Stereotactic Radiosurgery for Limited Brain Metastasis using Three Different Techniques; Helical Tomotherapy, Volumetric Modulated Arc Therapy, and Cone-Based Linac Radiosurgery.

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Abstract

Background: Specific radiation delivered to the tumor by stereotactic radiosurgery (SRS) has become widely used in the treatment of brain metastasis. This study aimed to compare radiation dosimetry and its parameters from SRS using three different modalities: Helical Tomotherapy (HT), Volumetric Modulated Arc Therapy (VMAT), and Cone-based Linac Radiosurgery (Cone-based).

Methods: Patients who had experienced oligo-brain metastasis received SRS in our treatment center. Each contouring dataset was re-planned to create radiation dosimetry in all three treatment systems (HT, VMAT, and Cone-based). The parameters of conformity index (CI), homogeneity index (HI), CI50, and gradient index (CGI) were analyzed to compare the effects of the three techniques.

Results: A total of 21 patients with 39 lesions were included in this study. For single lesion, Cone-based and VMAT revealed statistically identical CI, CI50, and CGI values, while exhibiting the poorest HI value. For multiple lesions, Cone-based provided the best CI50 and CGI values. VMAT displayed better CI50 and CGI values than HT. Moreover, VMAT exhibited the lowest BrainV5Gy value and displayed the shortest beam on time (BoT) calculation. Lastly, Decision Score analysis demonstrated better performance in VMAT when compared to the Cone-based approach.

Conclusions: Our data indicated the dosimetric comparison between three radiation techniques for single and multiple lesions. The Cone-based technique revealed the poorest HI value. On the other hand, VMAT provided the best estimated BoT value. Moreover, we have reported on the feasibility of SRS using HT, which has been associated with well-tolerability and an acceptable level of radiation output.

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Background

Brain metastasis is the most common form of intracranial malignancy. The approximate incidence of brain metastasis has been reported at 10%-30% among patients who developed extracranial primary cancers (1, 2). In Thailand, the prevalence of brain metastasis among intracranial tumors has been reported at 19.9% (3). The current brain metastatic rate actually may be higher due to improved imaging modalities in the detection of small cerebral disseminations by magnetic resonance imaging (MRI) and better extracerebral control resulting from novel systemic therapies. Lung, breast, and renal cell carcinomas, along with cutaneous melanoma, are extracranial forms of cancer that have a high propensity to disseminate into the brain (4, 5). Radiotherapy (RT) has been found to be the main treatment modality used to eradicate brain metastasis. Historically, whole brain irradiation (WBRT) remains a standard RT technique that can deliver radiation by simple feasibility and requires a short period of duration for each radiation session. However, radiation practically paints all parts of the brain which can result in neuro-cognitive impairment. With the development of novel chemotherapy, immunotherapy, and targeted therapy strategies, there is an increased possibility of eliminating cancer and enhancing the survival rate of cancer patients. Therefore, there is a need to better understand the effects of these treatments. Hippocampal avoidance WBRT (HA-WBRT) delivers radiation to the whole brain while minimizing the dose along bilateral hippocampal regions. The results of the Radiation Therapy Oncology Group (RTOG) 0933 have confirmed an improvement in memory decline in patients who have received HA-WBRT (6). Moreover, the addition of memantine to HA-WBRT has better preserved the neuro-cognitive outcomes and the related symptoms reported by patients (7). In contrast to WBRT, specific radiation precisely delivering radiation to gross tumors by stereotactic radiosurgery (SRS) has become widely used. This technique delivers radiation directly to the intracerebral mass which theoretically affects the small part of the brain. Thus, SRS can spare other parts of the brain parenchyma from radiation resulting in a degree of improvement in radiation-induced neurological consequences. This RT technique is usually administered in limited brain metastasis, in which there are no more than four disseminated intracranial lesions. Numerous radiation machines can be used to create the SRS technique through the arrangement of different radiation beams and multiple mechanical factors. Historically, Gamma-knife and Cone-based LINAC radiosurgery (Cone-based) techniques have been widely used as standard SRS modalities. Emerging advanced technologies have allowed intensity-modulated radiation therapy (IMRT) to operate with very steep radiation dose gradients. Thus, SRS by IMRT has become an extremely popular method of treatment. Various radiation devices are able to deliver IMRT, including helical tomotherapy (HT) and volumetric modulated arc therapy (VMAT), which have been installed in our center. This study aims to compare radiation dosimetry and the parameters of SRS through the use of three different modalities; HT, VMAT, and Cone-based Linac Radiosurgery.

