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Scientific Article

Dosimetric Analysis of Intra-Fraction Motion Detected by Surface-Guided Radiation Therapy During Linac Stereotactic Radiosurgery

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Abstract

Purpose: Stereotactic radiosurgery (SRS) immobilization with an open face mask is more comfortable and less invasive than frame based, but concerns about intrafraction motion must be addressed. Surface-guided radiation therapy (SGRT) is an attractive option for intrafraction patient monitoring because it is continuous, has submillimeter accuracy, and uses no ionizing radiation. The purpose of this study was to investigate the dosimetric consequences of uncorrected intrafraction patient motion detected during frameless linac-based SRS.

Methods and Materials: Fifty-five SRS patients were monitored during treatment using SGRT between January 1, 2017, and September 30, 2020. If SGRT detected motion >1 mm, imaging was repeated and the necessary shifts were made before continuing treatment. For the 25 patients with intrafraction 3-dimensional vector shifts of ≥1 mm, we moved the isocenter in the planning system using the translational shifts from the repeat imaging and recalculated the plans to determine the dosimetric effect of the shifts. Planning target volume (PTV) coverage, minimum gross tumor volume (GTV) dose (relative and absolute), and normal brain V12 were evaluated. Wilcoxon signed rank tests were used to compare planned and simulated dosimetric parameters and median 2 sample tests were used to investigate these differences between cone and multileaf collimator (MLC) plans.

Results: For simulated plans, V12 increased by a median of 0.01 cc ($P = .006$) and relative GTV minimum dose and PTV coverage decreased by a median of 15.8% ($P < .001$) and 10.2 % ($P < .001$), respectively. Absolute minimum GTV dose was found to be significantly lower in the simulated plans ($P < .001$). PTV coverage decreased more for simulated cone plans than for simulated MLC plans (11.6% vs 4.7%, $P = .011$) but median V12 differences were found to be significantly larger for MLC plans (-0.34 cc vs -0.01 cc, $P = .011$). Differences in GTV minimum dose between cone and MLC plans were not statistically significant.

Conclusions: SGRT detected clinically meaningful intrafraction motion during frameless SRS, which could lead to large underdoses and increased normal brain dose if uncorrected.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Introduction

Stereotactic radiosurgery (SRS) has been shown to provide good results for patients with brain metastases. SRS is an ablative treatment requiring effective immobilization, small margins, and sharp dose gradients to accurately treat the tumor and limit the volume of healthy brain receiving high doses. To improve patient comfort and enable multifraction dose schedules, both Gamma Knife and linac-based SRS now frequently use thermoplastic masks for patient immobilization, which have been shown to be sufficiently accurate for SRS in the image guided era.[1-4] Since transitioning from robotic radiosurgery to linac-based SRS, our clinic has used an SRS-specific open face mask for our patients in combination with surface guided radiation therapy (SGRT) with the AlignRT system (VisionRT, London, United Kingdom). The open mask allows the patient's face to be monitored during treatment, providing a means to detect intrafraction patient motion and correct it, as recommended by the American Society for Radiation Oncology and the American Association of Physicists in Medicine.[5] SGRT provides continuous patient monitoring with submillimeter accuracy without using ionizing radiation, and the SGRT system can be interfaced with the linear accelerator to stop the beam if the patient moves outside a predefined tolerance. Details of the system have been previously published.[6,7]

Several studies have shown that surface imaging is sufficiently accurate for SRS,[8] and ≥1 institution has transitioned to maskless SGRT-guided SRS[9] and has reported on their outcomes for frameless surface guided SRS.[10-12] However, there are no published studies of the potential dosimetric consequences of the detected intrafraction motion during SRS. The purpose of this study is to evaluate the dosimetric effects of intrafraction motion detected by SGRT during frameless linac-based SRS.

