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Dosimetric Evaluation of Fractionated Stereotactic Radiation Therapy for Skull Base Meningiomas Using HyperArc and Multicriteria Optimization

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Abstract

Purpose: Treatment planning of skull based meningiomas can be difficult due to the irregular shaped target volumes and proximity to critical optic structures. This study evaluated the use of HyperArc (HA) radiosurgery optimization and delivery in conjunction with multicriteria optimization (MCO) to create conformal and efficient treatment plans for conventionally fractionated radiation therapy to difficult base-of-skull (BOS) lesions.

Methods and Materials: Twelve patients with BOS meningioma were retrospectively planned with HA-specific optimization algorithm, stereotactic normal tissue objective (SRS-NTO), and conventional automatic normal tissue objective to evaluate normal brain sparing (mean dose and V20 Gy). MCO was used on both SRS-NTO and automatic normal tissue objective plans to further decrease organ-at-risk doses and target dose maximum to within clinically acceptable constraints. Delivery efficiency was evaluated based on planned monitor units.

Results: The SRS-NTO in HA can be used to improve the mid- and low-dose spread to normal brain tissue in the irradiation of BOS meningiomas. Improvement in normal brain sparing can be seen in larger, more irregular shaped lesions and less so in smaller spherical targets. MCO can be used in conjunction with the SRS-NTO to reduce target dose maximum and dose to organ at risk without sacrificing the gain in normal brain sparing.

Conclusions: HA can be beneficial both in treatment planning by using the SRS-NTO and in delivery efficiency through the decrease in monitor units and automated delivery.

Introduction

Base-of-skull (BOS) meningiomas account for nearly 35% to 50% of all intracranial meningiomas.[1] The extent of surgical resection is a prognostic factor of progression free survival rates; however, the challenge of resecting BOS meningiomas using microsurgical techniques is the proximity to cranial nerves II-VI, brain stem, and the

internal carotid arteries. In the 1990s, stereotactic radio-surgery (SRS) became an alternative treatment method, either as primary or adjuvant therapy for BOS lesions with similar 5-year tumor control rates and less morbidity than surgery.[2-4] In the 2000s, improvements in magnetic resonance imaging (MRI), image guided radiation therapy, and intensity modulated radiation therapy (IMRT), established radiation therapy (RT) as an effective method of managing BOS meningioma.

Hypo-fractionated stereotactic radiation therapy (hFSRT), in 5 to 10 fractions, or fractionated stereotactic radiation therapy (FSRT), in greater than 10 fractions, are techniques used when use of SRS may be prohibitive owing to tumor size, location adjacent to critical organs at risk (OARs), or other logistical reasons (such as inability of patient to lie supine for treatment duration). FSRT and hFSRT combine the precision of stereotactic immobilization and steep dose gradients while simultaneously providing the benefit of fractionation, allowing for normal tissue repair. Studies comparing SRS, hFSRT, and FSRT treatments for BOS meningiomas show no statistical significance in progression free survival and lower incidence of adverse effects using hFSRT and FSRT for larger lesions.[5-9] RT-related toxicities for large lesions include increased risk of edema, radiation necrosis, clinical worsening of neurologic functions, and permanent neurologic deficits.[10] The risk of secondary meningiomas developing after RT is also a concern for younger, pediatric patients.[11]

RT methods for BOS lesions include protons; carbon ions; and photons with conformal dynamic arc, tomotherapy, IMRT, and volumetric modulated arc therapy.[12-15] Particle-based RT is known to better spare normal tissue and OARs and is ideal for pediatric cases; however, photons are more readily available. Comparison of photon planning and delivery techniques has shown that IMRT achieves conformal dose distributions, whereas noncoplanar beams allow further sparing of normal tissues.[16]

HyperArc High Definition Radiotherapy (HA-HDRT) (Varian Medical Systems, Palo Alto, CA) is a commercial solution designed to improve plan quality and delivery efficiency for noncoplanar intracranial radiosurgery. The SRS normal tissue objective (SRS-NTO) in HyperArc (HA) optimization is a radiosurgery algorithm that focuses on creating sharp dose gradients at the edges of the target volume to decrease dose to surrounding normal tissues. The SRS-NTO is designed to control dose fall-off and dose bridging at the level of 17% of the prescription dose. It differs from the automatic-NTO (AutoNTO) used in conventional volumetric modulated arc therapy planning by using a set of spatially variant upper dose constraints that are weighted based on the size, shape, and position relative to the target. The AutoNTO uses a cost function that defines the shape of the dose fall-off, which is controlled by a set of internal parameters that are dynamically adapted during optimization.[17]

