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Is a single isocenter sufficient for volumetric modulated arc therapy radiosurgery when multiple itracranial metastases are spatially dispersed?

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ABSTRACT

Previous work demonstrated improved dosimetry of single isocenter volumetric modulated arc therapy (VMAT) of multiple intracranial targets when they are located ≤ 4 cm from isocenter because of narrower multileaf collimators (MLCs). In follow-up, we sought to determine if decreasing isocenter-target distance (d_{iso}) by using 2 to 3 isocenters would improve dosimetry for spatially dispersed targets. We also investigated the effect of a maximum dose constraint during VMAT optimization, and the dosimetric effect of the number of VMAT arcs used for a larger number of targets (*i.e.*, 7 to 9). We identified radiosurgery cases that had multiple intracranial targets with d_{iso} of at least 1 target > 5 cm. A single isocenter VMAT plan was created using a standardized 4-arc technique with 18 Gy per target. Each case was then replanned (1) using 2 to 3 isocenters, (2) including a maximum dose constraint per target, and in the case of 7 to 9 targets, (3) using 3 to 6 arcs. Dose evaluation included brain $V_{6\ Gy}$ and $V_{12\ Gy}$, and conformity index (CI), gradient index (GI), and heterogeneity index (HI) per target. Two isocenters were sufficient to limit d_{iso} to ≤ 4 cm and ≤ 5 cm for 11/15 and 13/15 cases, respectively; after replanning with 2 to 3 isocenters, d_{iso} decreased from 5.8 ± 2.8 cm (2.3 14.9) to 2.5 ± 1.4 cm (0 5.2). All dose statistics improved on average, albeit modestly: $V_{6\ Gy}$ = 6.9 ± 7.1%, $V_{12\ Gy}$ = 0.9% ± 4.4%, CI = 2.6% ± 4.6%, GI = 0.9% ± 12.7%, and HI = 2.6% ± 5.2%; however, the number of arcs doubled and monitor units increase by nearly 2-fold. A maximum dose constraint had a negative effect on all dose indices, increasing $V_{12\ Gy}$ by 9.7 ± 6.9%. For ≥ 7 targets, increasing number of arcs to > 3 improved CI, $V_{12\ Gy}$, and $V_{6\ Gy}$. A single isocenter is likely sufficient for VMAT radiosurgery of multiple intracranial metastases. Optimal treatment plan quality is achieved when no constraint is placed on the maximum target dose; for cases with many targets at least 4 arcs are needed for optimal plan quality.

Introduction

Radiosurgery is a well-established treatment technique for intracranial malignancies,[1,2] and has been implemented with a linear accelerator (LINAC) apparatus.[2] Typically on a LINAC-based system, this is achieved using dynamic conformal arcs collimated by high-definition multileaf collimators (MLCs)[3-5]; however, a recent development is single isocenter volumetric modulated arc therapy (VMAT) for radiosurgery of multiple intracranial targets.[6-13]

In a series of publications, a group at the University of Alabama outlined a single isocenter VMAT treatment planning strategy that includes 2 to 4 VMAT arcs; they also included guidelines for optimization and compared treatment plan quality with other multiisocenter radiosurgery techniques (dynamic conformal arcs and Gamma Knife).[7,8,12] Hardcastle *et al.*[9] compared treatment plan quality of single isocenter VMAT with a standard conformal arc technique; McDonald *et al.*[10] also performed a treatment planning study comparing single isocenter VMAT with Gamma Knife, although the MLCs used in this study had 5.0 mm rather than 2.5 mm resolution that is typical of other studies. Lau *et al.*[11,14] reported similar outcomes to conventional radiosurgery for patients treated with a single isocenter VMAT technique. The VMAT technique has the advantage of decreasing treatment time at the cost of

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added plan complexity; these complexities include potentially greater dosimetric effect of rotational errors,[13,15] and the use of larger MLCs (5.0 mm) for targets located > 4 cm from the isocenter[16-20] when a commonly available MLC system (Varian HD-MLC [Varian Medical Systems, Palo Alto, CA]) is used.

Recently, we addressed these challenges and showed the need for correcting rotational errors via image guidance for these cases.[13] We also quantified the dosimetric effect of target distance from the isocenter, and investigated various isocenter placement strategies to optimize plan quality. We found that all isocenter placement strategies were subject to the same plan quality tradeoffs: targets located proximal to the isocenter had improved conformity index (CI), gradient index, and heterogeneity index. In addition, our previous work showed that the optimal VMAT treatment plan typically results in a somewhat higher level of heterogeneity relative to conventional LINAC-based radiosurgery. For example, the maximum dose per target ranged from 135% to 165% of prescription dose, which corresponds to the 60% to 75% isodose line when the dose is normalized to the maximum point dose; in comparison, the heterogeneity for dynamic conformal arc radiosurgery is often more modest with a 110% to 120% max dose (83% to 90% isodose line).[21,22] These results raise the question of whether improved dosimetry could be achieved using more than 1 isocenter for select patients that have multiple intracranial targets located distal from each other, and whether a maximum dose constraint negatively affects normal tissue dose sparing for these cases.

To follow up, the primary objective of this study was to investigate whether improved dosimetry may be achieved by limiting the target distance from the isocenter to 5 cm using 2+ isocenters, thus minimizing the use of larger (5 mm) MLCs. We also investigated the dosimetric cost of including a maximum dose constraint within the optimization to more closely align the dose heterogeneity with conventional LINAC-based radiosurgery. Finally, many of the single isocenter VMAT cases that would have targets located distal from the isocenter have a large number of targets (7 to 9), which is on the upper end of the range of cases included in previous studies.[8-12,14] For these cases with a large number of targets, we investigated the number of arcs needed to achieve optimal VMAT plan quality.

