Treatment planning strategies for stereotactic Radiosurgery in managing Multiple brain metastases -An Institutional Experience.

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Abstract:

Managing multiple brain metastases poses a significant challenge in neuro-oncology. The Cyber Knife system, a robotic radiosurgery device, has become a crucial treatment modality due to its precision and efficacy. This study investigates treatment planning strategies for Cyber Knife stereotactic radiosurgery (SRS) in patients with multiple brain metastases[1,2]. We evaluated the treatment plans of 10 patients who underwent SRS using the Cyber Knife system. The primary objective was to assess the efficacy and precision of the treatment planning strategies employed. The study highlights the importance of individualized treatment plans based on the number, size, and location of metastases, as well as the patient's overall health and prognosis. Advanced imaging modalities, such as MRI and PET-CT, play a critical role in accurate target delineation. The findings aim to optimize treatment outcomes, minimize adverse effects, and improve the quality of life for patients with multiple brain metastases. Purpose of this study is to assess the delivery efficiency, plan quality, and dosimetry of planned treatment volume (PTV) and normal brain tissue in Cyber Knife planning approaches for multiple brain metastases (MBM).In our clinic, 10 cancer patients with multiple cranial metastases (2 to 6 tumors) were treated with Cyber Knife. The prescription dose was 20 Gy in a single fraction. Dosimetric properties were evaluated, with the new Conformity Index (nCI) and Gradient Index (GI) being 1.14 ± 0.09 and 3.96 ± 0.16, respectively, and the Homogeneity Index (HI) being 1.10 ± 0.05. For combined PTV, Dmin (Gy) was 18.95 ± 0.21, Dmax (Gy) was 22.21 ± 0.24, D2% (Gy) was 22.07 ± 0.05, and D98% (Gy) was 19.91 ± 0.3. For normal brain tissue, the dosimetric parameters evaluated were V12Gy (cm^3) at 4.98 ± 0.59, V10Gy (cm^3) at 7.77 ± 0.39, V5Gy (cm^3) at 22.99 ± 1.44, and V3Gy (cm^3) at 86.71 ± 3.27. The maximum doses (Gy) to organs at risk (OARs) were 0.12 ± 0.04 for lenses, 3.01 ± 0.31 for the brainstem, and 2.71 ± 0.29 for optic nerves.

Keywords: Cyber Knife, Iris, gradient index, conformity index, Stereotactic radiosurgery.

INTRODUCTION:

Stereotactic radiosurgery (SRS) and hypo-fractionated stereotactic radiotherapy (SRT) are both safe and effective treatment methods for brain metastasis patients. Both treatments have been shown to be highly effective in avoiding neurotoxicity and worsening of quality of life in patients with multiple brain metastases (MBM). SRS and SRT can be administered using some of the advanced technologies like the Gamma Knife (GK; Elekta AB, Stockholm, Sweden), Cyber Knife robotic radiosurgery system (CK; Accuray, Sunnyvale, CA, USA), and linear accelerators. These machines have distinct characteristics in terms of plan quality and delivery efficiency, particularly for the treatment of MBM[1,2].

The Cyber Knife system, on the other hand, has been linked to excellent overall survival and local control rates for MBM patients, but not with extremely high toxicity. This system is a 6-MV flattening filter-free (FFF) accelerator mounted on an arm robot that can deliver non-isocentric, non-coplanar beam arrangements. This is complemented by a high-resolution image-guided tracking system that offers precise positioning of the radiation beam on target during treatment, typically every 30–60 seconds. The fixed node locations and variable beam directions offer greater accuracy and efficiency in the treatment.