A patient protection zone in the HA-HDRT workflow, which incorporates the immobilization device, safely places the isocenter allowing for automated delivery of noncoplanar arcs with built-in clearance checks. These tools are valuable in radiosurgery planning and delivery, allowing for more consistent plan quality and avoidance of potential collisions.[18] Previous studies have shown the efficacy of HA-HDRT delivery for single isocenter radiosurgery of multiple lesions, as well as the ability to further decrease moderate-to-low normal brain dose using the SRS-NTO compared with conventional VMAT planning.[19,20]

BOS target volumes frequently overlap OARs once margins are added, which makes achieving both target coverage and OAR sparing challenging. Optimization of the overlap region is recommended in the NRG Oncology Radiation Therapy Oncology Group 0539 study, a phase II trial for RT of intermediate and high-risk meningiomas.[21] The overlap between the planning target volume (PTV) and planning OAR volume (PRV) is defined as the PTV_{PRV}. The PTV_{PRV} is optimized to receive as much of the prescription dose as possible while maintaining OAR max point dose (0.03 cm^3) constraints. Another technique is to use multicriteria optimization (MCO). MCO is used in many fields to help make optimal decisions when tradeoffs exist between 2 or more conflicting objectives.[22]

In treatment planning, MCO has been shown to be useful in multiple disease sites such as intracranial, head and neck, lung, and pancreas.[23-25] The Eclipse MCO algorithm uses an epsilon constraint method to generate a library of plans that cover the pareto surface. The user navigates the pareto surface in the MCO tradeoff workspace by using slider bars that interactively display dose tradeoffs.[17,26] Previous studies used MCO to maximize tradeoffs in cases with multiple OARs, decrease planning time, supplement knowledge-based-model creation, and allow physician navigation of best clinical tradeoffs.[27,28] MCO has yet to be used in conjunction with SRS-NTO to control tradeoffs between steep dose gradients and target dose maximum. Tradeoff for highly conformal dose distributions using the SRS-NTO in HA is a higher maximum dose, which is carefully regulated to minimize the risk of radiation necrosis. In this study, HA-HDRT was applied to conventionally fractionated BOS meningiomas, using the SRS-NTO to decrease normal brain dose, in conjunction with MCO to minimize hotspots from HA-HDRT and dose to adjacent OARs.

Methods and Materials

Patient selection

Twelve patients previously treated at our institution with BOS meningiomas were retrospectively replanned. All patients were World Health Organization grade I; 6
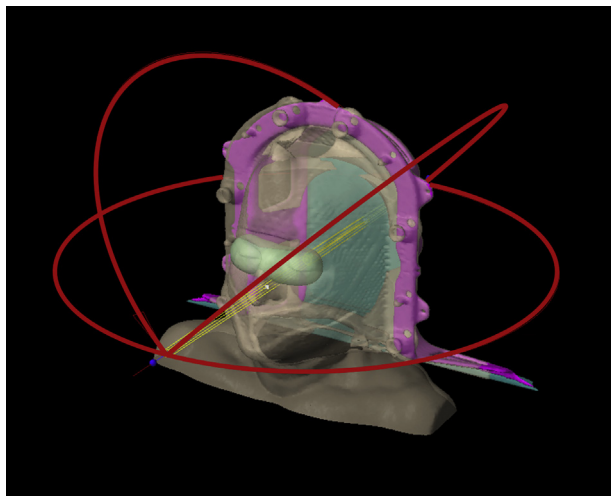
Figure 1 Patient immobilized in Encompass QFix SRS Immobilization system (cyan and magenta) with "virtual goggles" structure (light green) to avoid irradiation of orbits. Arc geometry shown with 2 180° coplanar arcs and 2 arcs with couch rotation of 45 and 315°. (A color version of this figure is available at https://doi.org/10.1016/j.adro.2021.100663.)

received subtotal or partial resection and the other 6 patients were not candidates for surgery owing to proximity and involvement of the optic pathway. These patients were specifically chosen due to the target volume located adjacent to 1 or more OARs. The gross target volume was contoured based on gadolinium-contrast enhanced MRI; a 2-mm margin was used to create the PTV. The average PTV volume was 38.02 cm^3 (0.90-114.68 cm^3). The original plans were prescribed to either 52.2 or 54 Gy in 1.8 Gy fractions to the PTV depending on OAR constraints.