Methods and Materials

When our clinic transitioned from robotic SRS to linac-based SRS in early 2017, we implemented intrafraction monitoring using VisionRT's AlignRT SGRT system to replace the frequent (~15 s) kV imaging used with robotic SRS. Patients were simulated in an SRS-specific open face thermoplastic mask[13] (Encompass, Qfix, Avondale, Pennsylvania) with bite plate; the treatment planning computed tomography (CT) scans had 1-mm thick slices. A 3-dimensional (3D) T1+C magnetic resonance image (MRI) with 1-mm slice thickness was fused to the planning CT, and the gross tumor volume (GTV) was contoured based off the MRI. GTV to planning target volume (PTV) margins ranged from 0 to 3 mm, depending on physician preference. Plans were designed using either multileaf collimator (MLC) or stereotactic cones, with the treatment device dependent on PTV size and shape. All patients treated using stereotactic cones had a 1-mm GTV to PTV margin, whereas 1 MLC patient had no margin, 8 had a 1-mm margin, 3 had a 2-mm margin, and 1 had a 3-mm margin. All patients were treated with 1 target per isocenter, which was placed at the geometric center of the PTV. Patients were treated on a Varian TrueBeam linear accelerator equipped with a Millennium 120 leaf MLC and stereotactic cones ranging from 4 to 17.5-mm diameter; PTVs larger than the largest cone were planned with MLC. MLC plans were a mixture of volumetric modulated arc therapy and dynamic conformal arc techniques. Prescriptions were 15 Gy, 18 Gy, or 21 Gy in 1 fraction or 27 Gy in 3 fractions, again depending on tumor size. All plans were prescribed such that ≥98% of the PTV was covered by the prescription dose. All plans were generated using a flattening filter-free 6 MV beam with patients initially set up using SGRT and then imaged using cone beam CT (CBCT). A reference SGRT surface was captured immediately before the initiation of the CBCT, allowing us to monitor the patient during the CBCT acquisition and match. The physician matched the CBCT to the planning CT, and once the couch shifts were made, a new SGRT surface was captured to use for intrafraction monitoring. The linac is equipped with a 6 degrees-of-freedom couch, allowing pitch and roll corrections in addition to yaw.

SGRT tolerances for these patients are 1 mm translations and 1° rotations. Since the SGRT system is interlocked with the linac, if the patient motion exceeded these thresholds, the beam automatically turned off and remained off while the patient was out of tolerance. Occasionally, the patient would return to tolerance within a few seconds and the treatment would resume, but if the patient did not return to tolerance within 20 to 30 seconds, we performed an intrafraction CBCT. The physician matched the CBCT and made any needed shifts. If intrafraction shifts were made, a new SGRT reference was captured and the treatment continued.

A Winston-Lutz test was performed each day before an SRS patient was treated and the accuracy of the SGRT system was tested using an in-house designed quality assurance procedure. The Winston-Lutz test was performed with a 2×2 cm^2 MLC defined field for MLC patients or with the planned cone unless it was <10 mm, in which case the 10-mm cone was used. Tolerance for the Winston-Lutz test was a maximum of 1-mm deviation for any single gantry/couch/collimator combination. The SGRT system quality assurance consisted of radiographic imaging and positioning/repositioning of a cube phantom that is tracked with the SGRT system and evaluation of the shifts determined from the imaging procedure and the

SGRT system. Tolerance for the image guided radiation therapy/SGRT quality assurance was also 1 mm.

Under an institutional review board-approved protocol, we retrospectively analyzed the 55 SRS patients who were treated between January 1, 2017, and September 30, 2020. For the 25 patients with intrafraction CBCT 3D vector shifts ≥1 mm, we simulated the dosimetric deviations in the planning system by translating the isocenter using the intrafraction shifts that were made. No rotations were included in the simulated plans. A threshold of 1 mm was chosen because that is the SGRT translational tolerance used for SRS patients in our clinic and our most commonly used GTV to PTV margin. The simulated plans were recalculated using the same beams and monitor units (MU) as the clinical plans, and the resulting minimum GTV point dose, PTV coverage, and the volume of normal brain receiving 12 Gy (V12) were compared between the clinical plans and the simulated plans. We evaluated the minimum GTV dose relative to the prescription dose and the absolute minimum GTV dose. V12 was chosen as a normal tissue metric since there are published guidelines recommending that V12 be limited to <10 cc (20 cc for 3 fractions) to limit the risk of radionecrosis.[14,15] The simulated plans provide an estimate of the dose delivered had the intrafraction shifts not been detected. We assumed the entire fraction was delivered with the shifted isocenter to simulate the worst-case scenario of a patient moving between the initial CBCT acquisition and the initiation of treatment. For patients receiving 3 fractions, a plan sum of the nonshifted fraction(s) and the shifted fraction(s) was created for evaluation.