The Cyber Knife robotic radiosurgery device (Accuray Inc., Sunnyvale, CA) is an advanced image-guided radiation therapy device that utilizes near-real-time imaging to dynamically align the radiation beam with the

target continuously. Its non-isocentric, non-coplanar design provides rapid dose falloff at the target boundary, a key dosimetric feature for minimizing radiation dose to nearby critical structures. This is usually quantified by the gradient index (GI), and studies indicate that an increasingly preferable GI with a more steplike dose gradient has the ability to reduce dose of radiation to normal brain tissue and reduce complication rates. This is especially helpful in the treatment of critical anatomical structures or for larger volumes, where selecting the plan with the minimum "penumbra dose" is most critical. Less than a GI of 3.0 is advisable in routine Gamma Knife surgery (GKS)[5] underlining the need for sharp dose falloff in stereotactic radiosurgery/radiotherapy.[8,10]

Fixed divergent circular collimators (cones) have been used historically to delineate X-ray beam shapes in the Cyber Knife system because of their low collimator transmission and steep penumbrae. Although up to three fixed cones can be used together in a single treatment plan for a target, as offered by the system, this is time-consuming since manual collimator changes are made during repeated traversals of the robotic manipulator along the patient.

We employ the CyberKnife S7 model, which is one of the most advanced robotic radiosurgery systems with high precision and efficacy in the treatment of numerous conditions in our clinic. It features a fixed cones collimator, an Iris variable aperture collimator, and the InCise2™ MLC, all of which combine to offer improved treatment precision and efficacy. The InCise2™ MLC is comprised of 26 pairs of leaves, 2.5 mm wide at isocenter, which permits very precise beam shaping and targeting of complex tumor shapes. It permits very accurate dose delivery with very low exposure to adjacent healthy tissue.

Collimator selection is typically based on clinical experience and specific target size. It can also be decided upon advice from a treatment planning system (TPS), e.g., Precision 3.2.0.0. Collimator selection plays a significant role in determining target coverage, sparing of organ at risk (OAR), and the efficiency of delivery. Figure 1 illustrates collimator selection in TPS, highlighting the critical role that collimator selection plays in optimizing treatment.

METHODS AND MATERIALS:

For this study, 10 cases of multiple brain metastases (MBM) were analyzed. In all treatment plans, the entire planning target volume (PTV) was covered by collimators. For plan quality validation, various parameters were compared, including monitor units (MUs), number of nodes and beams, estimated fraction treatment time (EFTT), new conformity index (nCI), dose gradient index (GI), homogeneity index (HI), PTV minimum/maximum dose (Dmin/Dmax), volume doses (D2% and D98%), and maximum doses to lenses, optic nerves, and brainstem. Doses to normal brain tissue at 3, 5, 10, and 12 Gy (V3Gy–V12Gy) were also compared. The lesions were two to six per patient.

Contour Delineation: Contours were delineated as per 1-mm CT and MRI slice thickness. PTV was the gross tumor volume (GTV) with a 1-mm margin. Each GTV was expanded individually to generate individual PTVs, and a composite PTV (PTVcombo) was created by combining all individual PTVs for analysis. Organs at risk (OARs) included normal brain, eyes, lenses, brainstem, cochlea, and optic nerves. The normal brain volume was contoured as the whole brain minus the PTVcombo.

