBM)

Introduction

Background

Glioblastomas (GBMs) account for almost half of all primary brain tumor cases diagnosed each year in the United States (US). More than 14,490 people will receive this diagnosis in 2023 (1,2). GBMs are usually rapidly fatal, with a historical 5-year overall survival rate of only 9% (3). Yearly, they claim over 10,000 lives in the US. The aggressive nature of these tumor is matched by their intense treatment course. The standard of care (SoC) treatment for GBMs consists of surgical resection, and post-operative concurrent chemoradiotherapy, followed by tumor treating fields (TTFields) administered alongside maintenance chemotherapy (4).

Rationale

TTFields are the latest addition to the GBM treatment paradigm and have significantly prolonged patients' lives (5). They deliver intermediate frequency (200 kHz) alternating electric fields transcranially, using cap-like transducer arrays affixed to the scalp. They wreak havoc on the cellular DNA repair and division machinery, stamping out cancer cell growth in the process (6,7).

TTFields only work while the transducer arrays are actively delivering the electric fields. They must hence be worn for more than 18 hours per day for optimal benefit (8). Unsurprisingly, this is a cumbersome undertaking made worse by the fact that these arrays can irritate the scalp that may have already been compromised by radiation.

Highlight box

Key findings
- Radiation scalp-sparing volumetric-modulated arc therapy (SSV) for glioblastomas (GBMs) can minimize radiation doses to the scalp without compromising target coverage or exceeding critical normal structure doses.

What is known and what is new?
- Radiation therapy (RT) causes significant scalp toxicity that can impact patients' quality of life.
- We demonstrate the feasibility of a scalp-sparing VMAT approach to minimizing undesirable radiation doses to the scalp.

What is the implication, and what should change now?
- Scalp-sparing VMAT can be safely and effectively used in the treatment of GBM to minimize RT-induced scalp toxicity.

Erythema, dermatitis, ulceration, and open wounds have all been reported due to their use in up to 35% of patients (9). These dermatologic side effects can ultimately affect patient com/pliance with the requirement for more than 18 hours of wear time (10).

Radiation itself is a scalp irritant as well. It causes local endarteritis, fibrosis, myofibroblast injury, and epithelial atrophy, which eventually translate into a loss of scalp thickness, elasticity, and vascularization (11-14). These changes increase the risk of post-surgical wound dehiscence, wound infection, flap loss, and bone plate infection (15-18). Reducing such risks could become even more important as TTFields are incorporated into the concurrent chemoradiation phase of the treatment. EF-32 clinical trial is an ongoing trial testing just that (19). By reducing radiation injury to the skin, we may be able to avoid exacerbating this injury with the subsequent use of TTFields.

Both clinicians and patients, therefore, have a vested interest in preventing or mitigating dermatologic toxicity.

Dermatologic toxicity

Dermatologic toxicity is usually managed either prophylactically or with treatment interventions. Prophylactic measures include educating patients on proper scalp care, hygienic ways to apply and remove the transducer arrays, and to periodically shift the arrays to different parts of the scalp. Treatment interventions can consist of topical corticosteroids if patients develop scalp dermatitis or topical antibiotics if they show signs of scalp infection. For more severe skin side effects, small treatment interruptions can also be considered to give the skin a chance to heal (9,20).

A novel way to mitigate such toxicities may be to reduce scalp radiation by contouring the scalp as an organ at risk (OAR) and using scalp dose constraints during treatment planning. This technique is termed scalp-sparing volumetric-modulated arc therapy (SSV) (21).

Such scalp avoidance, however, should not trade decreased scalp toxicity for optimal clinical outcomes or expose critical brain structures to unjustifiable risk. These outcomes depend on many factors, including the delivery of a sufficiently lethal radiation dose to the tumor as evidenced by the planning treatment volume (PTV) dose distribution (22). Harm to critical brain structures, including the brainstem, optic nerves, and optic chiasm, is minimized by respecting their radiation tolerances (23).

