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# Understanding & Optimizing Isocenter Placement In Single- and Multi-Isocenter Linear Accelerator-Based Radiosurgery Treatment Planning for Multiple Brain Metastases

Justin M. Napolitano PhD[1], James D. Ververs PhD[1] , Christina K. Cramer MD[1], Kenneth S. Berenhaut PhD[2], Michael T. Munley PhD[1], and J. Daniel Bourland PhD[1].

[1]Wake Forest University School of Medicine, Winston-Salem, NC, [2]Wake Forest University, Winston-Salem, NC

## ABSTRACT

### PURPOSE

Brain metastases (BM) can be treated with linear accelerator (LINAC)-based stereotactic radiosurgery (SRS). Treatment planning for this modality has evolved over time; plans typically have one, two, or n isocenters, where n is the number of targets. Common isocenter locations include the center of each target, the center of the brain or a region within it, the centroid of the targets, or coordinates determined by an expert clinician. The goals of this work are to 1) investigate the impact of isocenter quantity and location on treatment plan quality, and 2) explore isocenter designation options outside current and historical standards.

### METHODS

In a simulated phantom, thousands of configurations of targets, organs, and isocenters were optimized, and the resultant analysis served as the framework for advanced isocenter designation models. Next, ten anonymized GammaKnife® cases with 9–11 BMs were selected to be replanned for LINAC-based SRS with 1/2/3/4/5 isocenters. Three different isocenter designation models were utilized, each yielding 50 configurations.

### RESULTS

It was demonstrated that increasing isocenter quantity significantly improves integral dose, conformity, and organ sparing. That said, this relationship is non-linear; each new isocenter has diminishing and eventually potentially negative returns. It was also found that plan quality decreases as isocenter distance-to-target increases, and that factors such as target depth, size, and organ proximity influence this relationship—the models that accounted for these factors outperformed the simplest model. Finally, patient-specific quality assurance was performed to confirm plan deliverability.

### CONCLUSIONS

This work indicates that multi-isocenter solutions, when sufficiently configured and optimized, outperform single-isocenter solutions when treating 9–11 BMs. While the derived models show great promise, future work aims to 1) explore the potential impact of other parameters (e.g., arc configuration), 2) improve the modeling of identified significant phenomena (e.g., organ avoidance), and 3) investigate the models' handling of other quantities of BMs.

## DISCLAIMER

Napolitano JM. (2025). Radiation treatment planning methods, systems and computer program products. U.S. Provisional Application No. 63/750,475, filed January 28, 2025.

## CONTACT

Justin M. Napolitano, PhD
UPMC Hillman Cancer Center
Pittsburgh, PA
Justin.M.Napolitano@gmail.com
(631) 921-9572

## INTRODUCTION & METHODS

- Linear Accelerator (LINAC)-based Stereotactic Radiosurgery (LSRS) is an effective method for treating multiple brain metastases (MBM).
  - Plans traditionally have one isocenter, but more can be added to treat complex target/patient geometries.
- Physical parameters of LSRS include (not limited to):
  - Gantry start and stop angles and rotation direction, couch angle, collimator angle, field size, and dose rate and delivery time restrictions.
- Plan quality metrics include (not limited to):
  - Dose to normal tissue [*e.g.*, D80], integral dose / dose spillage [*e.g.*, V8Gy], conformity (CI) and homogeneity index (HI), and modulation [i.e., Monitor Units (MU)].

**Objective:** (1) Characterize the relationship between isocenter configuration (quantity and location) and treatment plan quality metrics and (2) apply these findings to optimize LSRS treatment planning.

A spherical representation of a brain containing metastases **(Fig 1)** was simulated in RayStation® for *in-silico* experiments, including:

- ONA – Single static target with 0.1 mm "micro adjustments" to isocenter location to elicit variation in resultant plans.
- TID – Single static target with a dynamic isocenter location.
- TED – Single dynamic target with a dynamic isocenter location.
- TSP – Single static target of variable size and prescription with a dynamic isocenter location.
- ODC – Single static target and an organ of varying distance-to-target/constraint with a dynamic isocenter location.
- ORL – Single static target and an organ of varying location with a dynamic isocenter location

Ten cases previously treated for MBM using GammaKnife™ **(Fig 2)** were replanned for LSRS with 1–5 isocenters chosen with various algorithmic strategies.

- Model 1 – *K*-means clustering of PTV centroids.
- Model 2 – *K*-means clustering of prioritized PTV centroids.*
- Model 3 – Modified *K*-means clustering of prioritized PTV centroids.**

All plans created with Model 1 underwent patient-specific quality assurance (PSQA), performed utilizing an SRS MapCHECK® with StereoPHAN™ and gamma analysis at 3%/1 mm ΔD/DTA.

*Prioritization based on target depth and size.