Patients were immobilized in the Encompass SRS Immobilization System (QFix, Avondale, PA). The QFix Encompass SRS system consists of a 2-piece clamshell style mask attached to a U-shaped carbon fiber couch insert. It is a prerequisite for HA-HDRT delivery because the Encompass system is used to demarcate the patient protection zone in the treatment planning system. Contrast-enhanced computed tomography images were obtained on a Philips Brilliance Big Bore CT scanner (Philips, Best, Netherlands) with 1-mm slice thickness and fused with the contrast-enhanced MR.

Plan setup and optimization

Treatment planning was performed in the Eclipse Treatment Planning System v15.6 (Varian Medical Systems, Palo Alto, CA) on an EDGE linear accelerator (Varian Medical Systems) equipped with a high-definition multileaf-collimator. Plans were optimized using the 6 MV flattened beam with a maximum dose rate of 600 MU/min and calculated with the default HA grid size of 1.25 mm. The HA template includes 2 180° coplanar arcs

and 3 additional noncoplanar arcs with couch rotations of 45, 315, and 90 or 270. For predominantly left or right sided disease, only 3 arcs were used with couch kicks of 0 and 45 or 315, whereas when the lesion was located more midline, an additional vertex (couch 90/270°) was added to the 3-arc beam arrangement.

HA-specific optimization algorithms used were the collimator angle optimization algorithm and SRS-NTO. The collimator angle optimization algorithm optimizes the collimator angles to reduce the dose to the normal brain; the optimized collimator angles from the HA plan were used for all plans so that beam geometry remained the same. Furthermore, "virtual goggles" were created to protect the optic structures. A no beam entry rule was placed on this structure during optimization to avoid beams entering through the anterior optic pathways (see Fig 1).

Plans were replanned to 54 Gy and normalized so 95% of the PTV received 100% of the prescription dose. No optimization structures were used, because MCO was used to determine the tradeoffs between PTV and OAR. In addition, no margins were used on OARs. During optimization, equivalent priorities were used for the NTO and PTV (100); OARs used priorities of less weight (20).

In the MCO tradeoff workspace, 3 tradeoff objectives were chosen for the PTV: an upper and lower objective to 0% and 100% of the target volume, respectively, as well as a homogeneity objective. The homogeneity objective assists in maintaining coverage to the target volume while minimizing the hot spot. Upper point objectives to 0% of the OARs (brain stem, chiasm, optic nerves) were used. In the tradeoff workspace, the priority was to achieve the OAR objectives. After OAR goals were achieved, the OAR tradeoffs were locked before navigating to the best PTV coverage and homogeneity. To compare the effects of the SRS-NTO to the Auto-NTO, the MCO process was repeated for the AutoNTO. Four optimized plans were created for each patient: a HA plan using the HA-specific algorithms, a HA_{MCO} plan using the HA plan as the base plan for MCO optimization, an AutoNTO plan using the AutoNTO, and an $AutoNTO_{MCO}$ plan using the AutoNTO plan as a base plan for MCO optimization.

Dosimetric comparison

All plans were normalized to achieve the same PTV coverage to 95% of the PTV volume ($PTV_{D95\%}$). The doses to 99% and 1% of the PTV ($PTV_{D99\%}$ and $PTV_{D1\%}$) were evaluated. Maximum point dose to the OARs ($D_{0.035cc}$) was evaluated to ensure all plans met clinical dose constraints and did not differ significantly in each plan. The normal brain volume (Brain-PTV-Brainstem) receiving 20 Gy (NBrainV20Gy) and the mean dose ($NBrain_{mean}$) were evaluated. Conformity of the high-dose region was evaluated using the Paddick conformity index (CI), and the low-dose region was

