






# Dosimetric Assessment of Intraoperative Radiation Therapy Utilizing Xofigo Axxent Electronic Brachytherapy for Intracranial Tumors

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## ABSTRACT

**Purpose:** It was aimed to investigate low-energy balloon electronic intraoperative radiation therapy (IORT) in terms of dosimetry, gradient indices (GI) and normal tissue complication probability (NTCP) for the treatment of intracranial tumors.

**Methodology:** For 23 patients with a single brain lesion, non-coplanar volumetric modulated arc therapy (ncVMAT) plans were generated in order to cover 95% of target volume with a prescription dose 20 Gy in 1 fraction. All CT data and structure sets were imported to BrachyCare treatment planning system to calculate IORT dose based on atlas plans. Based on two approaches, critical structure's dose, gradient indices and NTCP values for Brain-PTV were analyzed to evaluate IORT in terms of radiation dosimetry.

**Findings and Conclusion:** The mean Dmax of brainstem is  $(4.43 \pm 3.13)$  Gy in ncVMAT plans, and the dose by IORT delivery is  $(3.27 \pm 2.80)$  Gy. For eyes, lenses and optic nerves, IORT delivery dose is maximum 65% less than ncVMAT delivery dose and this difference is statistically significant for these structures ( $p \leq 0.05$ ). In ncVMAT and IORT techniques, the GI value is 2.65 and 2.24 respectively. NTCP value meet the criterion which is  $\leq 1.0$  in both approaches.

**Conclusion:** Xofigo Axxent eBX system is more capable to provide better control in low dose region at outside of the target and better to reduce critical structures dose which are close proximity to target due to its low energy nature. For that reason, it provides lower GI values and less probability to radiation necrosis. To treat single target high grade primary central nervous system (CNS) tumors and intracranial metastatic disease, IORT is safe considering the dosimetric assessments.

**Keywords:** Intracranial tumors, Gradient index, Intraoperative radiation therapy, NTCP, SRS, VMAT.

## INTRODUCTION

The most common brain tumors in adults are brain metastases. Surgical and radiation techniques continue to evolve to make the treatment more individualized and to control intracranial disease in many cancer types [1]. Based on current guidelines from neurosurgical, radiation oncology, and medical oncology professional organizations, the advantages in overall survival and progression free survival times were stated in patients treated with adjuvant radiation following surgical resection when the surgery was assumed to be a standard part of the treatment [2, 3]. Moreover, the adjuvant radiation therapy in the control of high-grade primary central nervous system

(CNS) tumors and intracranial metastatic diseases remains a standard of care in modern neuro-oncology. On the other hand, for optimal adjuvant radiation therapy, radiation delivery, dose fractionation, and time to initiation continue to be a subject of debate. Several factors including tumor size and location, exact target delineation, degree of mass effect and edema are essential to decide treatment modalities. Moreover, SRS can be applied to the small target volume, since the risk related to radiation induced side effects increases with larger volumes. The use of stereotactic radiosurgery (SRS) in this manner continues to expand, even though there are limitations based on cavity size and the potential development of radiation necrosis. [4].

In recent years, linac-based SRS are exclusively designed for SRS treatment to further improve the targeting accuracy and guarantee high dose rate delivery. In SRS techniques, a rapid dose fall-off from the surface of a target plays a crucial role to protect a normal brain tissue against radiation necrosis [5]. For that reason, recently developed sophisticated patient immobilization devices, multi leaf collimators (MLCs) and advanced imaging techniques, which are utilized during a treatment, are able to provide dose fall-off and accurate radiation dose delivery benefitting from linear accelerators [6]. Additionally, MLC device allows different delivery technique as the volumetric modulated arc therapy (VMAT), which is a novel plan optimization technique for efficient delivery of highly conformal plans using dynamically modulated arcs with continuously varying gantry speed [7].

Several factors such as tumor location and size, initiation time effect determining the best practice approaches in conjunction with disease control. Additionally, local control probability in tumors treated with SRS has been poor, due to surgical resection may be associated with increased risk of leptomeningeal failure. To overcome this obstacle and make the treatment more individualized, IORT has been introduced as another alternative treatment modality for intracranial diseases. With the advanced technology in delivery techniques, intraoperative radiation therapy (IORT) has become a crucial modality to deliver adjuvant radiation therapy and to improve outcomes of tumor control data [8, 9].