**Modifications include isocenter distance-to-target (IDT) anisotropy and organ-based repulsion.

**Fig 1. Simulated phantom experimental configurations.**

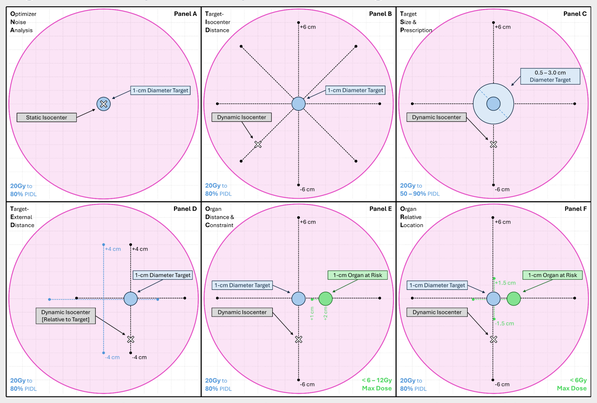
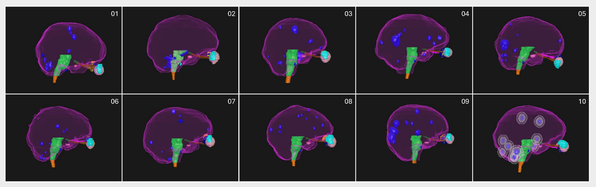
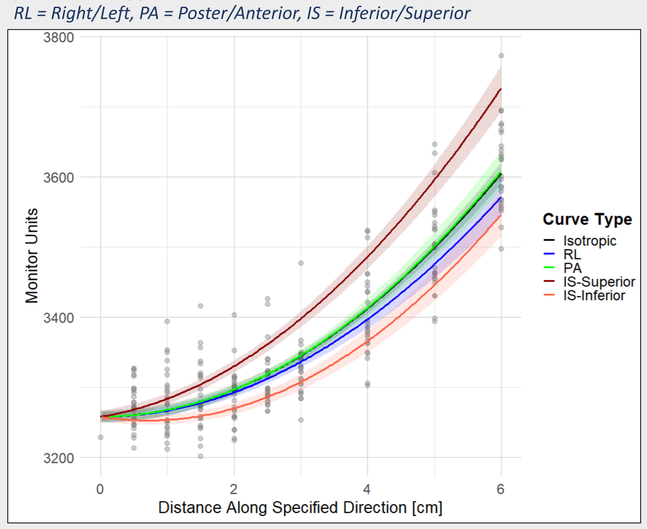



**Fig 2. Case Cohort.** BM PTVs with 1-mm margins are shown in blue. Case 10 shows 5 and 10 mm avoidance rings in white.



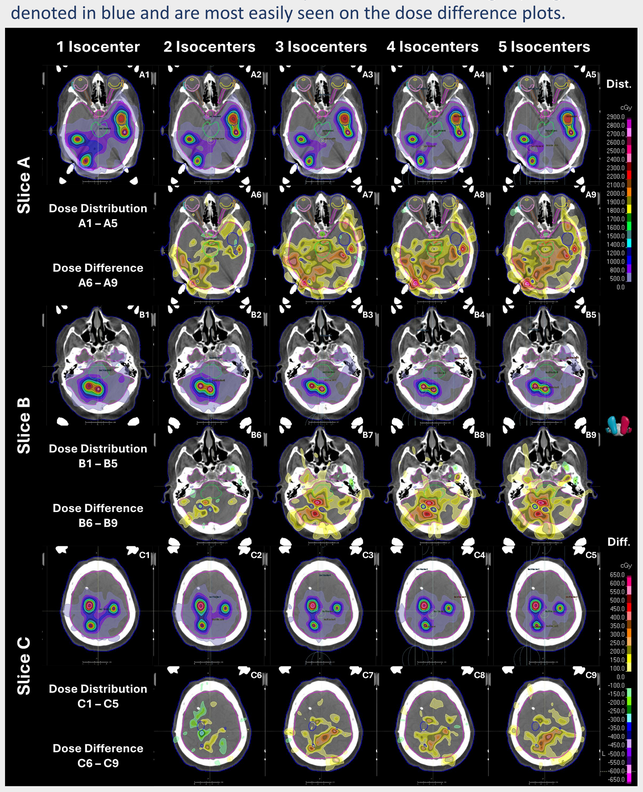

## RESULTS & DISCUSSION

**Fig 3. Isotropic versus Anisotropic Fit of TID Results.** Data points are shown in gray in the Euclidian ITD plane; curves are otherwise plotted against distance in their respective planes. The IS plane is split due to statistically significant IS-plane anisotropy.
*RL = Right/Left, PA = Poster/Anterior, IS = Inferior/Superior*




- MU found to exponentially increase as IDT increases.
- Relationship is anisotropic across planes and within the IS plane; optimal isocenter location found to be 7.2mm inferior to (below) the target.
- Relationship between IDT and MU found to change with other experimental characteristics (*e.g.*, target size and depth, and organ location and constraint).