Knowledge gap and objective

A single arm pilot study (clinicaltrials.gov Identifier: NCT03477110) investigated the safety of delivering SSV in conjunction with TTFields and reported favorable findings (14). To our knowledge, a head-to-head dosimetric comparison between SSV and traditional non-SSV approaches has not been reported in the literature. Herein we compare dosimetric parameters between the two approaches, including scalp, PTV, and Organ at Risk (OAR) doses, to test the efficacy of an SSV approach in reducing scalp dose without compromising PTV coverage or putting OARs at risk.

Such an approach has the potential to prevent or reduce scalp toxicities for GBM patients and increase compliance. A prospective trial evaluating the clinical benefit of this technique is ongoing (Clinicaltrials. gov, identifier: NCT03251027).

We present this article in accordance with the STROBE reporting checklist (available at https://cco.amegroups.com/article/view/10.21037/cco-23-15/rc).

Methods

This retrospective cross-sectional study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Thomas Jefferson University Hospital's (TJUH) institutional review board (No. FWA 00002109) and individual consent for this retrospective analysis was waived.

Patient selection

We retrospectively queried patient databases from TJUH and identified 19 patients with newly diagnosed GBMs, World Health Organization (WHO) Grade IV, who were treated at our institution between 2015 and 2018 with standard of care (SoC) treatment (24), including concurrent chemotherapy [temozolomide (TMZ): 75 mg/m^2] and conventional VMAT without scalp-sparing optimization to a total dose of 60 Gy. This included patients who received RT in a single course, 60 Gy in 30 fractions, as well as a split course, consisting of 46 Gy in 23 fractions to an initial volume followed by 14 Gy in 7 fractions to a cone-down, smaller volume. We excluded patients who received hypofractionated radiation treatment.

Scalp, OAR, and target volume contours

We generated scalp contours on the CT simulation scans used for the patients' original non-SSV treatment planning. The scalp was defined as a 5-mm thick, rind-like structure directly beneath the cranial skin surface. This scalp contour was extended caudally to the level of the foramen magnum (14). *Figure 1* shows the scalp contour for a representative patient in axial, coronal, and sagittal planes as well as a 3D rendering.

Radiation Therapy Oncology Group (RTOG/NRG) consensus guidelines were used to delineate OARs (25). European Organization for Research and Treatment (EORTC) and RTOG guidelines were used to generate the CTV, GTV, and PTV contours per the treating physicians (26). We used the original non-SSV contours without modifications for SSV treatment planning.

The EORTC guidelines define the gross tumor volume (GTV) as the enhancing lesion on T1 post-contrast MR imaging as well as the post-op surgical cavity. The GTV is expanded by 2 cm to generate the CTV, which is then edited to reflect the natural barriers to tumor growth. This includes the bones, tentorium, and falx. Finally, the PTV is generated by geometrically expanding the CTV by 3 mm. Ninety-five percent of the PTV receives 100% of the prescribed radiation dose (60 Gy in 30 fractions).

The RTOG/NRG guidelines, on the other hand, use a staggered approach to contouring the target volumes. They define GTV1 as the T1 post-contrast enhancing lesion and the post-op surgical cavity. In addition, they require a GTV2, which is defined as GTV1, and all areas of FLAIR abnormalities on T2 MR imaging. Both the GTVs are radially expanded to generate CTV1 and CTV2 respectively. These CTVs are then edited to respect the natural barriers to tumor growth mentioned before. PTV1 and PTV2 are generated by uniformly expanding CTV1 and CTV2 by 3 mm. PTV1 is prescribed 46 Gy in 23 fractions. PTV2 is prescribed an additional 14 Gy in 7 fractions for a total dose of 60 Gy in 30 fractions.

A prospective randomized trial revealed no difference in outcomes in patients treated with either the RTOG volumes or the smaller EORTC volumes. Hence, treating physicians were allowed to use the guideline of their choice.