IORT is a partial irradiation technique in which radiation therapy is delivered in a single dose of ionizing radiation applied directly over the tumor bed during surgery [10]. Based on the radiation source, several different treatment modalities such as Xoft Axxent Electronic Brachytherapy (eBx) or intraoperative electron radiotherapy (IOERT) are classified under the definition of IORT [11-13]. In recent years, the safety of IORT in the settings of recurrent glioblastoma has been established in conjunction with the post-radiation adjuvant Bevacizumab and its efficacy is being evaluated in Phase-II clinical trial [14].

These aforementioned treatment modalities have unique advantages and disadvantages based on dosing, incidence of radiation necrosis and local tumor control rates. On the same ground, a large amount of three-dimensional dose information is required to evaluate the relative merits of rival SRS and IORT treatment plans. In order to optimize an SRS plan, one method taken advantage of is to maximize the conformity of the prescriptive isodose

surface as well as maximizing the dose fall-off with respect to the distance with external surface of the target volume [15]. One of the most important factors in plan evaluation is dose conformity requiring consideration. The gradient index (GI) is merely defined as the quantification of the dose drop off [16-18]. The value of prescription isodose surface is selected with the aim of minimizing the dose radiated to non-target structures happening through precise conformation of the outer surface of the shell with highest level of precision. Moreover, to provide an information about treatment outcomes related to radiation hazards, normal tissue complication probability (NTCP) and equivalent uniform dose (EUD) plays a crucial role [19-21]. As known, the aim of radiation therapy is to deliver the prescription dose to the target while protecting the critical structure as much as possible. For the same ground, NTCP value is essential parameter to evaluate a risk of normal tissue complications while providing a high probability of local tumor control.

As known, SRS is a non-invasive approach that uses many precisely focused radiation beams to deliver high doses to target without surgical intervention. On the other hand, the present study aimed to analyze radiation dosimetry, gradient index (GI) for target IORT plans utilized with low energy Xoft Axxent eBx system by comparing it with linac-based non-coplanar VMAT SRS treatment delivery technique using Elekta Versa HD™ equipped with the Agility MLC in conjunction with the Elekta Monaco® treatment planning system (TPS version 5.51). In this study, the patients who have non-operated tumors were treated with linac-based SRS. However, it was investigated advantages of IORT to spare critical structures and reduce possible radiation necrosis in terms of NTCP value for Brain-PTV in the treatment of single target high grade primary central nervous system (CNS) tumors and intracranial metastatic disease.

## MATERIAL AND METHODS

### Target delineation for SRS

Baseline characteristics for the included 23 patients are listed in Table-1. A rigid immobilization was applied for patients with SRS dedicated micro perforation thermoplastic masks. Computed tomography (CT) images were acquired via Philips BigBore CT scanner with a 1.0 mm slice thickness. CT datasets were imported to Monaco® treatment planning system TPS, and fused with a T1 weighted gradient-echo magnetic resonance imaging (MRI)

sequence with contrast media and an axial slice thickness of 1 mm. Any residual gross tumor as well as any normal brain tissues of a thickness of 5 mm are observed in clinical target volume (CTV) which are attached to each tumor on MRI imaging since cystic lesions change in size during radiation therapy and residual tumors were possibly present. The planning target volume (PTV) was created by giving 2mm positive margin on CTV taking into account the potential systematic errors, setup errors and patient motions. Contours were delineated for the lenses, eyes, optic nerves, brainstem and whole brain as the organs at risk.

**Table 1.** Baseline characteristics for the included 23 patients.

Patient ID	Primer	Grade
1	Vestibular Schwannoma	II
2	Non-Small Cell Lung CA	IV (BM)
3	Non-Small Cell Lung CA	IV (BM)
4	Non-Small Cell Lung CA	IV (BM)
5	Meningioma	II
6	Meningioma	II
7	Meningioma	II
8	Meningioma	II
9	Low Grade Glial Tumor	II
10	Meningioma	II
11	Non-Small Cell Lung CA	IV (BM)
12	Non-Small Cell Lung CA	IV (BM)
13	High Grade Glial Tumor	IV
14	Meningioma	II
15	Non-Small Cell Lung CA	IV (BM)
16	Meningioma	II
17	Non-Small Cell Lung CA	IV (BM)
18	Gastric CA	IV (BM)
19	High Grade Glial Tumor	IV
20	Meningioma	III
21	Non-Small Cell Lung CA	IV (BM)
22	High Grade Glial Tumor	III
23	Breast CA	IV (BM)