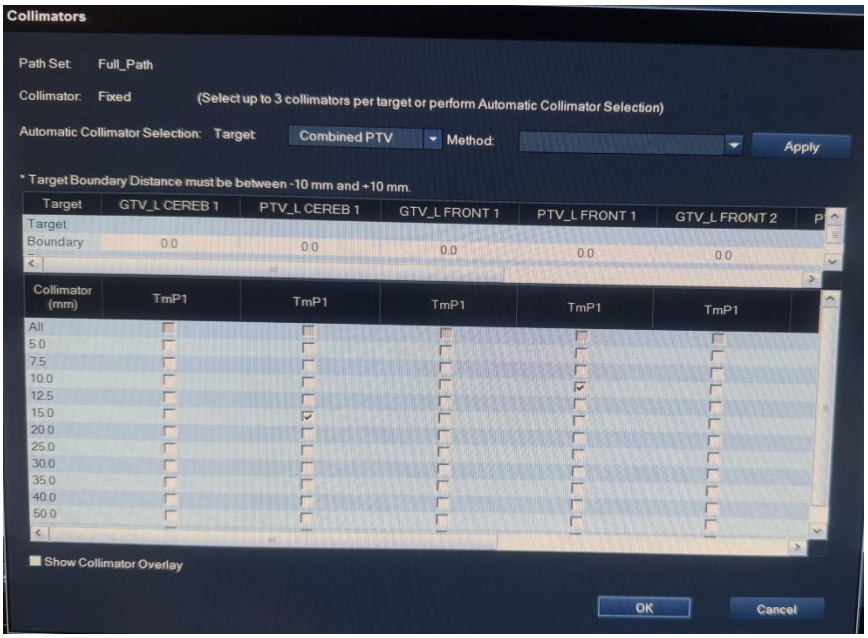

Figure.1- collimator selection in TPS.

TREATMENT PLANNING[3,4,9]

The prescription dose in all instances was 20 Gy in a single fraction, with target volumes less than 1 cm^3. The beam intersection model was arranged so that the eyes and lenses were spared. The optimization goal for the PTV was to achieve an optimized minimum dose (OMI) equal to the same value as the prescription dose. Normalization was used for all treatment plans in a way that 95% of the PTV would be covered by 100% of the prescription dose. The PTVcombo was the target, and collimators were selected based on the size of each lesion.

PLAN EVALUATION:

Treatment plans were evaluated based on several key metrics. Dose-volume histogram (DVH) parameters, including minimum dose (Dmin), maximum dose (Dmax), 2% volume maximum dose (D2%), and 98% volume minimum dose (D98%), were assessed for the planning target volume (PTV). Conformity of the dose distribution was evaluated using a new conformity index (nCI), calculated as

$$nCI = \frac{V_T V_P}{V^2_{TP}}$$

where V_T is the total target volume, V_P is the volume receiving the prescribed dose, and V_{TP} is the target volume receiving the prescribed dose. Homogeneity of the dose distribution within the target was quantified by the homogeneity index (HI), calculated as $HI = \frac{D_{max}}{PrescribedDose}$

The steepness of the dose gradient was evaluated using the dose gradient index (GI), calculated as GI=Vp V50%Dp, where V50%Dp is the volume enclosed by the 50% prescription isodose line, and Vp is the prescription volume. For normal brain tissue, volumes receiving 3, 5, 10, and 12 Gy (V3Gy, V5Gy, V10Gy, V12Gy) were evaluated. Maximum doses to the lenses, optic nerves, brainstem, and optic chiasm were recorded, with the optic chiasm evaluated using the same dose constraints as the other listed optical structures, as per departmental protocol. Treatment delivery parameters, including monitor units (MUs), number of nodes, and number of beams, were recorded. The estimated fraction treatment time (EFTT) was calculated by the treatment planning system (TPS), incorporating MUs, nodes, beams, user-defined estimated patient setup time, and estimated image time intervals.