Radiation simulation, treatment planning, and dose constraints

Patients were simulated in a supine position on an intensity-modulated radiation therapy (IMRT) board. Aquaplast masks were used to immobilize patients' head and neck areas in a neutral neck position.
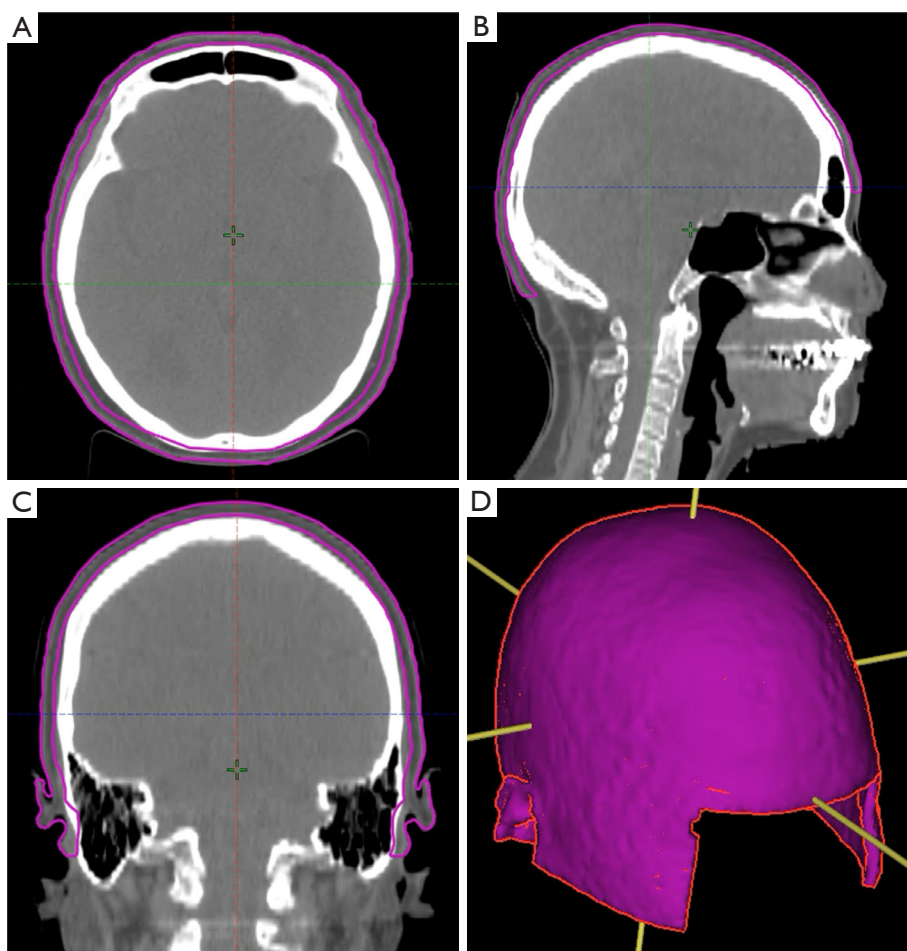
Figure 1 Scalp contour (magenta) for a representative patient in (A) axial, (B) coronal, and (C) sagittal planes. (D) shows a 3D rendering of the scalp. 3D, three-dimensional.

Volumetric modulated arc therapy (VMAT) technique was utilized for treatment planning. All plans were generated in Eclipse treatment planning system (Varian, Palo Alto, CA) using 6 MV photons. Initial treatment plans for all patients from 2015 through 2018 were planned in Eclipse version 11.0. Replanning with scalp sparing constraints for this study were done in Eclipse version 15.6.

Each plan utilized 2 clockwise and 2 counterclockwise (4 total) non-coplanar arcs. The arcs were primarily set ipsilateral to the PTV. A 0° couch angle was used for one set of arcs and a 90° couch angle was used for the other. If feasible, radiation beam entrance through the eyes was minimized by tilling the gantry angle away from the eyes. The same arc positions and range were used for the initial plans and replans.