## VMAT Treatment Planning

Non-coplanar VMAT (ncVMAT) plans were devised in 23 cases with all patients involved in the Monaco® TPS (version 5.51, Elekta, Stockholm, Sweden) and all patients are treated with ncVMAT technique. Six-megavolt flattening filter free (6 MV FFF) photon energies delivered by Elekta Versa HD Linac through Agility MLC were used for all plans. The treatment plan prescription is 20 Gy in single

fraction to planning target volume (PTV) with the coverage rate of 95% for all ncVMAT plans. Help contours were created through expanding target volumes by 2 cm and 4 cm, respectively for simplifying the optimization. Therefore, conformity and steep dose gradients around the targets were maximized as much as possible benefitting from the Monaco® cost function “Quadratic Overdose” (with a dose threshold of 10 Gy for 2 cm and 2 Gy for 4 cm). All patients underwent the same set of couch angles for 5 arc plannings. The provided couch angle and gantry start angle for 5 arc treatment plannings are presented in Table-2. Grid spacing was defined to be 0.2 cm along with statistical uncertainty selected as 0.5% per calculation. Beamlet width was 0.2 cm and maximum control points was 250. Monte Carlo algorithm was used for final dose calculation.

**Table 2.** 5arc ncVMAT treatment planning couch and gantry angles.

Number of Arcs	Gantry Rotation	Gantry Start (Deg)	Arc	Couch (Deg)
1	CCW	Atypical Meningioma 180	180	280
2	CW	Atypical Meningioma 180	180	315
3	CCW	IDH Mutant Astrocytoma 180	180	350
4	CCW	Atypical Meningioma 0	180	45
5	CW	Adenocarcinoma 180	180	10

## IORT Treatment Planning

IORT utilized with Xoft-Accuray eBx System is performed using a balloon applicator placed in the tumor cavity and a source producing 50 kVp soft x-rays. The S700 source model consists of a miniature (length = 10 mm, diameter = 2 mm) x-ray tube. Source properties were characterized according to the American Association of Physicist in Medicine (AAPM) Task Group 43 (TG-43) [22-24]. With the pre-calculated atlas plan for different applicator volumes and sizes, 20-21 Gy radiation dose in a single fraction is provided in IORT applications. While making these calculations, the water environment is taken as the basis, as in standard brachytherapy systems, and the dose distribution is assumed to be homogeneous [25].

For the dosimetric evaluation purposes, all structures and CT data sets were imported to BrachyCare treatment planning system to visualize the dose

distribution of IORT plans utilized with Xofig Axxent eBx System which is a 50 kVp low energy IORT system. PTV was assumed as the resection cavity which is filled spherical balloon applicator volume at the time of surgery. For all patients 3-4 cm balloon applicator was applied for the cavity volume. Standard atlas plans were selected based on applicator volume size ranging from a minimum of 18 cc and a maximum of 25 cc to simulate real case scenario. The prescription dose for the IORT was 20 Gy at the applicator surface. The treatment characteristics including tumor location, applicator volume and treatment time were detailed in Table-3. Final dose calculation was done based on dwell position and dwell time. Dwell position was shown in Figure-1 for the selected case.

### Plan Evaluation

The treatment plan prescription is 20 Gy in single fraction to planning target volume (PTV) with the coverage rate of 95% for all planning approaches. The option to limit dose optimization to the normal brain responded with plans minimizing low-dose isodose regions' volumes, however, plans present a lack of dose-limiting stipulation for normal brain tissue with a similar conformity. Besides, evaluating V2Gy, V10Gy and V12Gy for radiation necrosis indicator happened through Brain-PTV. Meanwhile, maximum dose Dmax for brainstem, lenses, optic nerves were taken to account for OARs dose. Knowingly, SRS plans include clinical evaluation in forms of general plan overview as well as evaluation of dosimetric indices which include the dose falloff index, i.e. gradient index (GI). Since help contours were created through expanding target volumes by 2 cm and 4 cm to restrict the high dose and low dose region in order to simplify the optimization and to maximize the conformity and steep dose gradients around the targets, GI was calculated based on Paddick formula which was given [26].

$$GI = \frac{PIV_{50}}{PIV} (1)$$

Where V50% is 50% of the prescription volume isodose line. GI is an indication of low-dose spillage, with lower GI values indicating greater dose falloff and better dose conformity outside the target volume. For single target SRS plan GI value of  $\leq 3.0$  is considered ideal.