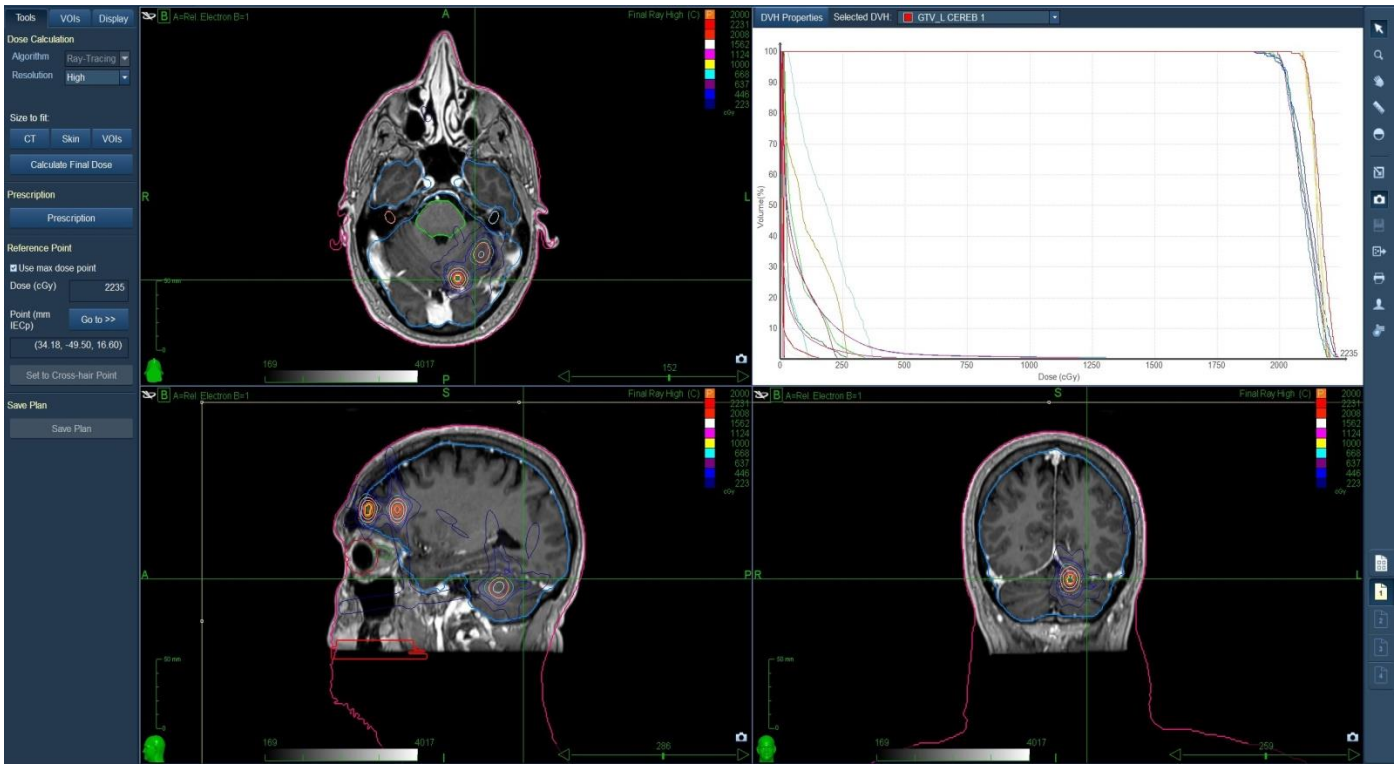

Figure.2: Dose Distribution and DVH for a patient plan having 4 lesions.

RESULTS:

The treatment delivery efficiency parameters were detailed in Table 2. Utilizing the same treatment approach but varying collimator settings, smaller collimator values led to an increase in monitor units (MUs), a reduction in the number of beams and nodes, and a shorter estimated fraction treatment time (EFTT), as presented in Table 3. The new conformity index (nCI) was measured at 1.14 ± 0.09, the gradient index (GI) at 3.96 ± 0.16, and the homogeneity index (HI) at 1.10 ± 0.05. For the combined planning target volume (PTV), the minimum dose (Dmin) was 18.95 ± 0.21 Gy, the maximum dose (Dmax) was 22.21 ± 0.24 Gy, the 2% volume maximum dose (D2%) was 22.07 ± 0.05 Gy, and the 98% volume minimum dose (D98%) was 19.91 ± 0.3 Gy. For normal brain tissue, the evaluated dosimetric parameters were: V12Gy, 4.98 ± 0.59 cm^3; V10Gy, 7.77 ± 0.39 cm^3; V5Gy, 22.99 ± 1.44 cm^3; and V3Gy, 86.71 ± 3.27 cm^3. The maximum doses to organs at risk (OARs) were also assessed, revealing values of 0.12 ± 0.04 Gy for the lenses, 3.01 ± 0.31 Gy for the brainstem, and 2.71 ± 0.29 Gy for the optic nerves.