Plans and replans were optimized to ensure that 95% of the PTV was covered by 100% of the dose. If the treatment consisted of initial and sequential boosts, each plan was normalized separately to cover 95% of the PTV with 100% of the dose, and then combined into a composite plan.

TJUH institutional dose constraints, derived from various protocols (27), were used for the initial plans and replans: Optic nerves D_{max} <58 Gy, Optic Chiasm D_{max} <56 Gy, Brainstem D_{max} <60 Gy, bilateral retina D_{max} <50 Gy, bilateral lens D_{max} <10 Gy Cochlea D_{max} <40 Gy, Scalp D_{mean} <20 Gy, Scalp D_{20cc} <50 Gy, Scalp V_{30cc} <40 Gy (25,28,29). Adequate PTV coverage was prioritized over scalp dose constraints.

Dosimetric evaluation

We compared various dosimetric parameters between non-

Table 1 Relevant baseline characteristics of patients used for our study

Baseline characteristics	Value
Age	
Median [range]	65 years [33–78]
Gender	
Male	84%
Female	16%
Resection	
GTR	37%
STR	63%
MGMT status	
Methylated	54%
Unmethylated	46%
IDH status	
Mutated	21%
Wild type	79%
Scalp volume, cm^3	
Median [range]	423 [379–468]
Treatment protocol	
EORTC	47%
RTOG/NRG	53%

MGMT, O6-Methylguanine-DNA Methyltransferase; IDH, isocitrate dehydrogenase; EORTC, European Organization for Research and Treatment; RTOG/NRG, Radiation Therapy Oncology Group.

SSV and SSV plans using dose-volume histograms (DVHs). To comprehensively quantify radiation doses to the scalp, we measured scalp D_{min}, D_{max}, D_{mean}, D_{20cc}, D_{30cc}, V_{30Gy}, V_{40Gy}, and V_{50Gy} for all plans. PTV D_{min}, D_{max}, and D_{mean} were measured to evaluate target volume coverage. Data on D_{max} to select critical structures including optic nerves and brainstem were also collected.

Statistical analysis

Two-sided student's *t*-test was used to compare the difference in doses to the parameters listed above between non-SSV and SSV plans. Statistical significance was defined at the 5% level (P<0.05). The analysis was performed using Prism version 10.0.40 for Mac (GraphPad Software Inc., La Jolla, California, USA).

Results

Nineteen patients treated at TJUH between 2015 and 2018 with SoC including non-SSV radiation plans were selected for our study. *Table 1* summarizes baseline patient characteristics. Eighty-four percent were male while 16% were female. Median age was 65 years (range, 33–78). Thirty-seven percent underwent a gross total resection while 63% received a subtotal resection. Fifty-four percent were O6-Methylguanine-DNA Methyltransferase (MGMT) methylated and 46% were unmethylated. Isocitrate dehydrogenase (IDH) was mutated in 21% of the patients while 79% were IDH wild type. Forty-seven percent of the patients received 60 Gy in 30 fractions in a single course, while 53% received split course radiation, with 46 Gy in 23 fractions followed by 14 Gy in 7 fractions delivered to initial and cone-down volumes respectively.

After adding the scalp as an OAR, new SSV plants were generated for all patients. *Table 2* compares median doses and doses delivered to different volumes for the scalp, PTV, and select OARs between non-SSV and SSV plans. SSV significantly reduced the minimum, maximum, and mean scalp doses, and doses received by 20 and 30 cc of the scalp.

The median scalp volume was 423 cm^3 (range, 363 to 468 cm^3). The median reduction in scalp D_{min} was 43.5% (range, –100% to 0%) from 0.3 to 0.1 Gy. The median reduction in scalp D_{max} was 2.8% (range, +13.4% to –24.9%) from 61.1 to 57.4 Gy. The median scalp D_{mean} reduction was 15.7% (range, +2.1% to –39.9%) from 13.3 to 11.1 Gy. Median reductions in scalp D_{20cc} and D_{30cc} were 19.5% (range, –2.7% to –54.5%), from 38.7 to 31.5 Gy, and 19.0% (range, –5.3% to –39.5%), from 34.5 to 27.4 Gy, respectively. Additionally, the median volumes of the scalp receiving 30 Gy, 40 Gy, and 50 Gy were reduced by 42.3% (range, –70.6% to –12.5%), 72% (range, –100% to –2.3%), and 92.4% (range, –100% to +5.4%) respectively.