**Table 3.** The IORT treatment characteristics.

Patient ID	Tumor Location	Balloon Volume (cc)	Treatment Time (s)
1	Right temporal	20	387.2
2	Right parietal	20	387.2
3	Right frontal	18	329.0
4	Right frontal	20	387.2
5	Right occipital	22	393.1
6	Right parietooccipital	22	393.1
7	Right frontal	20	387.2
8	Left frontoparietal	22	393.1
9	Right frontal	20	387.2
10	Right frontoparietal	22	393.1
11	Right parietal	20	387.2
12	Left frontal	22	393.1
13	Right frontoparietal	20	387.2
14	Left parietal	22	393.1
15	Left frontal	22	393.1
16	Left parietal	22	393.1
17	Left temporoparietal	20	387.2
18	Left temporoparietal	22	393.1
19	Left frontotemporal	25	422.8
20	Right parietooccipital	25	422.8
21	Left parietal	20	387.2
22	Right frontal	20	387.2
23	Right temporoparietal	22	393.1

In the published data, there is a difference in volumes which are used to correlate dose-volume exposure with radiation toxicity risk after SRS treatment. The size and location of the target as well as the planning



approaches determine calculated volume subtracted from surrounding brain tissue. As known, the NTCP value is an indicator of unfavorable reactions in the adjacent tissue at a particular dose. For the same reason, NTCP values were taken into account for Brain-PTV to compare both approaches regarding radiation necrosis. In this study, NTCP was calculated based on Lyman-Kutcher-Burman method which was given [27, 28].

$$NTCP = \frac{1}{1 + \left(\frac{TD_{50}}{EUD}\right)^{\gamma_{50}}} \quad (2)$$

TD50 is the tolerance dose for a 50% complication rate at specific time interval and  $\gamma_{50}$  is dimensionless parameters which defines the slope of the dose response curve.

$$TD_{50}(V) = \frac{TD_{50}(1)}{V^n} \quad (3)$$

For Brain-PTV, TD50(1) was 60, n was 0.25 and  $\gamma_{50}$  was 0.15. Since, maximum target volume is 25 cc which is approximately 2.5 cm abutting the brain surface, the V12Gy of the Brain-PTV shows the steepest dose/volume response regions. For that reason, NTCP was calculated based on V12Gy of Brain-PTV to evaluate possible risk of radiation necrosis. At the same time half of the dose distribution was shown in Figure-4 for the selected case. SPSS statistical software (SPSS, Statistics v22, Chicago, IL, USA) was used to examine the statistical differences in each of the parameters obtained from all plans. For statistical analysis, the significance test of the difference between two plan parameters was first applied to checked whether the variables provided the assumption of normality. If the differences are distributed normally, Paired – Samples t Test was applied, if the differences are not normally distributed, 2 Related – Samples test was applied. A p value < 0.05 was considered statistically significant for both tests.

## RESULTS

In the present study, the 23 patients, who have high grade primary central nervous system (CNS) tumors and intracranial metastatic disease, were retrospectively analyzed. The most common histology was non-small cell lung cancer (n=8) with brain metastases and meningioma (n=7). Frontal lobe (n=7) was the most common location and rest of the tumor location was in non-eloquent regions of the brain. The minimum tumor volume was 18 cc and

the maximum volume was 25 cc. All treatment plans were designed to delivered 20 Gy in single fraction. Additionally, PTV, which was defined for SRS treatment, was assumed as a tumor cavity filled with balloon applicator. All patients were treated with ncVMAT SRS plan and ncVMAT plans were compared to the IORT plan to evaluate the Xoft Axxent eBx System in terms of radiation dosimetry, gradient index and possible radiation necrosis by calculating NTCP values.

