

The Effect of MLC Leaf Width in Single-Isocenter Multi-target Radiosurgery with
Volumetric Modulated Arc Therapy

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of Master of Science in the
Graduate Program in Medical Physics in the
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ABSTRACT

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Abstract

Purpose

Single-isocenter multi-target (SIMT) Volumetric Modulated Arc Therapy (VMAT) technique can produce highly conformal dose distributions and short treatment delivery times for the treatment of multiple brain metastases. SIMT radiosurgery using VMAT is primarily limited to linear accelerators utilizing 2.5mm leaf width MLCs. We explore feasibility of applying this technique to linear accelerators utilizing MLCs with leaf width of 5mm to broaden the applicability of SIMT radiosurgery using VMAT to include the greater number of linear accelerators with standard 5mm MLCs.

Methods

Twenty patients with 3-10 intracranial brain metastases originally treated with 2.5 mm leaf width MLCs were re-planned using standard 5mm leaf width MLCs and the same treatment geometry (3-5 VMAT arcs). Conformity index, low (V30%[%]), and moderate (V50%[%]) isodose spill were selected for analysis. V12Gy[cc] was also analyzed for single fraction cases. We tested the effects of several strategies to mitigate degradations of dose quality values when 5 mm leaf width MLCs were used; these included duplicating each VMAT arc with altered collimator angles by 10°, 15°, and 90°, and adding 1-2 VMAT arcs, with all arcs equally spaced.

Results

Wider MLCs caused small changes in total MUs (5827 ± 2334 vs 5572 ± 2220 , $p = .006$), and Conformity Index (CI) ($2.22\% \pm 0.05\%$, $p = .045$), but produced more substantial increases in brain $V30\%$ and $V50\%$ ($27.75\% \pm 0.16\%$ and $20.04\% \pm 0.13\%$ respectively, $p < .001$ for both), and $V12Gy[cc]$ ($16.91\% \pm 0.12\%$, $p < .001$). Adding duplicate VMAT arcs with shifted collimator angle was not effective at mitigating the increases in low and moderate isodose spill. Adding 1-2 additional equispaced arcs improved CI, $V50\%$ and $V12Gy[cc]$ with less improvement for $V30\%$.

Conclusion

SIMT radiosurgery delivered via VMAT using 5mm leaf width MLCs can achieve similar CI compared to that using 2.5mm leaf width MLCs but with moderately increased isodose spill, which can be only partially mitigated by increasing the number of VMAT arcs.

Dedication

To my parents and childhood dreams.

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List of Abbreviations

AAA - anisotropic analytical algorithm

CBCT - cone-beam CT

CI - conformity index

CT - computer tomography

CTV - clinical target volume

DCA - dynamic conformal arc

FFF - flattening filter free

GTV - gross tumor volume

IMRT - intensity-modulated radiation therapy

LINAC - linear accelerator

MIDCA - multiple-isocenter dynamic conformal arcs

MLC - multi-leaf collimator

MRI - magnetic resonance imaging

MU - monitor unit

MV - megavolt

OAR - organ at risk

PTV - planned target volume

RN - radiation necrosis

SIDCA - single-isocenter dynamic conformal arcs

SIMT - single-isocenter multi-target

SIRMIT - single-isocenter radiosurgery for multiple intracranial targets

SRS - stereotactic radiosurgery

TPS - treatment planning system

V10Gy[cc] - volume of brain excluding PTV receiving greater than or equal to 10Gy

V100%[%] - percent volume of brain receiving 100% of the prescribed dose

V12Gy[cc] - volume of brain excluding PTV receiving greater than or equal to 12Gy

V16Gy[cc] - volume of brain excluding PTV receiving greater than or equal to 16Gy

V30%[%] - percent volume of brain excluding PTV receiving greater than or equal to 30% of the prescribed dose

V50%[%] - percent volume of brain excluding PTV receiving greater than or equal to 50% of the prescribed dose

V8Gy[cc] - volume of brain excluding PTV receiving greater than or equal to 8Gy

VMAT - volumetric modulated arc therapy

V_{PTV} - volume of PTV

WBRT - whole-brain radiation therapy

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Finally, to my caring, loving, and supportive family who has been continuously believing in me.

1. Introduction

1.1 *Brain metastases*

Brain metastases occur in 9% to 17% of cancer patients [1]. An autopsy of the brain revealed that 24% of patients have intracranial metastases and 20% of patients have intraparenchymal or leptomeningeal metastases [2]. The most common primary tumors which metastasize to brain are lung and breast carcinoma and melanoma [2-3]. The increased incidence of patients with brain metastases is due to the increased surveillance, improved control of systemic cancer, and prolonged survival [1,3]. The treatment methods of brain metastases can be classified as surgery, whole-brain radiation therapy (WBRT), and stereotactic radiosurgery (SRS) [2-3].

1.2 *Brain metastases treatment methods*

1.2.1 Surgery

Surgery is most commonly used for patients with a single brain metastasis from controllable systemic disease, the metastases diameter > 4cm, or the metastases that abut critical structures, such as the optic nerves. However, the recurrence rate of a single brain metastases after resection is higher without postoperative radiotherapy [1-2].