Methods

This study selected patients who fulfilled the following inclusion criteria:

- Known primary extracranial malignancy displaying clinical and diagnostic imaging compatible with brain metastasis
- MRI of the brain showing a limited number of brain metastatic lesions (no more than four lesions)
- Each intracranial tumor size less than 3 cm and at least 5 mm from critical structures (brainstem and optic apparatus)

Patients who participated in this study were subjected to computed tomography simulation (CT SIM) by applying 1-mm slice thickness. SRS-system mask (R406-1 SRS mask, Klarity, China) was used for non-invasive immobilization (Figure 1). MRI was registered into the CT SIM dataset to define targets and for delineation of the organs at risk (OARs).

Target

Gross tumor volume (GTV) was delineated by contouring the contrast-enhancing lesions observed on T1 gadolinium-weighted MRI images. No margin was added to create the clinical target volume (CTV). The planning treatment volume (PTV) was defined by 2 mm isotropic expansion of the GTV.

Organs at risk (OARs)

The whole brain, hippocampi, optic nerves, optic chiasm, pituitary gland, brainstem, both cochlea, bilateral globes, and the lens were contoured.

Virtual structures and treatment evaluation

Virtual structures and help organs were created following the method of Soisson et al (8). Help structures were created for Tomotherapy and VMAT which were inverse planning, whereas the cylindrical collimator was not. The clinical sub-volume (CSV) was created at the centroid of the GTV with a diameter of 2 mm (Figure 2). To create a steep dose gradient, the dose constraint to at least 1% volume of CSV was prescribed at 120% of the prescription dose to target. The surrounding dose was then compressed by the ring. These structures (rings) expanded by 5 mm and 10 mm from the PTV. The 5% volume of these 5 mm and 10 mm rings structures were constrained at 80%-85% and at 50% of the prescription dose, respectively. For all of the plans, the dose coverage was accepted for at least 75% of the maximal dose for Tomotherapy and VMAT, whereas the cylindrical collimator was accepted at 50% of the maximal dose. The prescription dose had to cover at least 99% volume of the PTV, while the distance of the dose gradient from 50–100% of the prescription dose had to be within 10 mm for the single lesion.

Treatment Planning

Treatment planning systems were composed of HT, VMAT, and Cone-based SRS. In our institution, the commissioning in VMAT was performed and SRS was initiated to deliver radiation treatments on December, 2018. Therefore, all patients that had experienced limited-brain metastasis before 2019 were actually treated by HT. After that point, patients received treatment by VMAT. Every contouring dataset was re-planned in order to create each radiation dosimetry for all three treatment systems (HT, VMAT, and Cone-based).

Helical Tomotherapy (HT)

Tomotherapy (Hi-Art equipped dynamic jaws, Tomotherapy, USA) delivers radiation by way of a helical megavoltage fan beam. Accuray® Planning System (HiArt® version 5.1.4, Tomotherapy, Inc) administers treatment plans through employment of the helical treatment mode. The field width was set to ten millimeters in the fixed jaw mode. Modulation factor and pitch were set to 1.800-2.500 and 0.125, respectively. Based on the helical fan beam, a single coplanar was used in all treatment plans. The finest calculation grid was selected (1.95·1.95 mm^2) for dose calculation.