To investigate whether 1 treatment device was more robust to intrafraction motion and would better maintain target coverage, we analyzed the MLC and cone patients separately to evaluate the differences between the 2 treatment techniques.

Statistical methods

Treatment characteristics were summarized with frequencies and proportions for categorical characteristics and medians and ranges for continuous variables. Wilcoxon signed rank tests were used for the paired comparisons of the actual versus simulated treatment plan dosimetric indices. To evaluate the difference between the cone and MLC simulated dosimetric indices, we used median 2 sample tests. P values were considered statistically significant if <0.05.

Results

All patients

The characteristics of the plans for the 25 patients analyzed for the study are shown in Table 1. The majority (>80%) of patients were treated with a single fraction with 1-mm margins. The patients were split evenly between cone and MLC plans. The median vector shift for all patients was 1.5 mm. Roll, pitch and rotation differences are also reported in Table 1 but were not used in the recalculation of the simulated plan. As shown in Table 2, differences between actual and simulated values in all 4 dosimetric indices are statistically significant. Median differences in relative GTV minimum dose and PTV coverage were −15.8% ($P < .001$) and −10.2% ($P < .001$), respectively, while the absolute minimum GTV dose difference was −308 cGy ($P < .001$). Median V12 increased in the simulated plans and the median difference was statistically significant ($P = .006$). Nineteen of the 25 GTVs received <100% of the prescription dose and were considered underdosed in the simulated plans. Figure 1 is an example of the original (left) and simulated (right) plan dose distributions. Figure 2 is the corresponding dose-volume histograms for the 2 plans. The Spearman correlation coefficient between PTV volume and difference in PTV coverage was −0.613 ($P = .001$), which is a strong correlation indicating that when PTV volume increases, the change in PTV coverage decreases. In other words, the coverage for larger PTVs was affected less by shifts than it was for smaller PTVs. There was no significant correlation between the GTV volume and change in relative GTV minimum dose.

Comparison of cone and MLC plans

Table 3 contains a comparison of the dosimetric indices between cone and MLC simulated plans. Differences in PTV coverage were statistically significant and were larger for cone plans than for MLC plans (11.6% vs 4.7%, $P = .011$). However, V12 was more sensitive to shifts in MLC plans than cone plans; median V12 increased in the simulated plans by 0.34 cc for MLC plans compared with 0.01 cc for cone plans. The median vector shifts for MLC and cone plans were not significantly different ($P = .551$, median 2 sample tests, data not shown), suggesting that the significant differences in PTV coverage and V12 could not be explained by differences in shift magnitudes. Possible explanations include the sharper dose gradients produced by circular cones and smaller lesion size for cone plans, which would be less robust to shifts. However, the correlation between PTV volume and PTV coverage change for the cone plans was 0.473 ($P = .121$), a moderate correlation, and for MLC plans the correlation was 0.349 ($P = .242$), which is a weak correlation. Neither correlation was statistically significant. Differences in minimum GTV dose were not statistically significant between the cone and MLC plans.

Discussion

Several studies have previously demonstrated the relationship between tumor dose and local control (LC) for

Table 1 Treatment characteristics for study patients

Characteristic	N = 25 subjects	
Treatment, n (%)		
MLC	13	52.0%
Cone	12	48.0%
Fractions, n (%)		
1	21	84.0%
3	4	16.0%
Dose per fraction, n (%)		
900 cGy	4 (MLC)	16%
1500 cGy	1 (MLC)	4%
1800 cGy	3 (MLC)	12%
2100 cGy	17 (12 cone, 5 MLC)	68%
GTV volume (cc)		
Median (range), all patients	1.05	0.03-29.48
Median (range), MLC	5.22	0.4-29.48
Median (range), cone	0.26	0.03-1.05
PTV volume (cc)		
Median (range), all patients	1.61	0.13-44.25
Median (range), MLC	8.38	0.79-44.25
Median (range), cone	0.56	0.13-1.61
Margin, n (%)		
0 mm	1 (MLC)	4%
1 mm	20 (12 cone, 8 MLC)	80%
2 mm	3 (MLC)	12%
3 mm	1 (MLC)	4%
Shift summaries, median (range), mm		
Vector	1.5	1.0-6.6
Vertical	0.3	0-1.1
Longitudinal	1.4	0.2-6.2
Lateral	0.5	0-2.2
Rotation	0.0	0-1.5
Roll	0.1	0-1.0
Pitch	0.3	0-2.1