1.2.2 Whole-brain radiation therapy

Historically, WBRT has been the standard treatment for brain metastases [1]. WBRT generally improves median survival and neurologic symptoms. The median survival ranges from 3 to 6 months with WBRT compared with 1 to 2 months long

survival without WBRT [2-3]. WBRT is preferred treatment for multiple brain metastases with poorly controlled or uncontrollable systemic diseases and brain metastases that are not surgically accessible [3-4]. However, WBRT is gradually being superseded by SRS, due to improved local control [1,3,5] and improved cognition after treatment [6,7].

1.2.3 Stereotactic radiosurgery (SRS)

SRS combines multiple focused radiation beams to deliver a highly conformal dose to the target while still sparing surrounding normal tissue [1-2]. SRS can treat multiple tumors simultaneously. SRS can be only used for tumors with < 3 cm in diameter [2]. SRS is also used postoperatively to decrease the risk of local recurrence after the tumor resection [1]. SRS can be delivered in one fraction with the prescription doses ranging from 15 Gy to 24 Gy [1] via multiple platforms including, multiple Cobalt sources [8-10], a linear accelerator mounted on a robotic arm [11-12], or isocentric linear accelerators [13-15].

1.3 Treatment delivery techniques using Linac SRS

Radiosurgery using isocentric linear accelerators has traditionally been carried out using dynamic conformal arcs (DCAs) to a single target [16,17], however a newer development is to treat multiple targets simultaneously using volumetric modulated arc therapy (VMAT). Clark et al. first demonstrated a single-isocenter VMAT radiosurgery technique which has the benefit of increased treatment efficiency [5,18] compared to traditional radiosurgery techniques. Single-isocenter multi-target (SIMT) VMAT

radiosurgery has been further developed in other studies with increasing clinical use [19,20].

With few exceptions, prior studies using a SIMT VMAT radiosurgery technique have utilized a 2.5mm leaf width MLCs within ± 4 cm of the isocenter [5,18-20]. However, a more common MLC width in use in standard linear accelerators is 5mm. The benefit of smaller MLC leaf widths is well-documented for single target conformal radiosurgery with DCAs and intensity-modulated radiation therapy (IMRT). Jin et al. showed that for DCAs, small leaf width MLCs provide better dose conformity than large leaf width MLCs especially for small target volumes. For IMRT technique, small leaf width MLCs have better sparing of small organs at risk (OARs) as compared to large leaf width MLCs [20]. Wu et al. also showed the dosimetric benefits of using of 2.5mm leaf width MLCs with IMRT technique for the treatment of small lesions [22]. Serna et al. performed a treatment planning study comparing 2.5mm and 5mm MLCs and reported that for 3D DCA therapy, the usage of small MLC leaf width decreases dose to OAR in close proximity to the planned target volume (PTV) and improves dose conformity [23]. While these benefits are well documented for DCA for a single target, it is not known whether they also apply to SIMT using VMAT. Indeed, a number of differences between these two techniques may diminish the benefit of smaller MLCs. For instance, it is reasonable to expect conformality of DCA plans to be highly sensitive to the MLC leaf width because the MLCs conform to the outline of the PTV; in contrast, for multi-target

VMAT the MLC trajectory dose is defined by the inverse optimization and thus may be less dependent on MLC leaf width.

In this study, we examined the effect of MLC leaf width on dosimetric quality of SIMT VMAT radiosurgery plans; we also considered several methods of mitigating any dosimetric plan quality degradations caused by 5mm leaf width MLCs.

2. Materials and methods

2.1 Summary

We re-planned 20 single-isocenter multiple brain metastases VMAT treatment plans using 5 mm leaf width MLCs which were originally created with 2.5 mm leaf width MLCs. The dosimetric quality comparisons between the plans were made using the V30%[%], V50%[%], V12Gy[cc], and Conformity Index (CI) metrics. Then we investigated several treatment plan modifications to mitigate degradations in dosimetric quality. These included duplicating each VMAT arc from the original plan, delivered with reverse rotation, and adjusting collimator angles (altered by 10°, 15°, and/or 90°). The rationale for this approach was that the additional arcs did not increase the number of couch angles and therefore would not significantly increase the treatment time. The second approach was to add an additional 1-2 VMAT arcs at a new couch position, with all arcs equally spaced.