Volumetric Modulated Arc Therapy (VMAT)

Treatment plans were performed with use of the Monaco® version 5.11.03 (Elekta, Inc) treatment planning system. Modulated broad beam in Linear accelerator (Synergy, Elekta, USA) was used with five millimeters of leaf width at the isocenter. All plans were created using the non-coplanar, single isocenter technique. Two full arcs (300 degrees) with a perpendicular collimator angle between each arc were used at zero degree of the couch angle. Specifically, 120 degrees of the treatment arc was used for three different couch angles (45°, 270°, 315°). The increment of the gantry angle was 10° for all arc beams. The dose optimization was calculated through the 2.00x2.00 mm^2 grid size whereas the fineness calculation grid (1.00 x 1.00 mm^2) was selected for the dose calculation.

Cone-based LINAC radiosurgery (Cone-based)

Treatment plans were carried out using the Monaco® version 5.11.03 (Elekta, Inc) treatment planning system. Different sizes (5-15 mm diameters) of the pencil beams in Linear accelerator (Synergy, Elekta, USA) were used in the non-coplanar technique. The directions of the arc beam were set in a half sphere and intersections between each beam were avoided through multiple isocenters in the targets. The weighting radiation dose of each isocenter was applied according to the experience of the planner. The finest calculation grid (1.00·1.00 mm^2) was selected to establish the dose calculation.

Dosimetric Comparison

Conformity index (CI), homogeneity index (HI), and gradient index were analyzed to compare the three techniques (9, 10, 11). Relevant formulars were as follows:

CI (9) = V_{pres}/V_{PTV}

V_{pres}: volume covered by prescribed dose

V_{PTV}: PTV volume

HI (10) = D_{max}/D_{Rx}

D_{MAX}: maximum dose in the PTV

D_{RX}: prescription dose

CI50 = $V_{50\%Rx}/V_{PTV}$

$V_{50\%Rx}$: volume of 50% prescription isodose volume

V_{PTV}: PTV volume

CGI (11) = 100-100x([$R_{eff,50\%Rx}$-$R_{eff,Rx}$]-0.3 cm)

$R_{eff,50\%Rx}$: effective radius of 50% of prescription isodose enclosing PTV

$R_{eff,Rx}$: the prescription isodose enclosing PTV

Beam On Time Calculation

HT represents the beam-on time (BoT) value of the unit of second, whereas the others were determined by the monitor unit (MU). The MU of the Cone-based SRS was converted to the unit of second by dividing the dose rate. The highest dose rate of our Cone-based approach provided 10 MU/sec. In the case of this approach, the dose rate could directly divide the total MU of each plan. In the VMAT technique, various dose rates were used in each plan. The treatment planning system (TPS) can be used to estimate BoT, but it is dependent upon the resolution of the calculation. A resolution of 2 mm was used in the optimization process to accelerate the optimization time, but a resolution of 1 mm was used to re-calculate the final absorbed dose. The result, then, was representative of the minimum BoT value, whereas various other dose rates were ignored in the VMAT technique.

Decision Score Analysis

The decision score was used to evaluate the performance among the different SRS techniques. The HT and VMAT approaches were benchmarked by applying the Cone-based technique. Significant differences of the plan quality indexes and dosimetric parameters were considered for the scoring procedure. Either plus one or minus one was granted to both the indexes and the parameters, which was indicative of either better or lesser performance than the Cone-based approach, respectively. The indexes and parameters received no score when no significant differences were observed.

Statistical Analysis

Descriptive analyses were summarized as medians with interquartile range (IQR) for continuous characteristics and as frequencies and proportions for categorical characteristics. The Friedman test was used to compare the dosimetric parameters and radiation painting to OARs, which were non-normally distributed between HT, VMAT, and the Cone-based planning techniques. A pairwise comparison was made and results were analyzed using Wilcoxon Signed Rank Test. The p value reports were two-tailed with an alpha level of 0.05 to establish statistical significance. All analyses were conducted using Stata version 16 (StataCorp LP, College Station, TX, USA).