Abbreviations: GTV = gross tumor volume; MLC = multileaf collimator; PTV = planning target volume.

SRS and stereotactic radiation therapy. In a study evaluating a 1-mm margin around the GTV, Noël et al found the addition of the margin to be predictive of LC, increasing LC at 2 years from 50.7% without a margin to 87.7% with a margin.[16] Margin (and thus the minimum GTV dose) was the only independent prognostic factor that was significant in multivariate analysis (P = .04). Schomas et al also found that after controlling for histology, volume, and prescription dose, the only predictive factor for LC to retain significance in a multivariate analysis was minimum tumor dose.[17] They found significantly worse LC at 1 year for a minimum dose of 12 Gy (66.7%) compared with higher minimum doses (>90%). Likewise, Vogelbaum et al showed that for Gamma Knife SRS, LC was significantly dependent on the dose at the tumor margin.[18] For fractionated SRS, the dose to 98% of the GTV ($D_{98\%}$) was found to be a significant predictive factor for LC by Dupic et al.[19] They prescribed 33 Gy to the GTV and 23.1 Gy to the PTV in 3 fractions and found that LC was 91.9% for a GTV $D_{98\%}$ ≥29 Gy and 69.6% for $D_{98\%}$

Table 2 Dosimetric comparison of actual and simulated plans for all patients

Dosimetric indices	Actual	Simulated	Median difference (actual - simulated)	*P* value*
V12 (cc), median (range)	2.78 (0.32-151.25)	3.02 (0.33-151.32)	−0.01 (−1.5-0.09)	.006
GTV minimum dose (%), median (range)	102.80 (91.70-118.60)	93.80 (15.00-106.00)	15.8 (−1.9-86.08)	<.001
PTV coverage %, median (range)	98.10 (98.00-99.00)	87.89 (36.60-99.56)	10.24 (−1.56-61.40)	<.001
GTV minimum dose (cGy), median (range)	2225.0 (1376.0-2719.0)	1901.8 (271.1-2752.3)	308.2 (−52.3-1548.3)	<.001

Abbreviations: GTV = gross tumor volume; PTV = planning target volume.
* Wilcoxon signed rank tests.

<29 Gy at 1 year. In the postoperative setting, worse dose conformality has been shown to improve LC, indicating that an overly conformal plan could be counterproductive.[20] The least conformal quartile (average confidence interval of 1.76) had an LC rate of 100% while the most conformal quartile (average confidence interval of 1.22) had an LC rate of 43%. The authors found no significant correlation between resection cavity size and LC and recommended using a 2-mm margin instead of less conformal plans. In a subsequent publication from the same institution, the authors performed a prospective study of margin and its effect on local failure.[21] They found that only the addition of a 2-mm margin was predictive of LC and found no increase in toxicity with the addition of the margin.

While there are several possible explanations for better LC when irradiating a larger volume (target volume delineation uncertainties, MRI distortion, microscopic spread of tumor cells outside of the imaging-defined tumor volume, imaging slice thickness), it is possible that the larger irradiated volume mitigates the effect of uncorrected intrafraction motion, whereas for highly conformal plans, the decrease in tumor dose due to intrafraction motion leads to worse LC. On the other hand, some studies evaluating margins for SRS did not find improved LC with additional margin added to the GTV.[22-24] Nevertheless, higher tumor doses continue to result in better LC,[25-27] indicating the importance of maintaining the planned dose distribution and safely delivering as high a dose as possible to the tumor while avoiding the irradiation of normal brain. As our study shows, uncorrected intrafraction motion can significantly reduce target coverage and increase V12 during linac-based frameless SRS.