**Table 4.** The mean OARs dose comparison based on ncVMAT and IORT from all patients' treatment plans.

Structure	Dose Criteria	ncVMAT	IORT	P Value ( $\leq 0.05$ )
Brainstem	$\leq 10$ Gy	4.43 $\pm$ 3.13	3.27 $\pm$ 2.80	0.000
Eye_Left	$\leq 8$ Gy	1.16 $\pm$ 0.72	0.44 $\pm$ 0.51	0.000
Eye_Right	$\leq 8$ Gy	1.28 $\pm$ 1.04	0.61 $\pm$ 0.85	0.000
Lens_Left	$\leq 2$ Gy	0.71 $\pm$ 0.44	0.21 $\pm$ 0.21	0.000
Lens_Right	$\leq 2$ Gy	0.73 $\pm$ 0.54	0.24 $\pm$ 0.28	0.000
Nerve_Right	$\leq 8$ Gy	1.85 $\pm$ 1.50	0.95 $\pm$ 1.39	0.000
Nerve_Left	$\leq 8$ Gy	1.89 $\pm$ 1.77	1.33 $\pm$ 1.91	0.000
Brain-PTV V2Gy	%	27.59 $\pm$ 5.40	16.78 $\pm$ 2.86	0.000
Brain-PTV V10Gy	%	2.32 $\pm$ 0.34	3.3 $\pm$ 0.63	0.000
Brain-PTV V12Gy	%	1.58 $\pm$ 0.22	2.62 $\pm$ 0.64	0.000

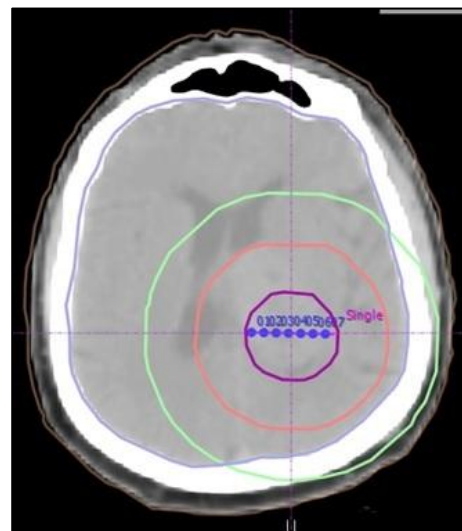


Figure 1: Dwell position of IORT treatment plan

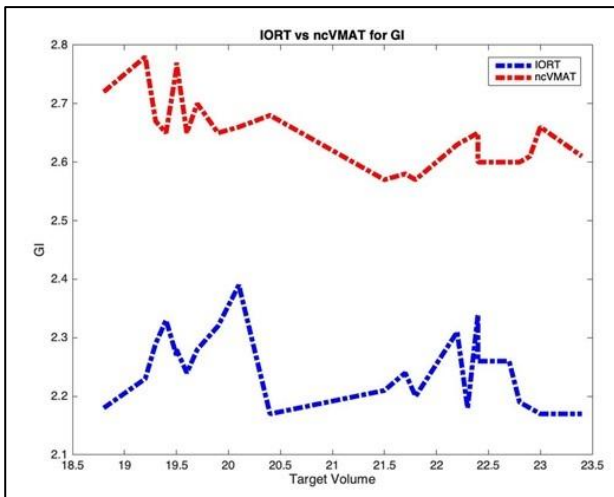


Figure 2: IORT vs ncVMAT treatment planning comparison for GI based on target volume

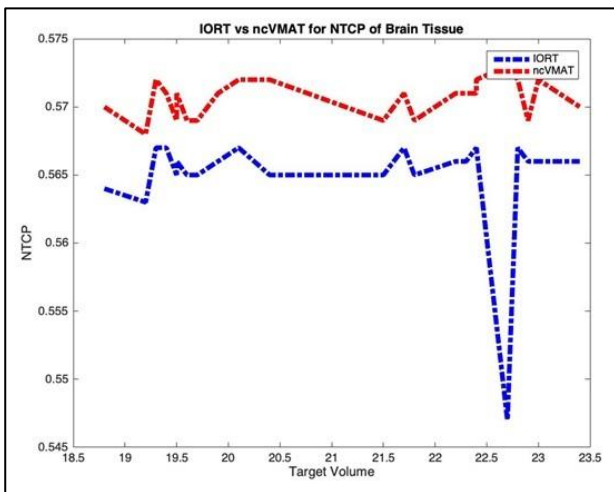


Figure 3: IORT vs ncVMAT treatment planning comparison for NTCP of Brain tissue based on target volume