Results

A total of 21 patients with 39 lesions were included in this study. The most common primary tumor site was lung cancer (14 patients, 66.7%). Nineteen patients classified as Recursive Partitioning Analysis (RPA) class II, while 2 patients were RPA class I (12). The most common tumor location was at parietal region (15 out of 39 lesions, 38.5%) followed by frontal (9), temporal (7), basal ganglion (3), occipital (3), and cerebellum (2), respectively. Ten patients had single lesion which located at parietal (3), frontal (2), temporal (2), occipital (1), basal ganglion (1), and cerebellum (1). The median tumor size, which was measured at the maximal diameter, was 1.2 cm. Median GTV and PTV values were 0.8 and 2.1 cc, respectively, as is shown in Table 1. The median prescription dose was 18 Gy. Eleven patients received SRS by HT and the other 10 patients received radiation therapy by VMAT. The isodose distributions comparing between three-different approaches for single and multiple lesions are demonstrated in Figure 3. All of the patients were well tolerant without displaying signs of radiation necrosis and had discontinued consumption of oral steroids after completing the SRS treatment.

Table 1
Tumor characteristics.

Characteristics	Median (IQR)
GTV (cc)	0.8 (0.2-4.7)
PTV (cc)	2.1 (0.8-8.4)
Tumor Size (cm)	1.2 (0.6-2.1)
Prescription dose (Gy)	18 (15-20)
IQR = interquartile range	
GTV = gross tumor volume. PTV = planning treatment volume	

Dosimetric Comparisons

Comparisons of median values of maximal dose (Dmax), HI, CI, CI50, and CGI were made between HT, VMAT, and the Cone-based approaches. The results are presented in Figure 4. For the whole cohort, the Cone-based approach had the highest Dmax value, which was significantly higher than HT and VMAT

approaches. Moreover, the Cone-based approach provided a more heterogenous and a less conformed radiation dose to the target as it had the highest HI and CI values in our study. In contrast, this technique delivered radiation with the best CGI value. HT and VMAT exhibited statistically identical Dmax, HI, and CI values; however, VMAT exhibited better CGI values than HT. VMAT also exhibited the lowest CI50 value when compared to the other two techniques.

Dosimetric parameters analyses for single lesion are showed in Figure 5. Cone-based and VMAT provided statistically similar CI, CI50, and CGI values. In contrast, HT approach exhibited the poorest CGI values. For multiple lesions, Cone-based revealed the best CI50 and CGI values, while HT providing the poorest values, as demonstrated in Figure 6. VMAT exhibited better CI value than Cone-based approach.

OARs and BoT comparisons were made and the results are presented in Tables 2 and 3. All three techniques delivered a similar integral dose (ID) to the whole brain. VMAT significantly provided the lowest whole brain volume, which was recorded at a dose of 5 Gy (BrainV5Gy) for multiple lesions. Lastly, VMAT also exhibited the lowest MU and shortest BoT calculation.

Table 2
Organs at risk and beam on time comparison of 3 techniques.