Figure 2 is a visual depiction of scalp dose reduction in a representative patient achieved via an SSV plan. *Figure 3* shows non-SSV scalp DVHs (thin solid red lines) overlaid with SSV scalp DVHs (thin solid green lines) for individual patients as well as the mean non-SSV (thicker dashed red line) and mean SSV (thicker dashed green line) scalp DVHs for the entire cohort.

The 9 patients treated in accordance with the EORTC

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Table 2 Median doses, and doses delivered to different volumes for the scalp, PTV, and select OARs

| Structures	Dose/Volume	Non-SSV median[1]	SSV median[2]	Median % change[3]	P value[4]
Scalp	D_{min} (Gy)	0.3	0.1	−43.5	<0.01
	D_{max} (Gy)	61.1	57.4	−2.8	0.04
	D_{mean} (Gy)	13.3	11.1	−15.7	<0.01
	D_{20cc} (Gy)	38.7	31.5	−19.5	<0.01
	D_{30cc} (Gy)	34.5	27.4	−19.0	<0.01
	V_{30Gy} (cm^3)	40.2	25.8	−42.3	<0.01
	V_{40Gy} (cm^3)	18.6	6.2	−72.0	<0.01
	V_{50Gy} (cm^3)	7.0	0.2	−92.4	<0.01
PTV	D_{min} (Gy)	47.9	51.3	2.0	0.50
	D_{max} (Gy)	64.9	65.8	1.4	0.57
	D_{mean} (Gy)	61.7	61.9	0.2	0.64
OAR					
Right optic nerve	D_{max} (Gy)	45.9	45.2	−0.8	0.68
Left optic nerve	D_{max} (Gy)	39.2	35.8	0	0.61
Optic chiasm	D_{max} (Gy)	51.6	52.1	0.8	0.27
Brainstem	D_{max} (Gy)	54.5	54.8	0.8	0.68