Several other studies have evaluated the effect of intrafraction motion on the dosimetry of SRS plans, though previous studies have used a radiographic method to measure motion by acquiring the images at the end of the fraction, thus making it not truly intrafraction.[28,29] These methods only provide a snapshot of the patient position and do not provide continuous monitoring as SGRT does; the patient position at time points other than the imaging procedure is unknown. A recent publication evaluated dosimetric implications of intrafraction motion for Gamma Knife Icon-based SRS using simulated patient motion rather than observed intrafraction motion, but the authors plan to use actual patient motion to validate the methods developed during the initial study.[30] We believe we are the first to publish results of the potential dosimetric consequences after applying observed intrafraction motion to the individual patient's treatment plan for frameless linac-based SRS.

Some limitations of this study exist. We did not evaluate dosimetric consequences of 3D vector shifts <1 mm; we are assuming that these patients would have had no significant dosimetric consequences without SGRT. We did not include rotations in the simulated plans because

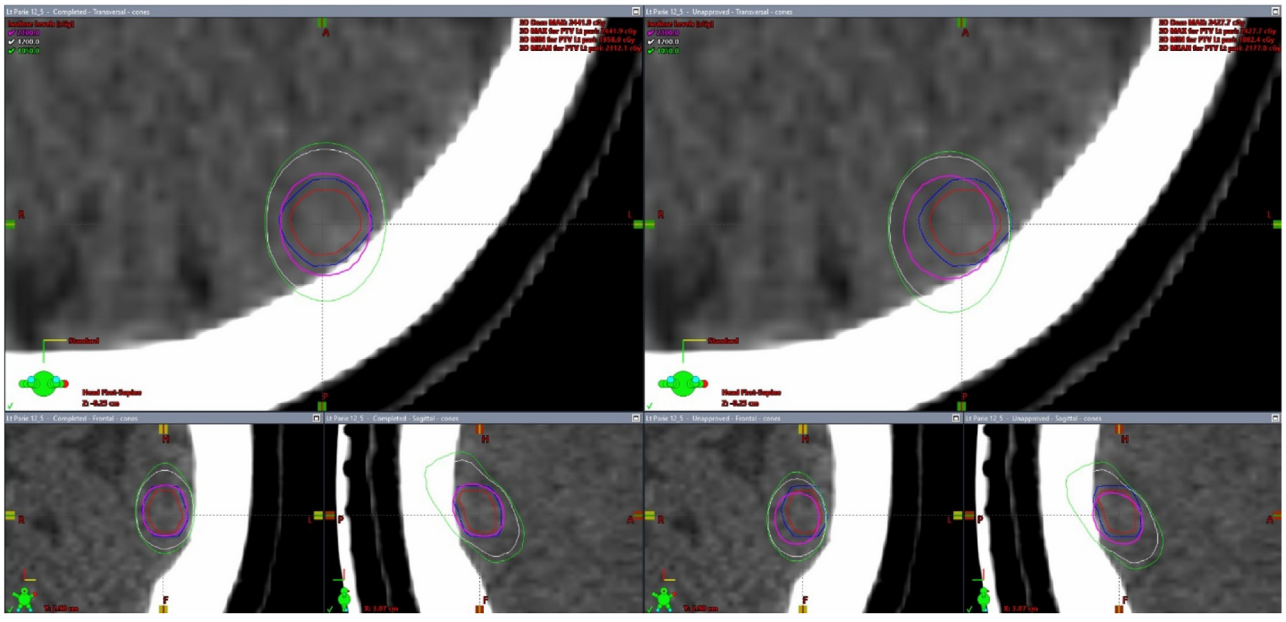

Figure 1 Clinical treatment plan on the left, simulated plan on the right.