2.2 Patient selection and treatment planning

In a retrospective institutional review board approved study, 20 patient plans used to treat 3-10 intracranial brain metastases with a SIMT technique in 2016 were selected for our study cohort. Our radiosurgery technique using a frameless SIMT technique has been described in detail previously [5,18-20]. In brief, patients were immobilized using noninvasive thermoplastic masks designed specifically for radiosurgery. The patients subsequently underwent computer tomography (CT) based

simulation with 1mm slices, which was fused with diagnostic magnetic resonance imaging (MRI) for treatment planning. Normal structures were contoured by a physicist or dosimetrist (verified by an attending radiation oncologist) using the CT and MRI including the brain, chiasm, optic nerves, eyes, and brainstem. For each metastatic lesion, the gross tumor volume (GTV) was delineated by the attending radiation oncologist and was equal to the clinical target volume (CTV). The PTV was equal to CTV + 1mm margin. The isocenter was generally placed at the geometric center of the combined PTV but was ultimately decided by the treatment planner. Treatment geometry included 3-5 VMAT non-coplanar arcs with flattening filter free (FFF) 6 MV photons. Single fraction dose was prescribed to sixteen cases and five fractions of dose was prescribed to the rest. All plans were normalized so that 99.5% of the combined PTV received the prescription dose. A TrueBeam machine (Varian Medical Systems, Palo Alto CA) equipped with 2.5mm leaf width MLCs within ± 4 cm of the isocenter, and 5mm leaf width for others was used for treatment planning and delivery of the clinical treatment. At each treatment fraction the patient was aligned prior to treatment using cone-beam CT (CBCT) with a 6-degree of freedom couch correction.

Each plan was re-optimized in the Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA) using the same beam geometry, prescription dose, optimization parameters, and dose normalization and planned to be delivered using a TrueBeam machine equipped with a 5mm leaf width MLCs. The commissioned

MLC parameters in the TPS included transmission factor and leaf gap; for the 2.5mm leaf width MLCs these were 0.012 and 0.4mm, respectively, and for the 5 mm leaf width MLCs were 0.016 and 1.2mm, respectively. Aside from MLC parameters, the models for the two beam energies were identically matched, using the anisotropic analytical algorithm (AAA) version 13.6.23 dose calculation model with 1mm dose grid size. The treatment plan geometry is shown in Figure 1.

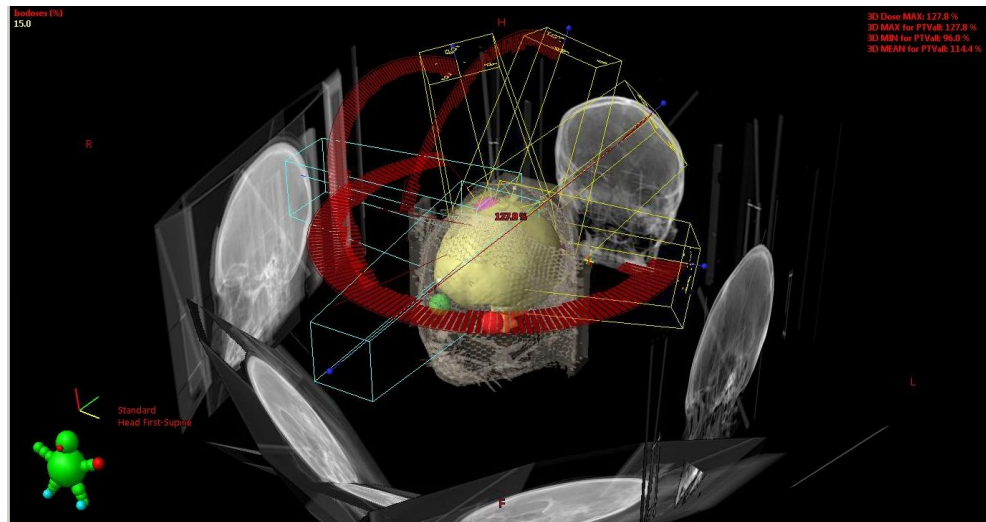


Figure 1: Plan geometry.

2.3 Plan evaluation

CI, as well as low and moderate isodose spills (brain V30%[%] and V50%[%]) were selected for analysis. We used the following definition of CI:

$$CI = \frac{V_{100\%}[cc]}{V_{PTV}[cc]}$$

where $V_{100\%[cc]}$ is the volume receiving 100% of the prescribed dose and V_{PTV} is the volume of the combined PTV. For perfectly conformal plan, $CI = 1$ and for less conformal plan CI is <1 or >1 . We defined $V_{30\%[%]}$ and $V_{50\%[%]}$ as the volume of brain excluding PTV receiving greater than or equal to 30% and 50% of the prescribed dose, respectively. For plans treated with a single fraction, we also evaluated $V_{12Gy[cc]}$, which is defined as the volume of brain excluding PTV receiving greater than or equal to 12Gy.