[1], non-SSV plan; [2], SSV plan; [3], median % change in dose between non-SSV and SSV plans; [4], P values with statistical significance defined at the 5% level (P<0.05). PTV, planning target volume; OAR, organ at risk; SSV, scalp-sparing volumetric-modulated arc therapy.
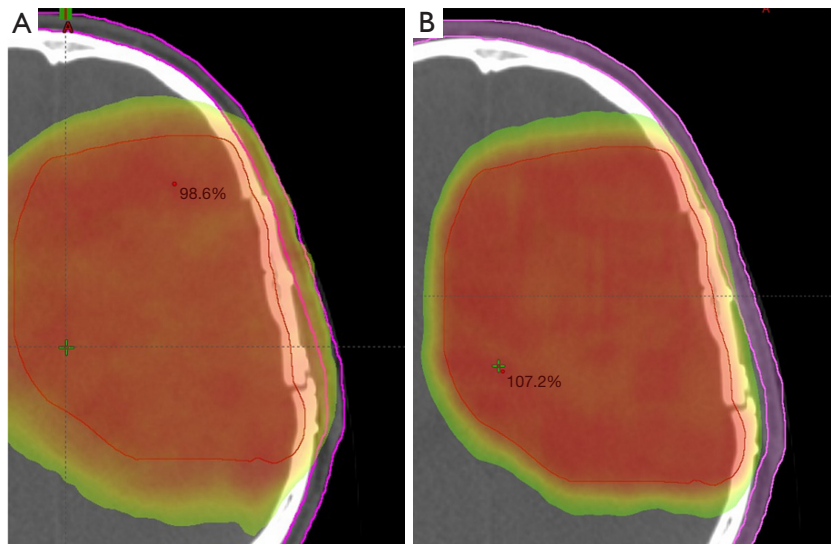
Figure 2 Reduction in dose to a patient's scalp (magenta contour) from a non-SSV plan (A) to an SSV plan (B). PTV is demarcated by the red contour. Dose wash encompasses an area covered by the 75% iso-dose line. PTV, planning target volume; SSV, scalp-sparing volumetric-modulated arc therapy.
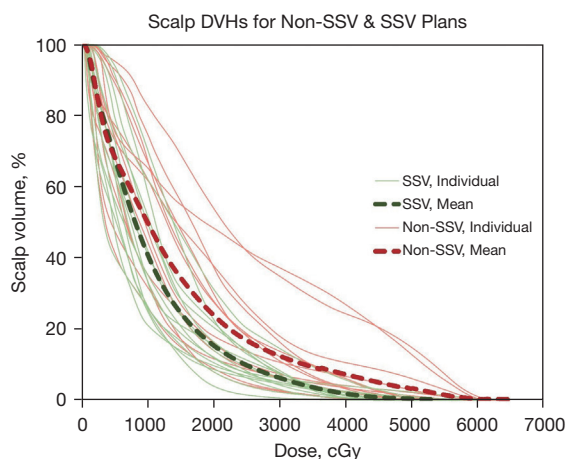
Figure 3 DVHs showing a reduction in scalp dose across all patients when planned using an SSV (green) versus a non-SSV approach (red). The thinner solid red lines represent individual non-SSV scalp DVHs, while the thicker dashed red line depicts the mean non-SSV scalp DVH. The thinner solid green lines represent individual SSV scalp DVHs and the thicker dashed green line depicts the mean SSV scalp DVH. DVHs, dose-volume histograms; SSV, scalp-sparing volumetric-modulated arc therapy.
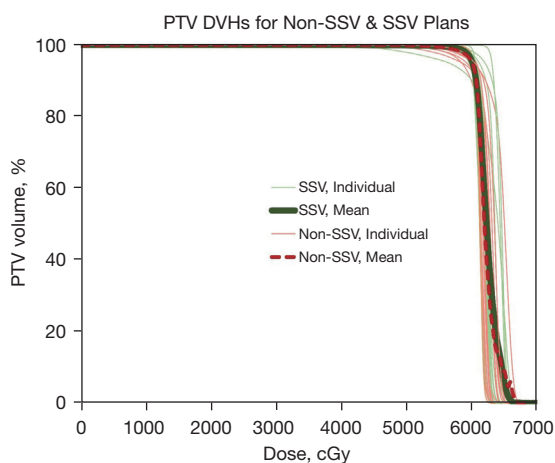
Figure 4 DVHs showing no significant difference in PTV doses across all patients when planned with either an SSV (green) or a non-SSV approach (red). The thinner solid red lines represent individual non-SSV PTV DVHs, while the thicker dashed red line depicts the mean non-SSV PTV DVH for all patients. The thinner solid green lines represent individual SSV PTV DVHs and the thicker solid green line depicts the mean SSV PTV DVH for all patients. PTV, planning target volume; DVHs, dose-volume histograms; SSV, scalp-sparing volumetric-modulated arc therapy.

protocol were analyzed separately. The median scalp volume was 410 cm^3 (range, 379 to 468 cm^3). The median reduction in scalp D_{min} was 90.6% (range, –100% to 0%) from 0.4 to 0 Gy. The median scalp D_{max} increased by 2.2% (range, –24.9% to +13.4%) from 62.6 to 63.1 Gy. The median scalp D_{mean} reduction was 23.5% (range, –39.9% to –1.4%) from 11.4 to 9.9 Gy. Median reductions in scalp D_{20cc} and D_{30cc} were 22.6% (range, –36.9% to –2.7%; P=0.92), from 37.4 to 33.5 Gy, and 25.5% (range, –39.5% to 5.3%; P=0.10), from 34.5 to 26.6 Gy, respectively. Additionally, the median volumes of the scalp receiving 30 Gy, 40 Gy, and 50 Gy were reduced by 58.4% (range, –70.6% to –15.1%), 76.4% (range, –100% to –2.3%), and 66.0% (range, –100% to +5.4%) respectively.