	The Whole Cohort. Median (IQR)				Single lesion. Median (IQR)				Multiple lesions. Median (IQR)			
	HT	VMAT	Cone-based	P-value†	HT	VMAT	Cone-based	P-value†	HT	VMAT	Cone-based	P-value†
Brain: V_{5Gy}	116.8 (50.2-182.8)	69.0 (29.1-105.2)	98.01 (26.2-126.2)	0.0001	45.3 (31.2-59.5)	31.8 (22.1-42.5)	26.2 (21.0-76.1)	0.0608	182.8 (136.3-225.9)	105.2 (89.8-162.4)	124.6 (98.9-178.9)	0.000
Brain: V_{12Gy}	27.0 (10.2-32.6)	20.5 (9.6-32.5)	21.7 (9.2-30.7)	0.0232	10.0 (7.1-17.5)	9.5 (6.4-15.6)	8.8 (4.8-17.9)	0.3012	32.6 (30.3-40.4)	32.5 (22.6-37.3)	30.7 (21.7-38.6)	0.059
Hippocampal Rt	1.7 (0 .3-3.9)	2.6 (1.0-3.8)	2.0 (0.4-3.9)	0.3499	1.7 (0.1-3.2)	0.8 (0.3-2.0)	1.5 (0.2-2.8)	0.4593	2.0 (0.5-4.6)	3.5 (2.4-4.1)	2.8 (1.5-5.8)	0.695
Hippocampal Lt	1.7 (0.2-2.4)	2.4 (1.2-3.5)	1.2 (0.4-2.7)	0.2122	1.0 (0.2-2.2)	1.4 (1.2-2.0)	0.7 (0.2-1.4)	0.4593	2.2 (0.4-4.3)	3.1 (1.2-4.8)	2.6 (0.5-3.9)	0.177
Optic nerve Rt	0.3 (0.1-1.7)	1.4 (0.6-2.3)	0.4 (0.2-1.0)	0.0051	0.27 (0.1-1.7)	1.0 (0.4-1.9)	0.4 (0.2-0.8)	0.4066	0.3 (0.1-2.0)	1.4 (0.8-2.6)	0.4 (0.2-2.4)	0.005
Optic nerve Lt	0.2 (0.1-1.4)	1.0 (0.7-1.3)	0.6 (0.2-0.9)	0.0099	0.2 (0.1-1.4)	0.8 (0.3-1.1)	0.5 (0.2-0.9)	0.6703	0.2 (0.1-1.5)	1.3 (0.9-1.9)	0.6 (0.2-1.6)	0.003
Optic Chiasm	0.4 (0.1-2.6)	1.3 (0.7-2.0)	0.8 (0.2-1.8)	0.0412	0.10 (0.04-0.26)	0.37 (0.13-1.02)	0.21 (0.19-0.81)	0.0253	0.2 (0.1-0.3)	0.8 (0.4-1.6)	0.5 (0.2-3.2)	0.078
Brainstem	1.2 (0.2-3.8)	2.4 (1.4-3.1)	1.7 (0.7-3.3)	0.2636	0.07 (0.05-0.11)	0.16 (0.09-0.24)	0.16 (0.08-0.20)	0.4966	0.2 (0.1-0.2)	1.1 (0.4-1.4)	0.4 (0.2-1.4)	0.002
Cochlea Rt	0.1 (0.1-0.3)	0.7 (0.3-1.1)	0.4(0.2-1.3)	0.0023	0.4 (0.1-3.5)	0.9 (0.7-1.8)	0.4 (0.2-1.7)	0.0672	0.4 (0.1-2.6)	1.7 (0.8-3.0)	0.9 (0.4-3.6)	0.306
Cochlea Lt	0.1 (0.1-0.2)	0.4 (0.1-1.2)	0.2 (0.2-0.5)	0.0048	1.2 (0.1-4.2)	1.6 (1.2-2.4)	1.1 (0.7-2.4)	0.6703	1.6 (0.2-3.6)	3.0 (2.0-3.5)	3.0 (0.7-8.0)	0.078
MU	13936.0 (12159.0-19734.0)	5745.0 (5287.3-7530.2)	14759.3 (9581.4-20993.1)	<0.0001	13081.5 (12159.0-14670.0)	5384.9 (4867.4-5673.0)	9099.4 (5151.3-12343.7)	0.0074	19734.0 (11774.0-47076.0)	7530.2 (6550.2-7891.4)	20993.1 (16824.6-30557.7)	0.001
Beam on Time	1098.0 (918.0-1884.0)	574.5 (528.7-753.0)	1475.9 (958.1-2099.3)	<0.0001	939.0 (864.0-1044.0)	538.5 (486.7-567.3)	909.9 (515.1-1234.4)	0.0136	1884.0 (1398.0-3324.0)	753.0 (655.0-789.1)	2099.3 (1682.5-3055.8)	0.000
Integral Dose	2029.0 (1316.6-3359.4)	2042.0 (1176.6-2956.4)	2203.5 (1218.0-2800.0)	0.1717	1262.1 (1047.7-1620.2)	1155.8 (724.3-1322.5)	1204.0 (714.5-1769.3)	0.2725	3359.4 (2714.0-3946.2)	2956.4 (2434.8-3782.1)	2800.0 (2381.6-3162.2)	0.233

†Based on Friedman test

HT = Helical Tomothearpy. VMAT = Volumetric Modulated Arc Therapy. MU = monitor unit. IQR = interquartile range.