TABLE 1: DVH parameters for PTV.

Patients	Dmin	Dmax	D2%	D98%
1	18.95	22.35	22.05	19.90
2	18.87	21.95	22.03	19.92
3	18.65	22.03	21.99	20.01
4	18.72	22.21	22.01	19.89
5	18.84	21.89	22.06	19.78
6	19.02	22.51	22.12	20.02
7	19.21	22.64	22.14	20.12
8	18.86	22.14	22.08	19.15
9	19.31	22.23	22.13	20.13
10	19.10	22.18	22.07	20.24
Mean	18.95	22.21	22.07	19.91
Median	18.91	22.20	22.07	19.97
Std div	0.21	0.24	0.05	0.30

TABLE 2: Dosimetric results for normal brain tissue, lens, optical nerves, and brainstem.

Patients	V12Gy (cm3)	V10Gy (cm3)	V5Gy (cm3)	V3Gy (cm3)	Lens(R) (Gy)	Lens(L) (Gy)	Brainstem (Gy)	Optic Nerves (Gy)
1	5.76	8.07	25.12	90.84	0.09	0.18	3.59	2.70
2	4.89	7.65	23.14	88.56	0.08	0.09	2.88	2.84
3	5.23	7.84	22.14	87.98	0.12	0.17	3.41	2.65
4	4.97	7.65	22.07	82.5	0.15	0.11	2.92	2.47
5	4.53	7.42	21.98	81.9	0.13	0.14	3.21	2.92
6	5.84	8.13	24.86	87.6	0.12	0.13	2.74	2.48
7	3.86	6.89	21.57	88.1	0.08	0.16	3.14	3.12
8	5.18	8.06	24.18	89.6	0.18	0.11	2.84	2.86
9	4.59	7.92	24.1	88.3	0.09	0.1	2.62	3.05
10	5.32	8.12	21.14	82.3	0.14	0.19	2.87	2.17
Mean	4.98	7.77	22.99	86.71	0.11	0.13	3.01	2.71
Median	5.08	7.88	22.64	88.04	0.12	0.14	2.90	2.77
Std div	0.59	0.39	1.44	3.27	0.03	0.04	0.31	0.29

DISCUSSION:

The management of greater than one brain metastasis (MBM) with the Cyber Knife (CK)[6,7] system is based on judicious planning consideration for the number and their association with critical and radiosensitive organs. The following article examines combined planning approaches, with focus on quality optimization parameters, delivery efficiency, and both PTV and normal brain dosimetry. In combined PTV planning, differences were seen in the minimum and maximum dimensions of Iris collimators but monitor units (MUs) remained the same. In past research, it has been proven that larger collimators reduce dose uncertainty and improve target coverage. However, with additional beams added with two PTVs, additional doses to inter-PTV space were delivered, resulting in increased normal brain dose in combined plans.

TABLE 3: Dosimetric results for plan quality.

Patients	nCI	HI	GI	PTV Vol(cm3)	MU's	EFTT (Minutes)	Nodes &Beams
1	1.25	1.12	4.10	0.98	12968.7	45	63&84
2	1.05	1.02	3.95	0.85	9758.4	29	42&44
3	1.02	1.03	4.08	0.93	19761.5	46	61&78
4	1.14	1.15	3.85	0.95	13170	38	42&55
5	1.12	1.14	3.68	0.87	8222.1	24	24&28
6	1.06	1.16	3.92	0.85	8870.8	25	22&26
7	1.15	1.12	4.11	0.79	10109.6	44	66&85
8	1.31	1.08	4.20	0.96	21728.2	56	68&98
9	1.24	1.07	3.87	0.97	41442.2	68	80&152
10	1.12	1.16	3.85	0.95	7392.9	24	0&34
Mean	1.14	1.10	3.96	0.91			
Median	1.13	1.12	3.94	0.94			
Std div	0.09	0.05	0.156	0.06			

We evaluated the impact of plan quality, delivery efficiency, and dosimetry with different optimization strategies against the number of collimators. A significant difference was noted in the number of nodes between the plans. With combined PTVs, targets had more than two or three collimators very frequently. As the number of collimators increased nodes, beams, EFTT, GI, and dose to normal brain, it reduced MUs and HI. Improved PTV coverage was achieved with increased PTV Dmin.