The 10 patients treated in accordance with the RTOG/NRG guidelines were similarly analyzed separately and then compared to the EORTC patients (P values noted in parenthesis). The median scalp volume was 417 cm^3 (range, 363 to 449 cm^3; P=0.46). The median reduction in scalp D_{min} was 41.0% (range, –83.6% to 0%; P=0.12) from 0.2 to 0.1 Gy. The median scalp D_{max} decreased by 8.0% (range, –23.1% to +6.7%; P=0.23) from 59.9 to 55.5 Gy. The median scalp D_{mean} reduction was 13.3% (range, –25.4% to +2.1%; P=0.16) from 13.9 to 12.0 Gy. Median reductions in scalp D_{20cc} and D_{30cc} were 18.6% (range, –54.5% to –13.2%; P=0.92), from 39.5 to 31.5 Gy, and 16.7% (range, –30.1% to –12.9%; P=0.10), from 35.3 to 28.2 Gy, respectively. Additionally, the median volumes of the scalp receiving 30 Gy, 40 Gy, and 50 Gy were reduced by 40.9% (range, –55.9% to –12.5%; P=0.26), 71.8% (range, –86.4% to –34.1%, P=0.68), and 96.1% (range, –100% to –14.9%, P=0.14) respectively. There was no statistically significant difference in these parameters between the EORTC and RTOG/NRG patients.

There is no significant dosimetric difference in the PTV between the non-SSV and SSV plans. The median D_{min} was 47.9 Gy and 51.3 Gy (+2.0% change, P=0.50), the median D_{max} was 64.9 Gy and 65.8 Gy (+1.4% change, P=0.57), and the median D_{mean} was 61.7 Gy and 61.9 Gy (0.2% difference, P=0.64) for the non-SSV and SSV plans respectively. Similarly, D_{max} to the brainstem, optic nerves, and optic chiasm did not change significantly between non-SSV and SSV plans (as shown in *Table 2*).

Figure 4 depicts non-SSV PTV DVHs (thin solid red lines) overlaid with SSV PTV DVHs (thin solid green lines) for individual patients as well as the mean non-SSV (thicker

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dashed red line) and mean SSV (thicker solid green line) PTV DVHs for the entire cohort.

Discussion

The toils of undergoing GBM treatment cannot be overstated. In addition to the logistical challenges that upend patients' lives, they must contend with treatment toxicity that takes a toll on their quality of life (QoL). This includes fatigue, dizziness, blood cytopenias, alopecia, and non-healing scalp wounds (30), among others (4), Scalp toxicity has become especially concerning due to the incorporation of TTFields in the GBM treatment package. TTFields use transducer arrays, which are secured to the same areas of the scalp with adhesives for long periods of time, leading to continuous thermal, mechanical, chemical, and moisture-related irritation to the scalp (9). Irradiated skin is especially vulnerable to these insults, as radiation compromises the highly ordered sequence of cellular events required for wound healing (31). Thus, reducing radiation doses to the scalp to minimize toxicity is a veritable clinical goal. Our study demonstrates that this goal is achievable through an SSV treatment approach applied to both the EORTC and RTOG guidelines for GBM treatment.

Of course, minimizing scalp toxicity should not take precedence over objectives critical to treatment success. Ensuring adequate target or PTV coverage and not dosing highly critical brain structures beyond their tolerances are goals of the highest priorities. Unsurprisingly, PTV underdosing is predictive of treatment failures (22). Ideal PTV coverage requires V100 ≥95% PTV, but this is not always possible, especially if the tumor is in the vicinity of critical structures (21). Therefore, V95% ≥95% PTV is an acceptable and likely more practical alternative. Our study shows that an SSV approach does not lead to inadequate PTV doses, and thus, does not cause an unjustifiable increase in the risk of treatment failure.