Table 3
Organs at risk and beam on time comparison of each technique. P-value of pair-wise* comparison.

	The Whole Cohort			Single lesion			Multiple lesions		
	HT vs VMAT	HT vs Cone-based	VMAT vs Cone-based	HT vs VMAT	HT vs Cone-based	VMAT vs Cone-based	HT vs VMAT	HT vs Cone-based	VMAT vs Cone-based
Brain: V_{5Gy}	0.0001	0.0157	0.0087	0.0051	0.5751	0.5076	0.0044	0.0128	0.0208
Brain: V_{12Gy}	0.0018	0.1395	0.4761	0.0166	0.5751	0.6465	0.0262	0.1542	0.4767
Optic nerve Rt	0.0208	0.2046	0.0496	0.3329	0.7213	0.1394	0.0099	0.1095	0.1307
Optic nerve Lt	0.0298	0.3392	0.0190	0.9594	0.8785	0.3329	0.0058	0.1549	0.0505
Optic Chiasm	0.1219	0.3219	0.2305	0.7989	0.8785	0.0166	0.0619	0.1307	0.9292
Cochlea Rt	0.0074	0.0091	0.7943	0.0662	0.0827	0.7989	0.0329	0.0754	0.8589
Cochlea Lt	0.0030	0.0386	0.3945	0.5076	0.6465	0.8785	0.0033	0.0619	0.3281
MU	0.0001	0.1396	0.0002	0.0051	0.0469	0.0367	0.0044	0.5337	0.0033
Beam on time	0.0001	0.2959	0.0002	0.0051	0.9594	0.0367	0.0051	0.1688	0.0033
HT = Helical Tomothearpy. VMAT = Volumetric Modulated Arc Therapy.									
MU = monitor unit									

Decision Score Analysis

Radiation dose characteristics were compared to those of the Cone-based approach by evaluating each dosimetric parameter, each radiation painting of normal structures, and by calculating BoT as presented in Table 4 (the whole cohort), Table 5 (single lesion), and Table 6 (multiple lesions). However, Dmax and HI values were excluded from this analysis as high maximal dose and heterogeneity in PTV were not affected the clinical outcome of SRS. For the whole cohort, VMAT displayed superior performance in both dosimetric and OARs parameters, while HT exhibited lower performance in dosimetric values but higher score in OARs parameters. For dosemetric parameters domain in single lesion, all three techniques revealed identical performance, while VMAT exhibiting better performance in OARs parameters. In contrast to multiple lesions, the Cone-based approach provided the best performance in dosimetric parameters. However, VMAT exhibited superior performance in OARs parameters, while HT displaying inferior performance than Cone-based approach.

Table 4
Decision Score analysis for the whole cohort.