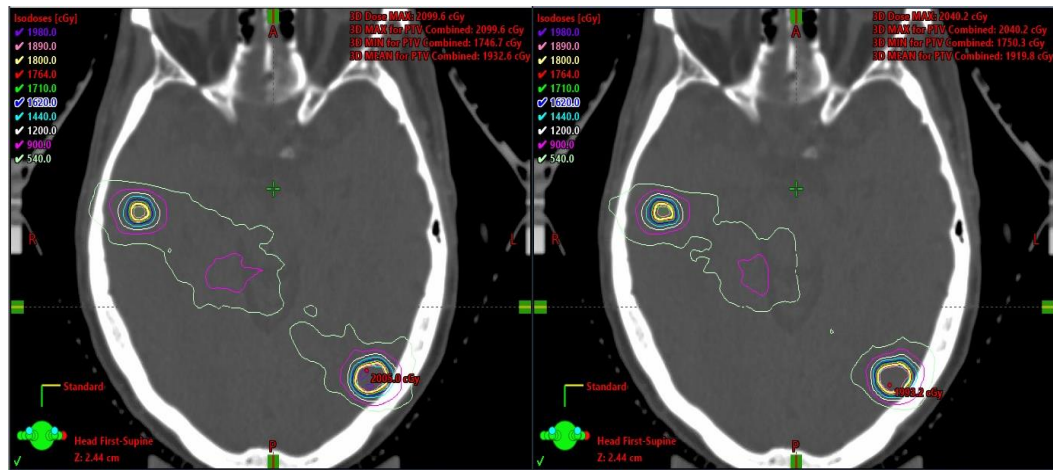


Figure 3: Dose distributions in axial views with both (left) 5 mm and (right) 2.5 mm leaf width MLCs – example 2.

Dosimetric parameters from reoptimized SIMT VMAT radiosurgery plans using the 5 mm leaf width MLCs were compared to those using the 2.5 mm MLCs. The average MU decreased from 5827 ± 2334 to 5572 ± 2220 ($p = .006$). The change in CI (mean \pm standard deviation) was $2.22\% \pm 0.05\%$ ($p = .045$). The V30%[%] and V50%[%] increased by $27.75\% \pm 0.16\%$ and $20.04\% \pm 0.13\%$ ($p < .001$ for both) respectively, while the V12Gy[cc] increased by $16.91\% \pm 0.12\%$ ($p < .001$). Total V12Gy[cc] and V12Gy[cc] per target for both 5 and 2.5mm leaf width MLCs are given in Table 1. The mean and standard deviation of V12Gy[cc] per target for 5 and 2.5mm leaf width MLC plans are $2.83\text{cc} \pm 1.17\text{cc}$ and $2.44\text{cc} \pm 1.03\text{cc}$ respectively. The change in dose indices is summarized in Figures 4.

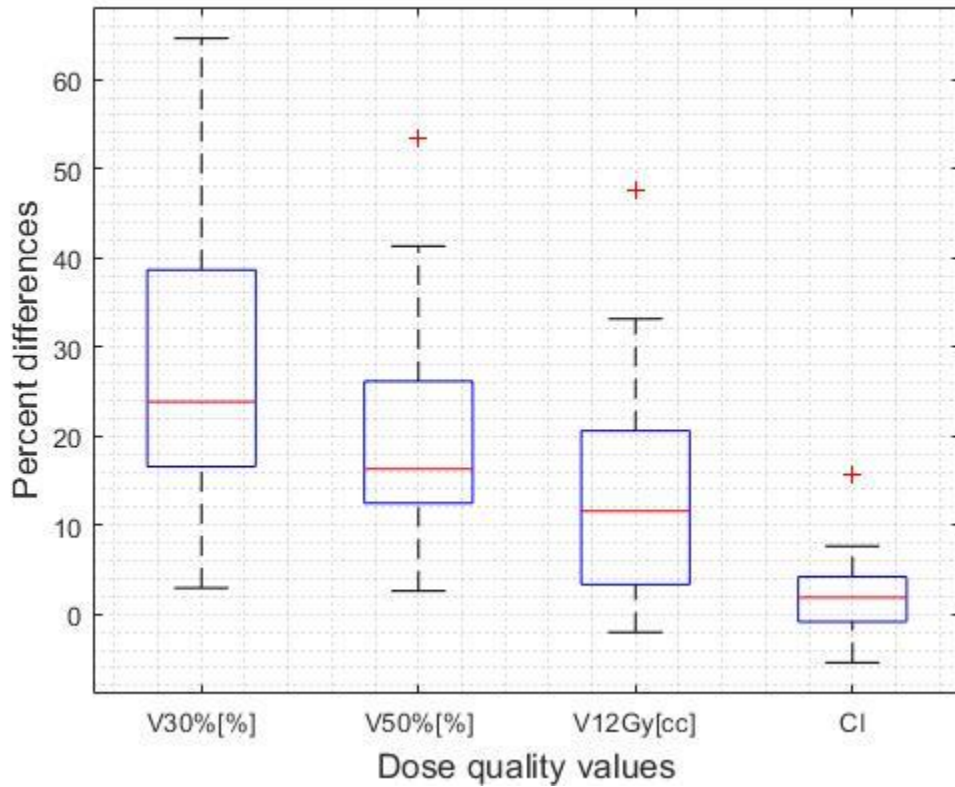


Figure 4: Percent differences of dose quality values between 2.5 and 5mm leaf width MLC plans.

Positive values in Figure 4 indicate an increase in the dose index when the larger MLCs are utilized. The central marks of boxplots indicate median, the edges of boxplots indicate 25th and 75th quartiles, and whiskers extend to most extreme data points not considered outliers, with outliers plotted individually using the '+' symbol".