Table 1   OARs and indices used in plan evaluation

Planning objectives		
OAR	Volume (cm^3)	Dose
Optic nerves and chiasm	0.035	54
Brainstem	0.035	54
Evaluation index		
Index	Description	Abbreviation
Normal brain (Brain − PTV − Brainstem)	Mean dose to normal brain	NBrain$_{mean}$
	Volume of normal brain receiving 20 Gy	NBrainV20Gy
Paddick conformity index	$\dfrac{TV_{RI}^2}{TV \times V_{100\%Rx}}$	CI$_{Paddick}$
Gradient index	$\dfrac{V_{50\%Rx}}{V_{100\%Rx}}$	GI

Abbreviations: OAR = organs at risk; PTV = planning target volume; TV = volume of target; TV$_{RI}$ = volume of target covered by the prescribed isodose line; V$_0$50$_{\%Rx}$ = volume of 50% prescription isodose; V$_{100\%Rx}$ = volume of 100% prescription isodose.

evaluated with the gradient index. Table 1 summarizes the evaluated OARs and indices.

Plan delivery and efficiency

To verify plan deliverability, plans were delivered and measured on the electronic portal imaging device. Using the portal dose image prediction algorithm, the calculated photon fluence was compared with the fluence delivered on the Varian amorphous silicon (aSi-1200) detector.[29] Gamma analysis was performed for each beam as well as the plan composite using a gamma passing criteria of 2% dose and 2 mm distance to agreement. Finally, to evaluate efficiency of delivery with HA automation, the monitor units (MU) were compared.

Results

Dosimetric comparison

Table 2 summarizes the doses to the target volume and OARs. Target hot spot, PTV$_{D1\%}$, was greater for the HA plans using the SRS-NTO compared with AutoNTO ($P = .003$). For SRS-NTO and AutoNTO plans, the addition of MCO increased target coverage (PTV$_{D99\%}$) and decreased PTV$_{D1\%}$ to achieve similar plan qualities. Compared with the AutoNTO, the SRS-NTO decreased both the NBrain$_{mean}$ and NBrainV20Gy without MCO ($P = .0002, .0007$) and with MCO ($P = .001, .003$). Figure 2a shows dose distributions and dose volume histograms (Fig 2b) from the 4 plans demonstrating the change in NBrainV20Gy. The NBrainV20Gy increased in HA$_{MCO}$ compared with HA plans on average by 10.16 cm^3 and in AutoNTO$_{MCO}$ compared with AutoNTO plans by 3.0 cm^3. HA$_{MCO}$ plans spared an additional 24 cm^3 of NBrainV20Gy compared with AutoNTO$_{MCO}$ plans. Although not typically evaluated, low doses to serial structures such as the optic pathway also showed a decrease in the HA plans using the SRS-NTO compared with AutoNTO plans, which can be observed in the shape of the dose volume histograms.

The sparing of NBrainV20Gy (AutoNTO$_{MCO}$ - HA$_{MCO}$) ranged from 0.97 to 66 cm^3. Due to the concavity of the volumes at the BOS and proximity to OARs, the change in NBrainV20Gy between AutoNTO$_{MCO}$ and HA$_{MCO}$ plans was compared with PTV sphericity (Fig 3). Sphericity quantifies how compact and similar an object is to a sphere, where a sphere has a sphericity of 1. The sphericity is calculated as the ratio of the surface area of a sphere with the same volume as the object to the surface area of the object. Sparing of greater than 20 cm^3 of NormBrainV20Gy occurred for PTV sphericity <0.85.

Table 2   Summary of DVH results of PTV coverage and organ-at-risk sparing showing average values ± standard deviation