Structure	Median (range) p-value			Decision Score	
	Cone-based	HT	VMAT	HT	VMAT
Dosimetric parameters					
CI	1.6 (1.4-2.0)	1.4 (1.3-1.8) 0.0097	1.4 (1.3-1.5) 0.0002	+1	+1
CI50	6.0 (4.9-8.8)	9.5 (5.2-12.7) 0.0001	5.7 (4.1-8.4) 0.0001	-1	+1
CGI	86.2 (58.8-92.9)	56.1 (41.5-62.9) < 0.0001	73.5 (66.8-77.5) 0.0409	-1	-1
Organs at risk and beam on time					
Brain: V_{5Gy}	98.01 (26.2-126.2)	116.8 (50.2-182.8) 0.0157	69.0 (29.1-105.2) 0.0087	-1	+1
Brain: V_{12Gy}	21.7 (9.2-30.7)	27.0 (10.2-32.6) 0.1395	20.5 (9.6-32.5) 0.4761	0	0
Hippocampal Rt	2.0 (0.4-3.9) 0.3499	1.7 (0.3-3.9)	2.6 (1.0-3.8)	0	0
Hippocampal Lt	1.2 (0.4-2.7) 0.2122	1.7 (0.2-2.4)	2.4 (1.2-3.5)	0	0
Optic nerve Rt	0.4 (0.2-1.0)	0.3 (0.1-1.7) 0.2046	1.4 (0.6-2.3) 0.0496	0	-1
Optic nerve Lt	0.6 (0.2-0.9)	0.2 (0.1-1.4) 0.3392	1.0 (0.7-1.3) 0.0190	0	-1
Optic Chiasm	0.4 (0.1-2.6)	0.4 (0.1-2.6) 0.3219	1.3 (0.7-2.0) 0.2305	0	0
Brainstem	1.7 (0.7-3.3) 0.2636	1.2 (0.2-3.8)	2.4 (1.4-3.1)	0	0
Cochlea Rt	0.4 (0.2-1.3)	0.1 (0.1-0.3) 0.0091	0.7 (0.3-1.1) 0.7943	+1	0
Cochlea Lt	0.2 (0.2-0.5)	0.1 (0.1-0.2) 0.0386	0.4 (0.1-1.2) 0.3945	+1	0
MU	14759.3 (9581.4-20993.1)	13936.0 (12159.0-19734.0) 0.1396	5745.0 (5287.3-7530.2) 0.0002	0	+1
Beam on Time	1475.9 (958.1-2099.3)	1098.0 (918.0-1884.0) 0.2959	574.5 (528.7-753.0) 0.0002	0	+1
Integral dose	2203.5 (1218.0-2800.0) 0.1717	2029.0 (1316.6-3359.4)	2042.0 (1176.6-2956.4)	0	0
Total score				**0**	**2**

HT = Helical Tomothearpy. VMAT = Volumetric Modulated Arc Therapy.

CI = conformal index. CGI = gradient index. MU = monitor unit

Table 5
Decision Score analysis for single lesion.

Structure	Median (range) p-value			Decision Score	
	Cone-based	HT	VMAT	HT	VMAT
Dosimetric parameters					
CI	1.6 (1.4-1.7)	1.3 (1.2-1.4) 0.0069	1.4 (1.3-1.5) 0.0593	+1	0
CI50	5.0 (4.4-5.4)	5.9 (4.8-9.0) 0.0593	4.6 (4.1-6.6) 0.0593	0	0
CGI	80.6 (59.7-95.0)	57.6 (54.2-62.9) 0.0284	75.6 (70.8-79.3) 0.7989	-1	0
Organs at risk and beam on time					
Brain: V_{5Gy}	26.2 (21.0-76.1) 0.0608	45.3 (31.2-59.5)	31.8 (22.1-42.5)	0	0
Brain: V_{12Gy}	8.8 (4.8-17.9) 0.3012	10.0 (7.1-17.5)	9.5 (6.4-15.6)	0	0
Hippocampal Rt	1.5 (0.2-2.8) 0.4593	1.7 (0.1-3.2)	0.8 (0.3-2.0)	0	0
Hippocampal Lt	0.7 (0.2-1.4) 0.4593	1.0 (0.2-2.2)	1.4 (1.2-2.0)	0	0
Optic nerve Rt	0.4 (0.2-0.8) 0.4066	0.27 (0.1-1.7)	1.0 (0.4-1.9)	0	0
Optic nerve Lt	0.5 (0.2-0.9) 0.6703	0.2 (0.1-1.4)	0.8 (0.3-1.1)	0	0
Optic Chiasm	0.4 (0.2-1.7) 0.0672	0.4 (0.1-3.5)	0.9 (0.7-1.8)	0	0
Brainstem	1.1 (0.7-2.4) 0.6703	1.2 (0.1-4.2)	1.6 (1.2-2.4)	0	0
Cochlea Rt	0.21 (0.19-0.81)	0.10 (0.04-0.26) 0.0827	0.37(0.13-1.02) 0.7989	0	0
Cochlea Lt	0.16 (0.08-0.20)	0.07 (0.05-0.11) 0.6465	0.16 (0.09-0.24) 0.8785	0	0
MU	9099.4 (5151.3-12343.7)	13081.5 (12159.0-14670.0) 0.0469	5384.9 (4867.4-5673.0) 0.0367	-1	+1
Beam on Time	909.9 (515.1-1234.4)	939.0 (864.0-1044.0) 0.9594	538.5 (486.7-567.3) 0.0367	0	+1
Integral dose	1204.0 (714.5-1769.3) 0.2725	1262.1 (1047.7-1620.2)	1155.8 (724.3-1322.5)	0	0
Total score				**-1**	**+2**