Table 1: Total V12Gy[cc] and V12Gy[cc] per target for both 2.5 and 5mm leaf width MLC plans.

Cases	Number of targets	V12Gy[cc]		V12Gy[cc] per target	
		5mm leaf width MLC	2.5mm leaf width MLC	5mm leaf width MLC	2.5mm leaf width MLC

1	4	8.75	5.93	2.19	1.48
2	3	7.36	6.59	2.45	2.20
3	7	14.09	12.97	2.01	1.85
4	4	5.99	5.02	1.50	1.26
5	4	7.7	6.56	1.93	1.64
6	4	7.82	7.98	1.96	2.00
7	3	10.36	8.36	3.45	2.79
8	6	9.1	8.4	1.52	1.40
9	4	12.72	11.92	3.18	2.98
10	3	5.54	4.78	1.85	1.59
11	4	11.21	8.42	2.80	2.11
12	3	17.54	15.36	5.85	5.12
13	6	23.73	19.48	3.96	3.25
14	4	13.67	11.12	3.42	2.78
15	3	12.54	11.45	4.18	3.82
16	3	9.22	8.27	3.07	2.76
Mean ± standard deviation	4.1±1.2	11.08±4.68	9.54±3.98	2.83±1.17	2.44±1.03
Paired t-test		p<0.001		p<0.001	

3.2 Modified treatment planning to mitigate dosimetric quality degradation

3.2.1 Adding duplicate arcs with unique collimator angle

In an attempt to mitigate the increase in low and moderate isodose spill, we investigated adding duplicate arcs with altered collimator angles for all cases. The rationale for duplicating each arc is that doing so would not increase the number of couch angles in the plan; the duplicated arc could be delivered in reverse direction from the original, thus having negligible effect on treatment delivery time.

While this mitigation strategy resulted in lower CI, V50%[%], V30%[%], and V12Gy[cc] in select cases compared to 5mm leaf width MLC plans, on average the improvement was modest or non-existent, and these values did not reach the values of the original 2.5mm leaf width MLC plans. The percent differences of the dosimetric quality values are provided in Table 2.

Table 2: Percent differences between original plans and re-planned plans using 5mm leaf width MLCs and the plans with duplicated VMAT arcs.

Dosimetric values/Methods	Re-planned	Duplicated, altered by 10°	Duplicated, altered by 15°	Duplicated, altered by 90°
V30%[%]	27.75%±0.16%	24.11%±0.14%	29.51%±0.19%	35.84%±0.21%
V50%[%]	20.04%±0.13%	19.39%±0.14%	22.13%±0.15%	21.02%±0.14%
V12Gy[cc]	16.91%±0.12%	16.78%±0.1%	18.84%±0.11%	18.53%±0.11%
CI	2.22%±0.05%	0.3%±0.09%	0.17%±0.07%	-0.18%±0.08%

3.2.2 Increasing the number of arcs

In a second attempt to mitigate increased low and moderate isodose spill, we added one and two more VMAT arcs and equally spacing all VMAT arcs. By comparing the percent differences of the dosimetric qualities of 5mm leaf width MLC plans and 5mm leaf width MLC plans with one and two added VMAT arc, we can see that as arcs were added all indices improved on average, with the exception of V30%[%]. While this strategy did improve most dosimetric indices, they still did not completely reach the values of the original 2.5 mm leaf width MLC plan. The percent differences of

dosimetric quality values are shown in Table 3.

Table 3: Percent differences between original plans and re-planned plans using 5mm leaf width MLCs and the plans with additional one and two VMAT arcs.

Dosimetric values/Methods	Re-planned	+1 VMAT arc	+2 VMAT arcs
V30%[%]	27.75%±0.16%	24.51%±0.18%	27.94%±0.28%
V50%[%]	20.04%±0.13%	18.24%±0.13%	17%±0.13%
V12Gy[cc]	16.91%±0.12%	16.18%±0.09%	15.57%±0.1%
CI	2.22%±0.05%	1.33%±0.08%	0.55%±0.07%

Figures 5, 6, 7, and 8 depict the percent differences between original 2.5mm leaf width MLC plans and 5mm leaf width MLC plans and other modified 5mm leaf width MLC plans for dosimetric quality values V30%[%], V50%[%], V12Gy[cc], and CI. The central marks of boxplots indicate median, the edges of boxplots indicate 25th and 75th quartiles, and whiskers extend to most extreme data points not considered outliers, with outliers plotted individually using the '+' symbol".