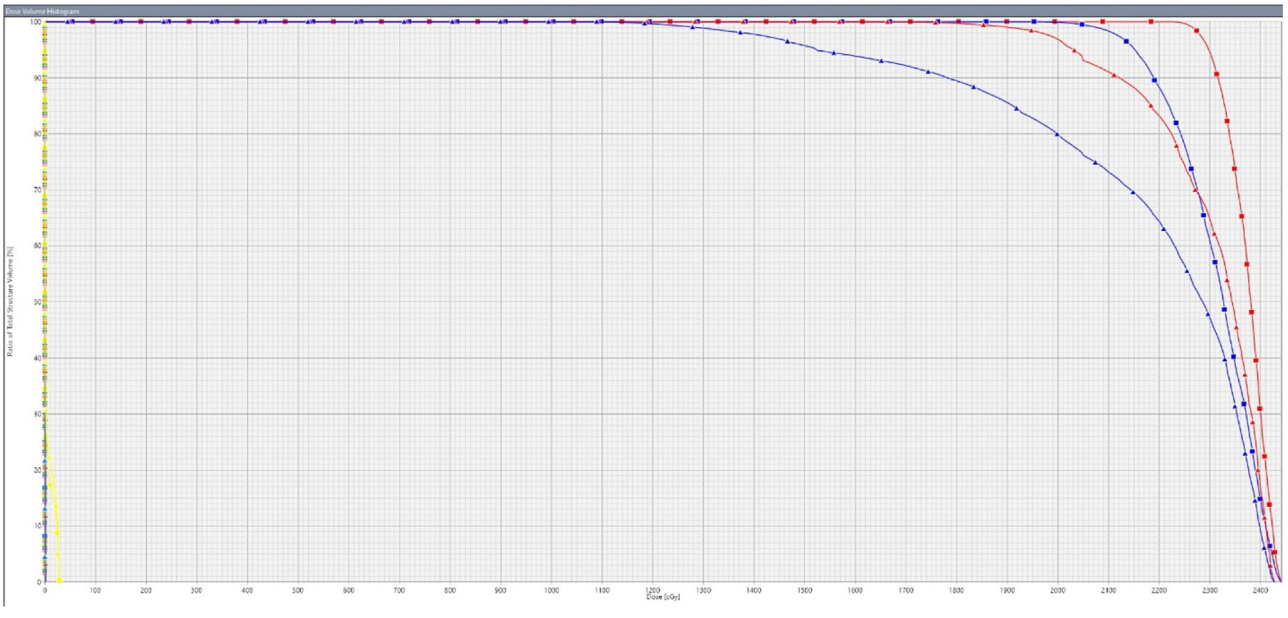

Figure 2 Dose-volume histogram comparing clinical plan and simulated plan. Clinical plan indicated by squares and simulated plan indicated by triangles. PTV is indicated by the blue curves and GTV by red curves. *Abbreviations:* GTV = gross tumor volume; PTV = planning target volume.

of the median intrafraction rotations being <0.5° and previous studies having shown that, for single isocenter/single target plans such as the ones analyzed in this study, rotations make <2% difference in the target dose.[28,29] Additionally, since the cone plan MU calculation depends on the global maximum dose and the maximum dose changes when the isocenter is shifted, the MU in the simulated plans could not be matched exactly to the original plans. The maximum difference in total plan MU was 0.3%, and the largest difference in MU for any single beam was 1%. We also assumed that the motion occurred between the initial image guided radiation therapy procedure and the initiation of treatment, thus representing a worse-case scenario when no intrafraction monitoring is used. While not common, SGRT detected >1 mm motion before initiating treatment in 2 of our patients; 1 patient

Table 3 Comparison of simulated dosimetric indices for cone and MLC plans

	Cone, n = 12			MLC, n = 13			
Dosimetric indices	Actual	Simulated	Median difference (actual - simulated)	Actual	Simulated	Median difference (actual - simulated)	*P* value*
V12 (cc), median (range)	1.1 (0.3-2.8)	1.2 (0.3-2.8)	−0.01 (−0.15-0.05)	15.2 (2.5-151.3)	15.2 (3.0-151.3)	−0.34 (−1.50-0.09)	0.011
GTV min dose (%), median (range)	107.5 (102.8-118.6)	91.4 (55.8-106.0)	16.8 (4.0-57.2)	100.7 (91.7-103.1)	93.8 (15.0-101.9)	6.5 (−1.9-86.1)	0.330
PTV coverage %, median (range)	98.3 (98.0-98.8)	86.8 (42.7-92.6)	11.6 (5.4-55.9)	98.0 (98.0-99.0)	93.3 (36.6-99.6)	4.7 (−1.6-61.4)	0.011
GTV min dose (cGy), median (range)	2293.8 (2159.0-2490.8)	1918.8 (1172.9-2226.1)	351.9 (176.1-1202.9)	2121.1 (1376.0-2719.1)	1901.8 (271.1-2752.3)	136.5 (−52.3-1548.3)	.079