Methods and Materials

Patient cohort

All analyses were retrospective; under an internal review board–approved protocol, radiosurgery cases within our department from the past 6 years were reviewed. Cases that received single isocenter VMAT to multiple targets and were immobilized with the U-frame thermoplastic mask immobilization system (BrainLAB, Heimstetten, Germany) were identified. An additional criteria was to select those who had at least 1 target located > 5 cm from the isocenter when treated with a single isocenter.

Treatment plan and evaluation

We used the Eclipse v11.0 treatment planning system (Varian Medical Systems, Palo Alto, CA). The LINAC(s) used for the treatment planning and delivery were specialized for stereotactic applications and were equipped with an high-definition MLC with 2.5-mm wide leaves within ± 4 cm from the isocenter and 5-mm leaves at greater distance.

The arc geometry (couch angle, gantry rotation, and collimator angle) were chosen as described in previous studies,[7,13] with each single isocenter VMAT plan consisting of the following 4 VMAT arcs: 1 full arc with no couch rotation and 3 half rotation arcs equally spaced in the superior hemisphere. The isocenter was placed in the centroid of all targets, with each target weighted equally. Optimization criteria have also been described in detail previously,[7,13] and include ring structures to minimize the normal tissue dose; the optimization priorities were modified on a case by case basis to achieve similar coverage between targets.

Dose statistics were tabulated for each plan, including brain $V_{12\ Gy}$, low dose volume (brain $V_{6\ Gy}$), total number of monitor units. For each individual target of each plan we tabulated CI, gradient index, and heterogeneity index. We define CI as

$$CI = \frac{(V_{PTV} \cap V_{100\%})^2}{V_{PTV} \times V_{100\%}}, \quad (1)$$

or in other words, as the square of the intersection of the target volume (V_{PTV}) with the prescription isodose volume ($V_{100\%}$). We define the gradient and heterogeneity indices as

$$GI = \frac{V_{50\%}}{V_{100\%}}, \quad (2)$$

$$HI = \frac{D_{max}}{D_{Rx}}, \quad (3)$$

where $V_{50\%}$ is the volume receiving greater than or equal to 50% of the prescription dose, and D_{max} and D_{Rx} are the maximum and prescription doses, respectively. With these definitions, CI is perfect at 1.0, whereas additional or lacking coverage results in a CI < 1.0. Smaller GI values indicate a faster dose fall-off.

Single vs. 2+ isocenters

We replanned each of the 15 single isocenter VMAT plans as a multiple isocenter VMAT plan with the following procedure. Targets were strategically assigned to one of the isocenters to minimize the overall and maximum distance of the targets from their respective isocenters, and the isocenter was placed in the centroid of its respective targets (weighted equally). For cases with many targets and for which the optimal isocenter assignment was not obvious, we iteratively changed the isocenter assignment until the maximum distance from the isocenter for any target was minimized. Each isocenter used 4 VMAT arcs, with the jaws collimated to just include the associated targets. A third isocenter was included if targets were still > 5 cm from the isocenter when using 2 isocenters; these cases included a total of 10 VMAT arcs that were divided among the 3 isocenters (4-4-2 or 4-3-3). For all cases, all isocenters were inverse optimized simultaneously using the same optimization criteria and procedures as with the single arc VMAT plans.

Plan geometry for many targets

Many of the cases have a large number of targets (7 to 9), which is on the upper end of the range of single isocenter VMAT cases included in prior studies.[8-12,14] For these cases with a large number of targets, we investigated the number of arcs needed to achieve optimal plan quality in the VMAT. For cases with ≥ 7 targets, we created single isocenter plans with 3, 4, 5, and 6 VMAT arcs. Each plan had 1 full arc with no couch rotation, and 2 to 5 half rotation arcs that are equally spaced in the superior hemisphere. In addition to the dose statistics described above, we also tabulated the maximum skin dose for these cases, to identify whether 3 arcs was sufficient to achieve adequate dose fall-off at the skin. Skin dose was calculated as maximum dose within 5 mm of the patient surface.

Maximum dose constraint

As the plans optimized in this study had higher heterogeneity relative to conventional LINAC-based radiosurgery, we also investigate the dosimetric cost of including a maximum dose constraint within the optimization. Each plan was reoptimized with each target having an additional constraint to limit the maximum dose to 112%, with a priority of roughly 90% that of the planning target volume lower dose constraint.

Results

We identified 15 single isocenter radiosurgery patients who had at least 1 target located > 5 cm from the isocenter when treated with a single isocenter; approximately 65% of single isocenter VMAT plans to multiple targets met this criteria. The mean number (± standard deviation) of targets per plan was 4.9 ± 2.4 (median = 4), and ranged from 3 to 9. Of these plans, 5 had ≥ 7 targets.

Single vs. 2+ isocenters

Using 2 isocenters decreased the maximum distance from the isocenter per target to ≤ 5 for all but 2 cases; for these cases 3 isocenters were used. Using 2 to 3 isocenters rather than a single isocenter decrease d_{iso} from a mean ± standard deviation of 5.8 ± 2.8 cm (range = 2.3 to 14.9 cm) to 2.5 ± 1.4 cm (range = 0 to 5.2 cm). The number of targets assigned to each isocenter reduced from 4.9 ± 2.4 (range = 3 to 9) to 2.3 ± 1.5 (range = 1 to 6). Total