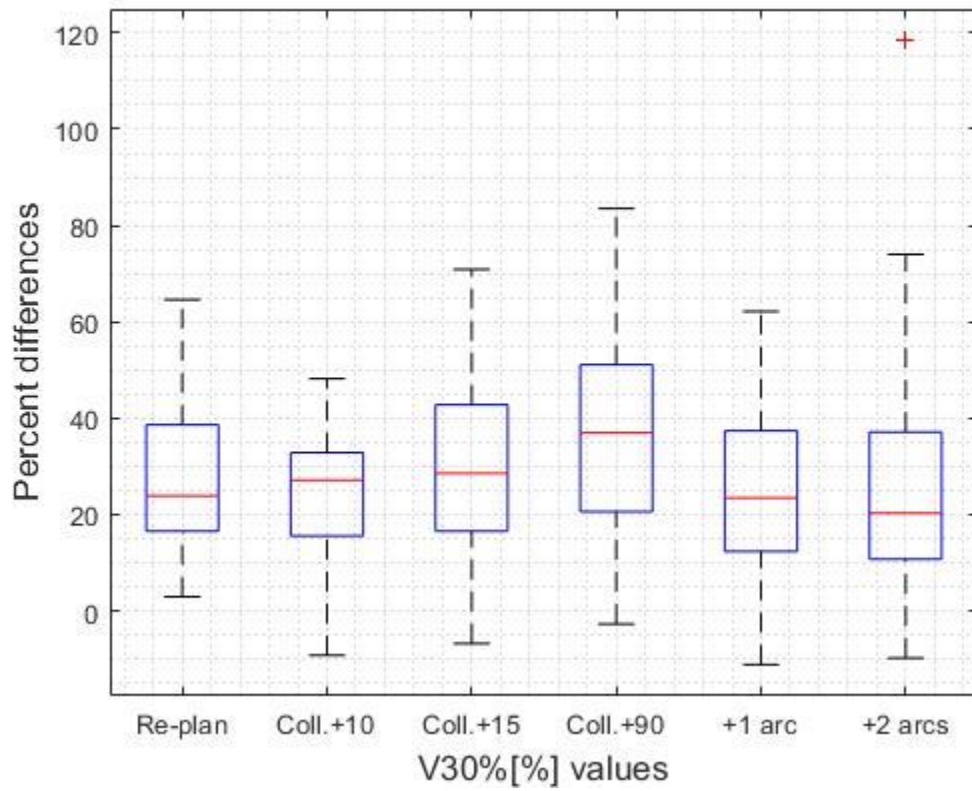


Figure 5: Percent differences of V30%[%] between original and re-planned plans, re-planned plans with duplicated arcs, and re-planned plans with additional arcs.

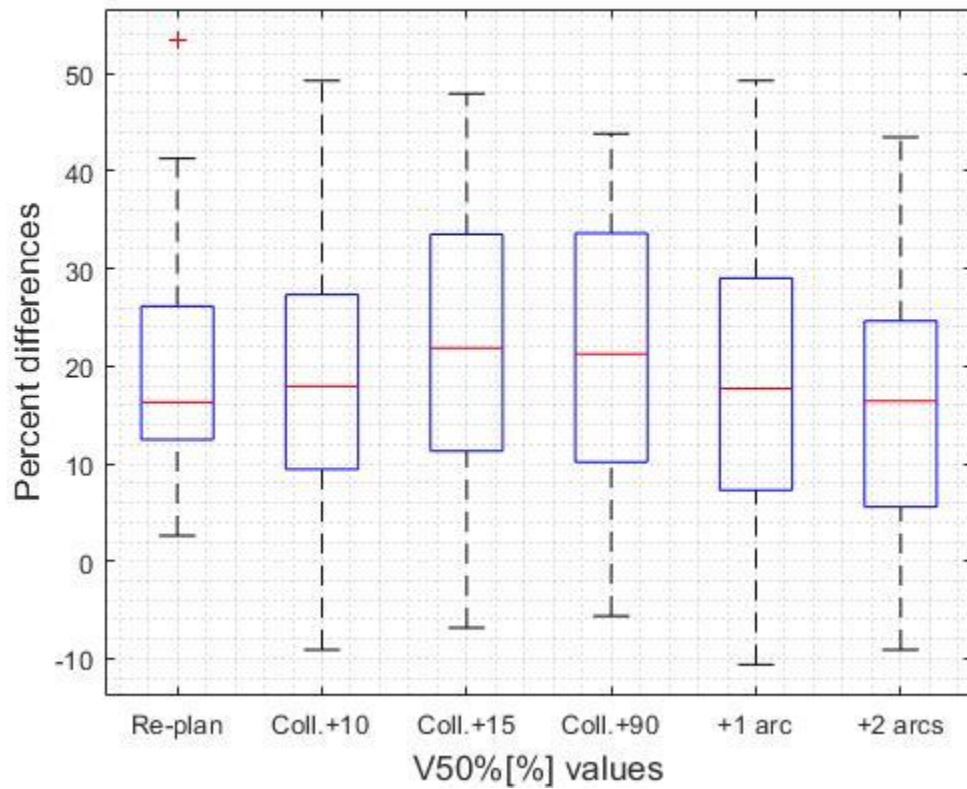


Figure 6: Percent differences of V50%[%] between original and re-planned plans, re-planned plans with duplicated arcs, and re-planned plans with additional arcs.