Two-collimator plans significantly reduced the dose to normal tissue, improved GI, and reduced beams and EFTT. With three collimators, PTV coverage was improved by increasing PTV Dmin and D98% and decreasing PTV Dmax, D2%, and HI. Optimization of conformity and homogeneity of the PTV versus protection of the OARs is of utmost importance. The increase in the number of Iris collimators tends to produce little improvement in PTV dose coverage and plan quality (HI), longer treatment time, and worsening normal brain dosimetry. Therefore, collimator numbers should be optimized to achieve an optimal balance between the aim of treatment and OARs.

To be consistent, all the cases from this study were normalized to constant parameters. The lens and brainstem were unilaterally spared at beam intersections in order to maintain their doses according to planning strategies. In cases with more than six lesions, there are workarounds that are not lower in plan quality, such as irradiating the two eyes simultaneously rather than one at a time to support the inclusion of an additional target. Separate planning for PTVs in such cases is not suitable with big OARs and clearly defined lesions. The results of this study underscore the need for individualized treatment planning in CK-based SRS for MBM. By proper choice of collimator number and optimization of planning parameters, one can balance the effective target coverage with normal brain tissue sparing and OARs sparing. Improvement in these strategies is an area for further research with the aim of improving further the treatment outcomes and limiting adverse effects.

CONCLUSION:

The CyberKnife system has proven to be a highly effective tool for achieving high-quality treatment plans in stereotactic radiosurgery (SRS) and hypo-fractionated stereotactic radiotherapy (HFSRT) for patients with multiple brain metastases (MBM). This study underscores the importance of balancing treatment efficiency, plan quality, and dosimetric outcomes when selecting the number of collimators.

The use of an increased number of collimators in the Separate approach significantly improved the coverage of the planning target volume (PTV) and overall plan quality. This enhancement is crucial for ensuring that the entire target receives the prescribed dose, thereby maximizing the therapeutic effect. However, the increased number of collimators also led to a decrease in treatment efficiency, evidenced by longer estimated fraction treatment times (EFTT) and a higher number of monitor units (MUs) required. These factors can impact patient throughput and overall treatment delivery time.

While more collimators improved PTV coverage, they also resulted in higher doses to normal brain tissue. Minimizing radiation exposure to healthy brain tissue is essential for reducing potential side effects and preserving cognitive function. Therefore, the selection of the number of collimators must strike a balance between achieving optimal PTV coverage and sparing normal tissue. Using two collimators can reduce the dose to normal tissue and improve the gradient index (GI), while three collimators can enhance PTV coverage by increasing PTV Dmin and D98% and decreasing PTV Dmax, D2%, and homogeneity index (HI).

The findings underscore the importance of individualized treatment planning. By carefully selecting the number of collimators and optimizing planning parameters, clinicians can tailor treatments to the specific needs of each patient, considering the number, size, and location of metastases, as well as the proximity to critical structures. Further research is needed to refine these approaches and explore new optimization strategies that can enhance treatment outcomes. The integration of advanced imaging modalities and real-time tracking systems will continue to play a pivotal role in improving the precision and efficacy of CyberKnife treatments.

In conclusion, the CyberKnife system offers a versatile and effective tool for treating MBM. By balancing PTV coverage and normal tissue sparing, clinicians can achieve high-quality treatment plans that optimize patient outcomes and quality of life.

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