Structure	Parameter	HA	HA$_{MCO}$	AutoNTO	AutoNTO$_{MCO}$
PTV	PTV$_{D99\%}$ (Gy)	52.52 ± 0.62	52.99 ± 0.48	53.04 ± 0.37	53.11 ± 0.42
	PTV$_{D1\%}$ (Gy)	64.60 ± 3.10	57.37 ± 1.50	61.41 ± 1.65	58.08 ± 1.66
	CI$_{Paddick}$	0.85 ± 0.06	0.80 ± 0.08	0.82 ± 0.05	0.79 ± 0.06
	GI	2.86 ± 0.59	3.14 ± 0.63	3.61 ± 1.04	3.54 ± 0.80
Optic chiasm	D0.035 cm^3 (Gy)	54.93 ± 2.67	52.06 ± 1.42	52.32 ± 2.34	52.40 ± 0.89
Brainstem	D0.035 cm^3 (Gy)	44.23 ± 15.50	43.40 ± 16.50	46.42 ± 13.92	44.10 ± 15.77
OpticNerve(L)	D0.035 cm^3 (Gy)	38.36 ± 18.81	34.61 ± 18.50	37.10 ± 17.28	35.24 ± 18.49
OpticNerve(R)	D0.035 cm^3 (Gy)	40.89 ± 19.24	38.14 ± 17.86	40.67 ± 15.69	39.75 ± 16.46
Normal brain	NBrain$_{Mean}$ (Gy)	5.95 ± 2.42	6.42 ± 2.63	7.20 ± 3.046	7.32 ± 3.16
	NBrainV20Gy (cc)	47.96 ± 26.95	58.12 ± 33.11	79.13 ± 48.27	82.13 ± 50.75
	Monitor units (MU)	742 ± 165	885 ± 179	1307 ± 383	1269 ± 438