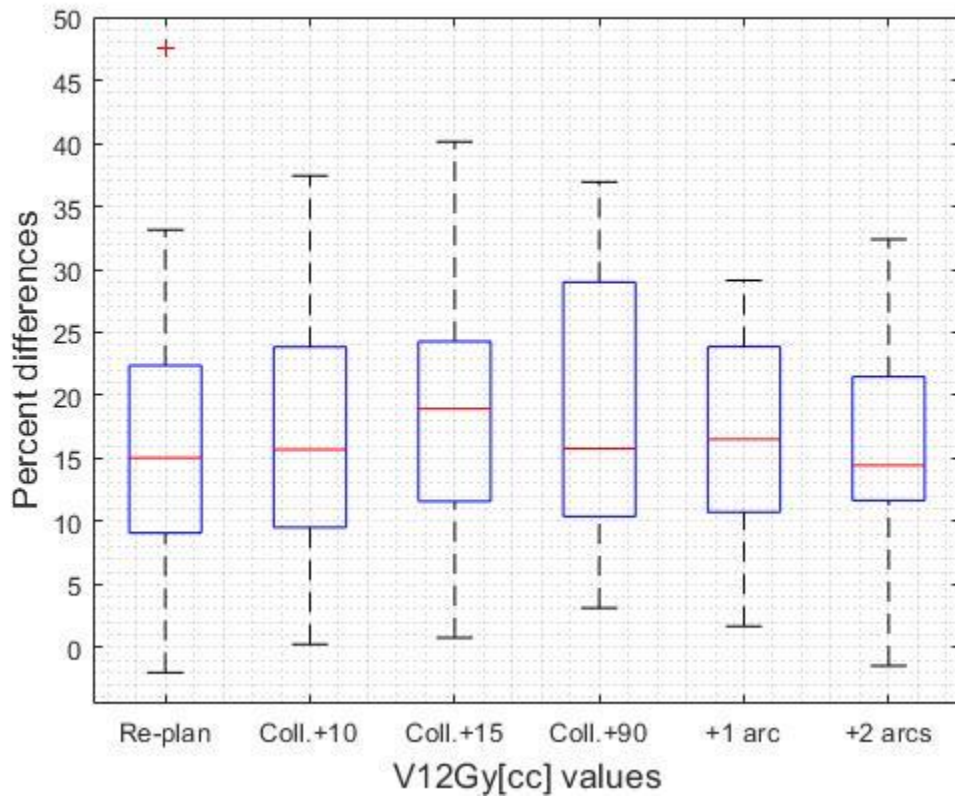


Figure 7: Percent differences of V12Gy[cc] between original and re-planned plans, re-planned plans with duplicated arcs, and re-planned plans with additional arcs.

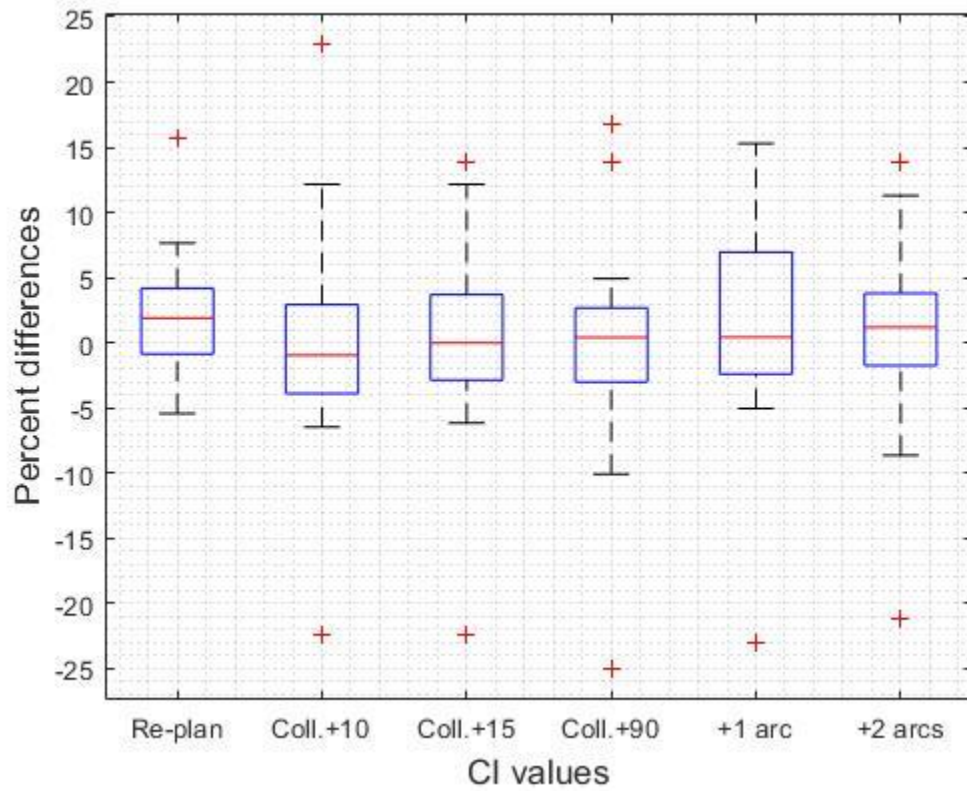


Figure 8: Percent differences of CI between original and re-planned plans, re-planned plans with duplicated arcs, and re-planned plans with additional arcs.