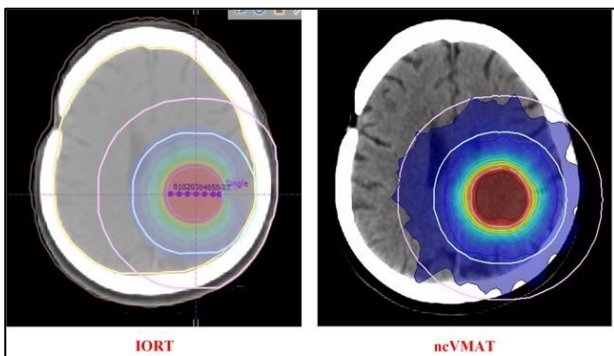


Figure 4: Dose distribution form IORT and ncVMAT for the selected case.

All OARs dose based on ncVMAT plan and IORT are shown in Table-4. The maximum dose (Dmax) was considered for brainstem, eyes, lenses and optic nerves. Based on the results, the mean Dmax is  $(4.43 \pm 3.13)$  Gy in ncVMAT plans, and it is  $(3.27 \pm 2.80)$  Gy in IORT plans. Since tumor location has the close proximity to the brainstem, the dose criteria which is  $\leq 10$  Gy for brainstem ( $D_{\max} \approx 11$  Gy) could not be achieved with ncVMAT plan in three patients. On the other hand, IORT has great advantageous to reduce brainstem dose even if the tumor location is close to critical structures. Moreover, the IORT meets the dose criteria for brainstem in all patients. Dose to the Eye was also evaluated and both treatment plan approaches meeting the criteria of  $D_{\max} \leq 8$  Gy. However, IORT dose is approximately 65% less than ncVMAT dose and this difference is statistically significant. The same results were observed for lenses and optic nerves. The difference between IORT and ncVMAT plan is 68% for lens dose and IORT has better result in reducing lens dose comparing the ncVMAT plans. Furthermore, for the mean Dmax of optic nerves is  $(1.87 \pm 1.50)$  Gy and  $(1.14 \pm 1.65)$  Gy in ncVMAT plan and IORT respectively. Additionally, V2Gy, V10Gy, V12Gy of Brain-PTV were also analyzed for radiation necrosis. Since, Xofigo Axxent eBx System is utilized with low energy (50 kVp) miniaturized x-ray source, this system is crucial to provide better V2Gy result for Brain-PTV due to the nature of source energy. On the other hand, ncVMAT plan is superior to control high dose region and Monaco TPS provides better solution to reduce high dose outside of PTV with the help of several cost function namely quadratic over dose. As a result, V10Gy and V12Gy are 1% higher in IORT plans comparing to ncVMAT plan. Even though the difference is not crucial, it is statistically significant.

In the second part, Xofigo Axxent IORT was evaluated based on gradient index and NTCP by comparing the plans with ncVMAT treatment plans. For single target SRS plan GI value of  $\leq 3.0$  is considered ideal. Both treatment approaches meet this criterion. The GI value is 2.65 and 2.24 in ncVMAT plan and IORT respectively. Based on this result, Xofigo Axxent eBx System is superior to provide low-dose spillage, with lower GI values indicating greater dose falloff and better dose conformity outside the target volume. IORT and ncVMAT plan comparison for GI results was shown in Figure-2. As known, NTCP is the probability that a radiation dose absorbed by organ or normal tissue causes a complication considering the specific biological cell of the organ or structure. So NTCP is an indicator to evaluate radiation necrosis probability in treatment planning as a tool to differentiate among treatment plans. In this study

NTCP values were calculated for Brain-PTV by using Lyman-Kutcher-Burman method. In both approaches NTCP value meet the criterion which is  $\leq 1.0$ , however, IORT (mean NTCP  $\approx 0.555$ ) is superior to ncVMAT (mean NTCP  $\approx 0.575$ ) for NTCP results as expected. NTCP value comparison in ncVMAT vs IORT plan for Brain-PTV was shown in the Figure-3. Based on NTCP value, Xofter Axxent eBx System is crucial to reduce radiation necrosis for the treatment of high grade primary central nervous system (CNS) tumors and intracranial metastatic disease.