Abbreviations: CI = conformity index; DVH = dose volume histogram; GI = gradient index; HA = HyperArc; MCO = multicriteria optimization; NTO = normal tissue objective; PTV = planning target volume.
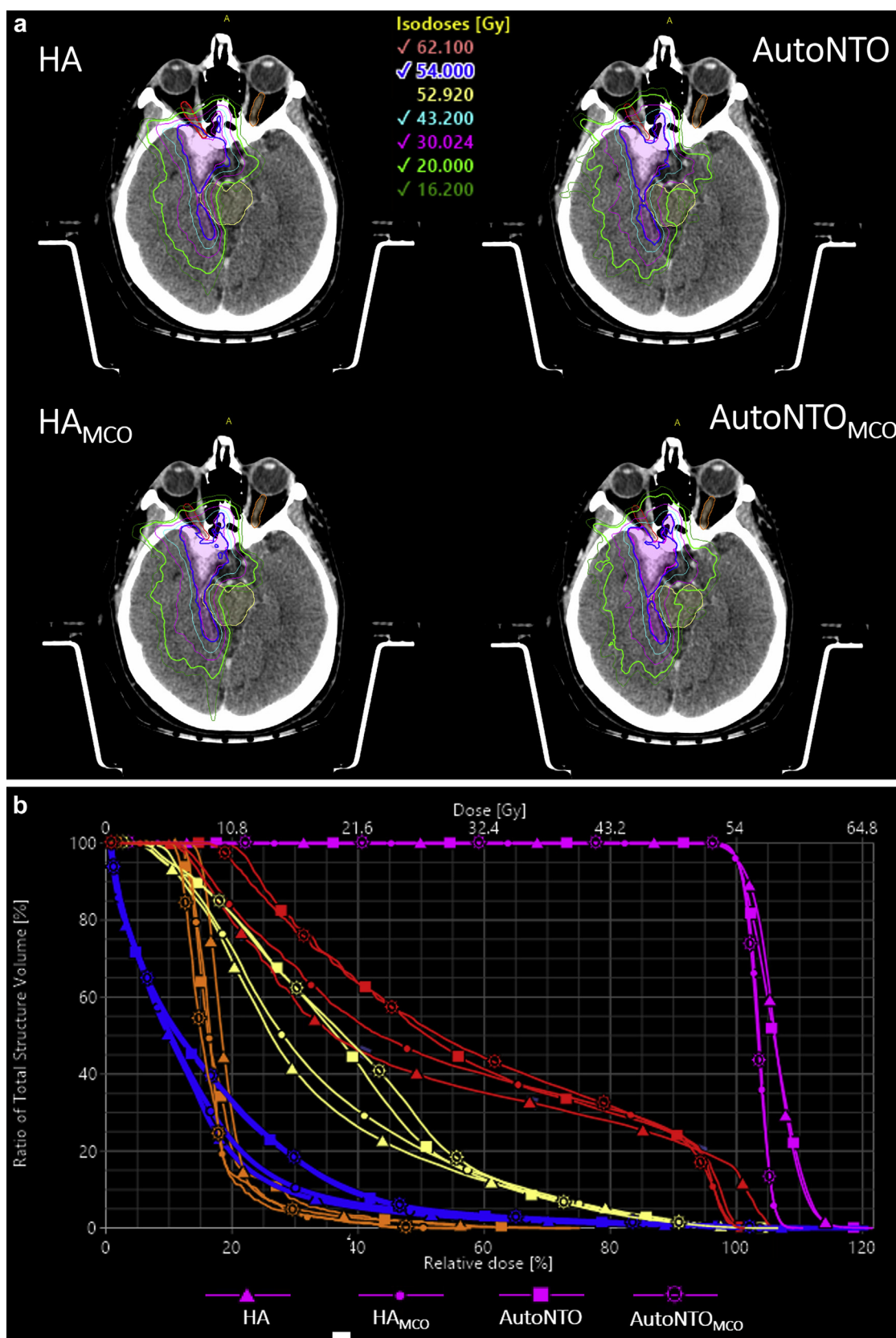
Figure 2 (a) Prescription dose (blue), mid-dose 43.2 Gy (cyan), and V20 Gy (light green). Note changes in conformality between upper and lower images with the addition of multicriteria optimization (MCO), with tradeoffs in normal brain dose. (b) Dose volume histogram (DVH) of planning target volume (PTV) (magenta), OpticNerve(L) (orange), OpticNerve(R) (red), Normal Brain (blue), and Brainstem (yellow). (A color version of this figure is available at https://doi.org/10.1016/j.adro.2021.100663.)
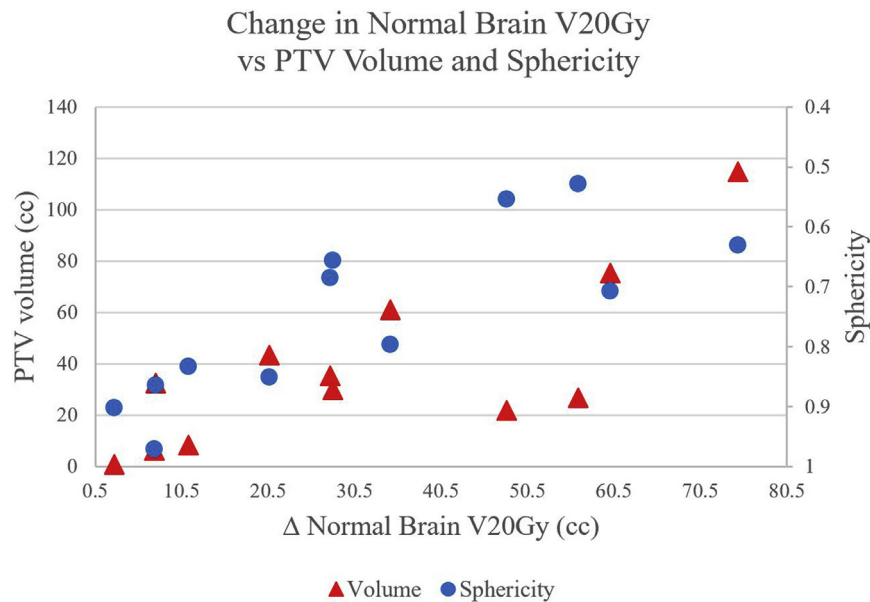
Figure 3   Change in normal brain volume receiving 20 Gy (NBrainV20Gy) between automatic-normal tissue objective multicriteria optimization (AutoNTO$_{MCO}$) and HyperArc (HA)$_{MCO}$ compared with planning target volume (PTV) and sphericity.

For OARs, neither SRS-NTO nor AutoNTO plans resulted in greater OAR doses. After MCO, all OAR objectives were met with no significant difference. The tradeoff in achieving OAR tolerance can be observed in the decrease in the CI$_{Paddick}$. HA and AutoNTO both have better conformality than their MCO counterparts ($P = .002$). After MCO optimization, both plans achieved similar conformality with no statistical difference ($P > .05$). The GIs of HA compared with AutoNTO plans were significantly better before MCO ($P = .0003$) as well as after MCO ($P = .0004$).