4. Discussion

In the present study we have evaluated the dosimetric differences in using MLC leaf widths of 2.5mm and 5mm for SIMT radiosurgery with VMAT. Given the higher clinical prevalence of 5mm leaves and increasing use of SIMT radiosurgery, we analyzed clinical plan quality of SIMT radiosurgery delivered via VMAT using 5 mm leaves. The dosimetric values CI, V50%[%], V30%[%], and V12Gy[cc] were used for single fraction cases for the comparison between two plans which were taken from the dose volume histograms. We also tested several ways to mitigate the dosimetric value degradations after the re-planning with 5mm width MLCs. We found that 5mm MLCs had plan degradation compared to 2.5mm leaf width MLC delivery. By adding two more VMAT arcs and equally spacing them, we were able to improve the dose quality values, beginning to approach the plan quality of the original 2.5mm leaf width MLC plan.

Prior studies have found that V12Gy[cc] is highly predictive for the development of radiation necrosis (RN) in patients receiving multi-isocenter, single-fraction SRS [24-26]. Therefore, part of our analysis included quantifying the absolute volume receiving V12Gy[cc] and the V12Gy[cc] per target. As expected, we found that using the larger leaves caused the V12Gy[cc] to increase from 9.54 ± 3.98 cc to 11.08 ± 4.68 cc (mean \pm standard deviation), which corresponded to an increase in V12Gy[cc] per target from 2.44 ± 1.03 cc to 2.83 ± 1.17 cc. Minniti et al. investigated the factors affecting survival and toxicity in patients treated with SRS with no history of WBRT. They analyzed V10-

V16Gy[cc] as predictors for brain RN and found out that V10Gy[cc] and V12Gy[cc] were the strongest predictors and that lesions with V12Gy[cc] >8.5 cc have a risk of RN >10% [24]. Korytko et al. performed a retrospective review of patients with non-arteriovenous malformation (non-AVM) intracranial tumors and found that the risk of symptomatic RN correlated with V12Gy[cc] and that the risk of RN increases significantly for V12Gy[cc]>10 cc per lesion [25]. Finally, Blonigen et al. performed a retrospective analysis of 63 patients treated with SRS for brain metastases to investigate patient and treatment factors for predictors of RN and found that V8Gy[cc]-V16Gy[cc] were the best predictors for symptomatic RN. They also found that patients with V12Gy[cc] >10.8 cc had a 68.8% rate of RN, however it should be noted that 63 % of patients received WBRT prior to SRS, which has been shown in other studies to increase the risk of RN [26]. To the author's knowledge, there have been no trials to date that have reported on the incidence of RN following SIMT SRS and/or describing patient or treatment specific factors that are predictive of the development of RN. Additionally, the aforementioned studies primarily considered the probability of RN in the context of a single target volume, as a majority of the patients reported had only 1 lesion. It is doubtful that these same rates would apply to a total volume of V12Gy[cc] in the setting of multiple isolated targets and for this reason both total volume of V12Gy[cc] and volume per target V12Gy[cc] were reported.

It is important to note that in this study only Varian MLCs and their specific characteristics as well as the Varian Eclipse modeling of those MLCs was analyzed. MLCs from different vendors with different leakage characteristics and leaf edge design may have different results. Additionally, the results may be dependent on how well the leakage and leaf edges are modeled in the treatment planning system.

One of the purposes of this study was to broaden the applicability of SIMT radiosurgery using VMAT to include the greater number of linear accelerators with standard 5mm MLCs. However, it should be noted that leaf size is not the only consideration as to whether a SIMT VMAT technique can and should be used. For instance, Stanhope et al in their study considered the challenges of the increased sensitivity to rotational uncertainties which results from distance of the targets from isocenter and potential for decreased plan quality from larger multi leaf collimator width $N > 4$ cm from isocenter with single-isocenter radiosurgery for multiple intracranial targets (SIRMIT). They showed the need for rotational corrections via image guidance for SIRMIT when a thermoplastic mask is used for immobilization [19]. Given this, a separate requirement for SIMT VMAT radiosurgery is the ability to apply 6D-couch corrections, which also greatly limits the number of linear accelerators to which it can be applied. However, many radiosurgery immobilization systems have the ability to adjust pitch and roll manually, which could potentially serve the same purpose. Additionally,

6-degree couches are now commonly offered on LINACs with 5mm MLC width, making this combination commonly commercially available.

5. Conclusion

Using 5mm MLCs for SIMT VMAT radiosurgery leads to minor increases in conformity index and moderate increases in low and moderate isodose spill. Duplicated VMAT arcs could not mitigate the changes in the dosimetric values of 5mm leaf width MLC plans compared to 2.5mm leaf width MLC plans. We were able to see the decrease trend of the percent differences of the dosimetric quality values when adding one more and two more VMAT arcs.

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