Abbreviations: GTV = gross tumor volume; Min = minimum; MLC = multileaf collimator; PTV = planning target volume.
* Median 2-sample tests.

could not be treated at all because of an inability to remain still. In addition, though the difference in V12 is statistically significant, it is likely not clinically relevant.

Conclusions

SGRT detected clinically meaningful intrafraction motion during frameless SRS, which could potentially lead to large underdoses to the targets, worse LC, and increased normal brain dose if not corrected. Dosimetric differences between planned and simulated plans were statistically significant. Patients treated with stereotactic cones exhibited PTV coverage being more sensitive to uncorrected patient shifts than patients treated with MLC SRS plans. MLC plan PTV coverage is more robust to intrafraction motion but V12 increases more when uncorrected patient motion occurs for MLC plans compared with cone treatments. This study provides evidence that uncorrected intrafraction motion can produce significant dosimetric deviations during linac-based frameless radiosurgery that could negatively affect patient outcomes.

References

1. Solberg TD, Medin PM, Mullins J, et al. Quality assurance of immobilization and target localization systems for frameless stereotactic cranial and extracranial hypofractionated radiotherapy. *Int J Radiat Oncol Biol Phys*. 2008;71:131-135.
2. Verbakel WFAR, Lagerwaard FJ, Verduin AJE, et al. The accuracy of frameless stereotactic intracranial radiosurgery. *Radiother Oncol*. 2010;97:390-394.
3. Bilger A, Frenzel F, Oehlke O, et al. Local control and overall survival after frameless radiosurgery: A single center experience. *Clin Transl Radiat Oncol*. 2017;7:55-61.
4. Grimm MA, Köppen U, Stieler F, et al. Prospective assessment of mask versus frame fixation during Gamma Knife treatment for brain metastases. *Radiother Oncol*. 2020;147:195-199.
5. Solberg TD, Balter JM, Benedict SH, et al. Quality and safety considerations in stereotactic radiosurgery and stereotactic body radiation therapy: Executive summary. *Pract Radiat Oncol*. 2012;2:2-9.
6. Peng JL, Kahler D, Li JG, et al. Characterization of a real-time surface image-guided stereotactic positioning system. *Med Phys*. 2010;37:5421-5433.
7. Zhang L, Vijayan S, Huang S, et al. Commissioning of optical surface imaging systems for cranial frameless stereotactic radiosurgery. *J Appl Clin Med Phys*. 2021;22:182-190.
8. Oliver JA, Kelly P, Meeks SL, et al. Orthogonal image pairs coupled with OSMS for noncoplanar beam angle, intracranial, single-isocenter, SRS treatments with multiple targets on the Varian Edge radiosurgery system. *Adv Radiat Oncol*. 2017;2:494-502.
9. Cerviño LI, Detorie N, Taylor M, et al. Initial clinical experience with a frameless and maskless stereotactic radiosurgery treatment. *Pract Radiat Oncol*. 2012;2:54-62.
10. Pan H, Cerviño LI, Pawlicki T, et al. Frameless, real-time, surface imaging-guided radiosurgery: Clinical outcomes for brain metastases. *Neurosurgery*. 2012;71:844-851.