## DISCUSSION

Definitive therapy and adjuvant radiation therapy after surgery are well established treatment modalities in achieving local control of high grade primary central nervous system (CNS) tumors and intracranial metastatic disease. On the other hand, in surgical resected brain metastases, the optimal delivery technique of adjuvant radiation therapy is the subject of debate. Several factors such as tumor location and size, initiation time effect determining the best practice approaches in conjunction with disease control [29]. Additionally, local control probability in tumors treated with SRS has been poor, due to surgical resection may be associated with increased risk of leptomeningeal failure. To overcome this obstacle and make the treatment more individualized, IORT has been introduced as another alternative treatment modality for intracranial diseases. In comparison to SRS treatment utilized with linac-based treatment, low energy (50 kVp) IORT systems plays a crucial role to deliver higher linear energy transfer (LET) thereby producing a relatively higher proportion of lethal DNA lesions. However, effectiveness of IORT in terms of radiation necrosis and long term neurocognitive functions is under research.

Twenty patients IORT treatment plan utilized with 50 kV X-rays on the INTRABEAM® 600 (ZEISS International, Jena, Germany) were analyzed by comparing the data with SRS treatment plan for large brain metastases. IORT plans were generated to delivered 10-30 Gy in single fraction to applicator surface and OAR's dose including Dmax of optic chiasm, brainstem and V12Gy of brain-GTV were evaluated. Based on findings, IORT provided the significantly lower doses to optic nerves and brainstem. Additionally, in 86% of patients treated with IORT radiographic and symptomatic radiation necrosis have not been observed [30].

In another study, IORT was evaluated in terms homogeneity index (HI) by comparing its dose volume value with SRS and fractionated stereotactic radiotherapy. The IORT dose was 30 Gy at the applicator surface, while gamma knife SRS and IMRT plans were designed to deliver 16 Gy and 24 Gy respectively. When HI was used as primer radiation parameters for adjuvant radiation therapy after surgical resection in brain metastases, IORT offered better dose homogeneity comparing with single fraction gamma knife based SRS, however, linac based IMRT in multisession stereotactic radiosurgery was superior with respect to the HI [31].

In another study, the potential benefits of intraoperative balloon electronic brachytherapy (IBEB) was evaluated for local control of recurrent glioblastomas (GBM). Prospective data from two different centers were compared with ongoing follow-up. The first group was treated with IBEB and the second group underwent re-resection with adjuvant chemoradiotherapy options. Overall survival and local progression free survival were evaluated, however, no dosimetric evaluation were stated [14].

On the other hand, this presented study focused on radiation dosimetry and reliable parameters to evaluate IORT plans utilized with Xofter Axxent eBx System which is a 50 kVp low energy IORT system comparing them with linac based noncoplanar VMAT SRS treatment plans. Twenty three patients treated with SRS treatment plans with non-coplanar 5 arc VMAT techniques using Elekta Versa HD™ equipped with the Agility MLC in conjunction with the Elekta Monaco® treatment planning system (TPS version 5.51) were retrospectively analyzed. Based on our result, IORT was superior to reduce critical structure doses. Additionally, it plays a crucial role to meet the dosimetric criteria when the target has close proximity to the critical structure. Moreover, low energy Xofter Axxent eBx System provides low-dose spillage, with lower GI values indicating greater dose falloff and better dose conformity outside the target volume comparing to the ncVMAT plan. Radiation necrosis is the challenging obstacle in the treatment of high grade primary central nervous system (CNS) tumors and intracranial metastatic disease. On the same ground, the NTCP value, which is an indicator to evaluate radiation necrosis probability in treatment planning as a tool to differentiate among treatment plans, was also calculated. Based on our findings, Xofter Axxent eBx System has significant potential to reduce radiation necrosis.

## CONCLUSION

In the present study, low energy Xofter Axxent eBx System was evaluated in terms of radiation dosimetry, GI and NTCP in the treatment of high grade primary central nervous system (CNS) tumors and intracranial metastatic disease by comparing the plans with single target non-coplanar 5 arc VMAT SRS plan. It as shown that, low energy Xofter Axxent eBx system provides better organ sparing comparing ncVMAT technique especially which has close proximity to target. Additionally, it is superior to other technique for low dose region control at outside of the target resulting lower GI values indicates sharp dose fall-off. As a result, increasing radiobiological advantages to provide local control is possible with the unique dosimetry of Xofter Axxent eBx System. However, detailed investigation in conjunction with radiation necrosis and novel systemic treatments after surgery is crucial for IORT evaluation.

## Conflict of Interest

There are no conflicts of interest and no acknowledgements.

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