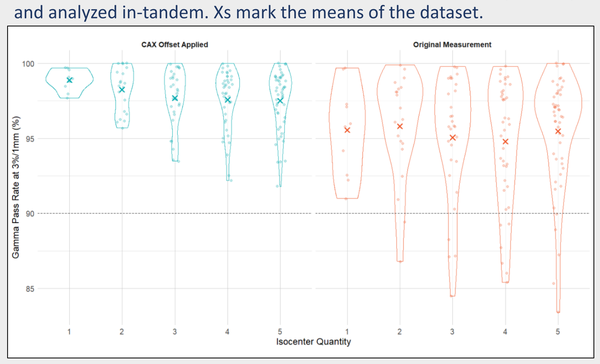
**Fig 4. Case 03 Dose Distribution.** Dose distributions for plans with one through five isocenters (Model 1) at three different axial slices. Dose differences versus the single-isocenter plan are also displayed. Slice A, B, and C refer to different axial slices that capture nine of the 11 targets; targets are denoted in blue and are most easily seen on the dose difference plots.




- Case 03 shows 33–43% reduction in V5/8/12/16Gy in the five- versus single-isocenter plan.
- Average reduction to V12Gy (relative to single-isocenter) across all Model 1 plans found to be -14.7%, -19.5%, -23.7%, and -25.9% percent for two, three, four, and five isocenters, respectively.
- Target coverage (D80) was scaled and CI improved.

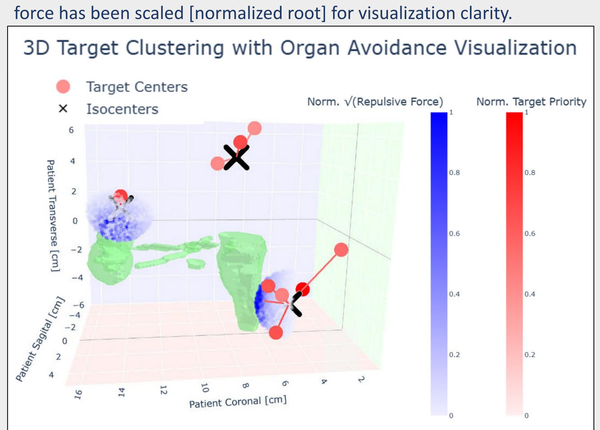
## RESULTS & DISCUSSION

**Fig 5. Gamma Passing Rates.** Delivery was performed "iso-by-iso", such that all beams associated with an isocenter were delivered sequentially and analyzed in-tandem. Xs mark the means of the dataset.



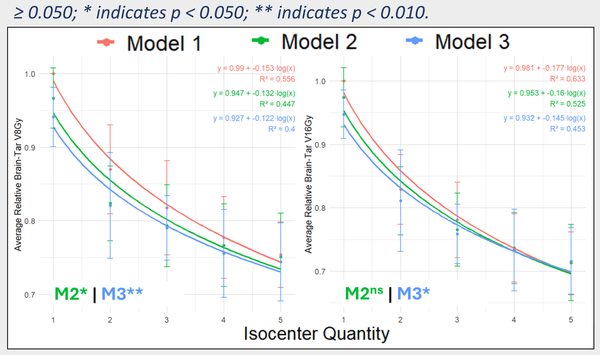

- 89.3% of all isocenters passed QA with a gamma passing rate (GPR) of ≥90% at 3%/1 mm.
- There is no statistically significant relationship between isocenter quantity and GPR.

**Fig 6. Case 07 M3 Clustering.** OARs are shown in green. The repulsive force has been scaled [normalized root] for visualization clarity.




- Each model returned unique isocenter configurations.
- Repulsive force only had substantial impact in one case (Case 02), which was caused by target proximity to the brainstem and optics.

**Fig 7. Relative Outcome Metric Trends.** All values are defined as the average of the raw values divided by the values at that case's Model 1 single-isocenter plan. Logarithmic regressions are fit to the relative datapoints, not the averages. *ns (not statistically significant) indicates p ≥ 0.050; * indicates p < 0.050; ** indicates p < 0.010.*




- Relative V8Gy and brainstem D0.5cc statistically significantly decreased between Model 2 and 3 versus Model 1; V5/12/16Gy did for Model 3 only.

## CONCLUSIONS

- Isocenter quantity and location impact plan quality; each case has an optimal "sweet spot" isocenter quantity.
- Accounting for anatomical and pathological factors can improve isocenter designation methods.
- Single- and multi-isocenter are comparably deliverable.