11. Pham NLL, Reddy PV, Murphy JD, et al. Frameless, real-time, surface imaging-guided radiosurgery: Update on clinical outcomes for brain metastases. *Transl Cancer Res*. 2014;3:351-357.
12. Paravati AJ, Manger R, Nguyen JD, et al. Initial clinical experience with surface image guided (SIG) radiosurgery for trigeminal neuralgia. *Transl Cancer Res*. 2014;3:333-337.
13. Komiyama R, Ohira S, Ueda H, et al. Intra-fractional patient motion when using the Qfix Encompass immobilization system during HyperArc treatment of patients with brain metastases. *J Appl Clin Med Phys*. 2021;22:254-260.
14. Milano MT, Grimm J, Niemierko A, et al. Single- and multifraction stereotactic radiosurgery dose/volume tolerances of the brain. *Int J Radiat Oncol Biol Phys*. 2021;110:68-86.
15. Gondi V, Bauman G, Bradfield L, et al. Radiation therapy for brain metastases: An ASTRO clinical practice guideline. *Pract Radiat Oncol*. 2022;12:265-282.
16. Noël G, Simon JM, Valery CA, et al. Radiosurgery for brain metastasis: Impact of CTV on local control. *Radiother Oncol*. 2003;68:15-21.
17. Schomas DA, Roeske JC, MacDonald RL, et al. Predictors of tumor control in patients treated with linac-based stereotactic radiosurgery for metastatic disease to the brain. *Am J Clin Oncol Cancer Clin Trials*. 2005;28:180-187.
18. Vogelbaum MA, Angelov L, Lee SY, et al. Local control of brain metastases by stereotactic radiosurgery in relation to dose to the tumor margin. *J Neurosurg*. 2006;104:907-912.
19. Dupic G, Brun L, Molnar I, et al. Significant correlation between gross tumor volume (GTV) D98% and local control in multifraction stereotactic radiotherapy (MF-SRT) for unresected brain metastases. *Radiother Oncol*. 2021;154:260-268.
20. Soltys SG, Adler JR, Lipani JD, et al. Stereotactic radiosurgery of the postoperative resection cavity for brain metastases. *Int J Radiat Oncol Biol Phys*. 2008;70:187-193.
21. Choi CYH, Chang SD, Gibbs IC, et al. Stereotactic radiosurgery of the postoperative resection cavity for brain metastases: Prospective evaluation of target margin on tumor control. *Int J Radiat Oncol Biol Phys*. 2012;84:336-342.
22. Nataf F, Schlienger M, Liu Z, et al. Radiosurgery with or without a 2-mm margin for 93 single brain metastases. *Int J Radiat Oncol Biol Phys*. 2008;70:766-772.
23. Kirkpatrick JP, Wang Z, Sampson JH, et al. Defining the optimal planning target volume in image-guided stereotactic radiosurgery of brain metastases: Results of a randomized trial. *Int J Radiat Oncol Biol Phys*. 2015;91:100-108.
24. Badloe J, Mast M, Petoukhova A, et al. Impact of PTV margin reduction (2 mm to 0 mm) on pseudoprogression in stereotactic radiotherapy of solitary brain metastases. *Tech Innov Patient Support Radiat Oncol*. 2021;17:40-47.
25. de Azevedo Santos TR, Tundisi CF, Ramos H, et al. Local control after radiosurgery for brain metastases: Predictive factors and implications for clinical decision. *Radiat Oncol*. 2015;10:63.
26. Moraes FY, Winter J, Atenafu EG, et al. Outcomes following stereotactic radiosurgery for small to medium-sized brain metastases are exceptionally dependent upon tumor size and prescribed dose. *Neuro Oncol*. 2019;21:242-251.
27. Redmond KJ, Gui C, Benedict S, et al. Tumor control probability of radiosurgery and fractionated stereotactic radiosurgery for brain metastases. *Int J Radiat Oncol Biol Phys*. 2021;110:53-67.
28. Guckenberger M, Roesch J, Baier K, et al. Dosimetric consequences of translational and rotational errors in frame-less image-guided radiosurgery. *Radiat Oncol*. 2012;7:63.
29. Sagawa T, Ohira S, Ueda Y, et al. Dosimetric effect of rotational setup errors in stereotactic radiosurgery with HyperArc for single and multiple brain metastases. *J Appl Clin Med Phys*. 2019;20:84-91.
30. Schasfoort J, Ruschin M, Sahgal A, et al. Quantifying the sensitivity of target dose on intrafraction displacement in intracranial stereotactic radiosurgery. *Pract Radiat Oncol*. 2022;12:e221-e231.