Deliverability and quality assurance

The HA plan used an average of 742 MUs whereas the AutoNTO plan required nearly double the MUs (Table 2). The MUs for the MCO plans increased on average by 146 MUs for the HA$_{MCO}$ plans but decreased by 38 MUs for the AutoNTO$_{MCO}$ plans.

The average plan composite gamma pass rate for the HA, HA$_{MCO}$, AutoNTO, and AutoNTO$_{MCO}$ plans was 99.5%. HA plans had the lowest plan composite pass rate of 98.1%. Per beam, no significant differences were observed between HA and AutoNTO plan delivery results. However, a slight decrease in per beam gamma pass rate was observed in the HA$_{MCO}$ compared with HA plans ($P = .04$).

Discussion

One risk of treating benign meningiomas with radiation is the risk of secondary malignancy and damage to normal brain and OARs. The risk of developing a meningioma after cranial irradiation was reviewed by Strojan et al,[11] with concern that irradiation of neighboring meninges would increase risk of secondary meningiomas. Indications of increased risk include younger age at presentation, a higher female:male ratio, and atypical histology. The use of SRS-NTO in HA optimization would significantly decrease the irradiated volume of normal brain for large, irregular shaped lesions, effectively lowering the inherent risk.

HA optimization algorithms not only have a dosimetric benefit, but the automated delivery of couch rotations in the HA-HDRT workflow allows for additional patient safety and treatment efficiency. For clinics that use noncoplanar beams sparingly, this allows an additional comfort level when clearance can be guaranteed before patient treatment, whereas for clinics that use noncoplanar beams frequently, automation of couch kicks assists in treatment efficiency, allowing rotations to be applied from the treatment console and no pause in treatment while waiting for beam mode-up. From the evaluation of MUs, the SRS-NTO HA optimizer converges to a more efficient solution compared with the AutoNTO.

Although delivery efficiency is increased when using HA, the planning time increases with the addition of the MCO library plan creation. The MCO algorithm creates $3n + 1$ plans for each objective, which can be time consuming if there are many objectives. To improve the efficiency, a new MCO feature available in v15.6 and above is hybrid optimization. This allows for faster calculation of the tradeoff plans using a hybrid IMRT technique that uses the graphics processing unit for IMRT optimization. HA-HDRT and MCO v15.6 does not allow for hybrid optimization without removing HA-HDRT delivery automation; automation cannot be added after

removal. Due to the benefits in delivery automation for HA plans, the hybrid optimization was not investigated in the study. Future investigations into the cost benefit in efficiency of using hybrid optimization may be performed.

The shortcoming of any planning study is the inherent plan bias. Comparison to the original treated plans was not performed owing to variability in use of noncoplanar arcs that affects the low-dose distributions. Similarly, owing to variability in planning techniques, some original plans were unable to meet OAR constraints and thus were not treated to 54 Gy. Although further investigation is needed, preliminary results show that MCO can achieve more consistent plan quality and perhaps allow for dose escalation with high-grade tumors as in Radiation Therapy Oncology Group 0539. In the MCO tradeoff-exploration space, the user controls slider bars where small changes lead to large changes in the final plan dose, making the process extremely user-dependent. Furthermore, in the tradeoff-exploration space, dose visualized in the workspace is not the final dose distribution because machine parameters and MLC motions need to be accounted for in the dose calculation. This can lead to slight changes in the target coverage and OAR sparing between MCO plans. In this study, we used the best effort to navigate to the same objectives in the tradeoff space and verify that dose constraints were met after final dose calculation. Because there are multiple solutions in the MCO space, the solution is user-dependent. It is not fair to say that the plan evaluated was objectively the best plan; however, it was optimized in a similar method for both SRS-NTO and Auto-NTO. Further investigation is warranted in exploring the MCO workspace to evaluate if the plan quality can be further improved.

Conclusions

HA and MCO can be used to improve the mid- and low-dose spread to normal brain tissue in the irradiation of BOS meningiomas. Greater improvement in normal brain sparing is seen in larger, more irregular shaped lesions and is less significant in smaller spherical targets. HA is beneficial both in treatment planning by using the SRS-NTO and in delivery efficiency through the decrease in MUs and automated delivery.

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