PTV volumes, especially in the case of peripheral tumors, can also encroach on the scalp (32). This can necessitate violating the scalp dose constraints, and therefore, strict sparing may not always be practical. Even in such cases, minimizing scalp dose to reasonably achievable levels may avoid the degree of scalp toxicity that may otherwise result from total scalp non-avoidance.

Another treatment planning consideration is the abundance of critical structures (OARs) in the vicinity of GBM tumors. Firstly, GBM severely curtails patients' lifespan, making optimizing the QoL a prime consideration

for many. Any damage to critical brain structures and the consequent sequalae naturally run counter to this consideration (33). Brainstem injury, for example, can lead to gait instability, debilitating muscle weakness, and facial paralysis (23,34). Injury to the optic nerves may result in vision loss (35). Secondly, GBM has an undesirable knack for recurrence, which can require additional radiation for management (36). The feasibility of any retreatment hinges on the doses delivered to the OARs during prior courses of radiotherapy. All in all, radiation oncologists are doubly incentivized to respect dose constraints to critical structures. Our analysis shows that sparing the scalp did not violate these constraints, establishing the safety of the SSV approach.

Our study has limitations inherent to all retrospective analyses, such as selection biases. We included a small cohort of 19 patients. It is possible that this represents a patient population with tumors unusually amenable to an SSV approach. There could be GBM tumors unlike the ones in our study where the scalp cannot be meaningfully spared unless PTV dose or OAR safety is compromised. Additionally, we did not treat patients with the SSV plans. Therefore, we cannot conclude whether this approach would translate into an effective decrease in scalp toxicity. Preliminary results from an ongoing prospective phase II trial evaluating this benefit (clinicaltrials.gov Identifier: NCT03251027) were encouraging. Patients treated with an SSV approach had a median 13% decrease in scalp thickness 9 months post-radiation as compared to a 30% decrease reported for the non-SSV cohort (2). A decrease in scalp thickness correlates with scalp toxicity.

SSV is a feasible technique to significantly reduce scalp radiation doses without sacrificing tumor coverage or overdosing critical brain structures. This could translate into reduced short and long-term toxicity to the scalp. This is especially important as TTFields, now a staple in the GBM treatment paradigm, come with their own scalp side effects that can compound radiation-induced dermatologic injuries. By circumventing such injuries, we can greatly improve patients' QoL. This may lead to reduced acute and late radiation toxicity to the scalp. A prospective trial evaluating the clinical benefit of this technique is ongoing (clinicaltrials.gov Identifier: NCT03251027).

Conclusions

Scalp-sparing VMAT is a feasible technique that can significantly reduce scalp radiation dose without

compromising target coverage or critical normal structure doses. This may lead to reduced acute and late radiation toxicity to the scalp. A prospective trial evaluating the clinical benefit of this technique is ongoing (clinicaltrials. gov Identifier: NCT03251027).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Chinese Clinical Oncology* for the series "Recent Advances in Neuro-Oncology". The article has undergone external peer review.

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://cco. amegroups.com/article/view/10.21037/cco-23-15/rc

Data Sharing Statement: Available at https://cco.amegroups. com/article/view/10.21037/cco-23-15/dss

Peer Review File: Available at https://cco.amegroups.com/ article/view/10.21037/cco-23-15/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cco.amegroups. com/article/view/10.21037/cco-23-15/coif). The series "Recent Advances in Neuro-Oncology" was commissioned by the editorial office without any funding or sponsorship. WS served as the unpaid Guest Editor of the series and serves as an unpaid Associate Editor-in-Chief of *Chinese Clinical Oncology* from October 2019 to September 2023. WS also received consulting fees from Brainlab, Novocure, Zai Lab, and Varian, and participated in the advisory board for Novocure. HL received funding from Brainlab and participated in BrainLAB Novalis circle educational webinar. The other authors have no other 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Thomas Jefferson University Hospital's (TJUH) institutional review board (No. FWA 00002109) and individual consent for this retrospective analysis was waived.

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