HT = Helical Tomothearpy. VMAT = Volumetric Modulated Arc Therapy.

CI = conformal index. CGI = gradient index. MU = monitor unit

Table 6
Decision Score analysis for multiple lesions.

Structure	Median (range) p-value			Decision Score	
	Cone-based	HT	VMAT	HT	VMAT
Dosimetric parameters					
CI	1.5 (1.4-2.2)	1.6 (1.3-1.9) 0.1363	1.4 (1.3-1.6) 0.0016	0	+1
CI50	6.9 (6.0-9.6)	10.4 (6.3-17.8) 0.0010	7.5 (4.7-9.3) 0.0010	-1	-1
CGI	87.3 (58.4-89.4)	44.5 (40.0-62.7) 0.0005	72.7 (66.1-75.9) 0.0174	-1	-1
Organs at risk and beam on time					
Brain: V_{5Gy}	182.8 (136.3-225.9)	105.2 (89.8-162.4) 0.0128	124.6 (98.9-178.9) 0.0208	+1	+1
Brain: V_{12Gy}	32.6 (30.3-40.4) 0.0597	32.5 (22.6-37.3)	30.7 (21.7-38.6)	0	0
Hippocampal Rt	2.0 (0.5-4.6) 0.6952	3.5 (2.4-4.1)	2.8 (1.5-5.8)	0	0
Hippocampal Lt	2.2 (0.4-4.3) 0.1777	3.1 (1.2-4.8)	2.6 (0.5-3.9)	0	0
Optic nerve Rt	0.3 (0.1-2.0)	1.4 (0.8-2.6) 0.1095	0.4 (0.2-2.4) 0.1307	0	0
Optic nerve Lt	0.2 (0.1-1.5)	1.3 (0.9-1.9) 0.1549	0.6 (0.2-1.6) 0.0505	0	0
Optic Chiasm	0.9 (0.4-3.6) 0.3067	0.4 (0.1-2.6)	1.7 (0.8-3.0)	0	0
Brainstem	3.0 (0.7-8.0) 0.0784	1.6 (0.2-3.6)	3.0 (2.0-3.5)	0	0
Cochlea Rt	0.5 (0.2-3.2) 0.0784	0.2 (0.1-0.3)	0.8 (0.4-1.6)	0	0
Cochlea Lt	0.4 (0.2-1.4)	0.2 (0.1-0.2) 0.0619	1.1 (0.4-1.4) 0.3281	0	0
MU	20993.1 (16824.6-30557.7)	19734.0 (11774.0-47076.0) 0.5337	7530.2 (6550.2-7891.4) 0.0033	0	+1
Beam on Time	2099.3 (1682.5-3055.8)	1884.0 (1398.0-3324.0) 0.1688	753.0 (655.0-789.1) 0.0033	0	+1
Integral dose	2800.0 (2381.6-3162.2) 0.2335	3359.4 (2714.0-3946.2)	2956.4 (2434.8-3782.1)	0	0
Total score				**-1**	**+2**

HT = Helical Tomotherapy. VMAT = Volumetric Modulated Arc Therapy.

CI = conformal index. CGI = gradient index. MU = monitor unit

Discussion

The targeted-therapy and immunotherapy era is associated with improvements in the survival rate for tumor-controlled patients. Thus, treatment-associated toxicities must be closely concerned. The management for oligo-metastasis to the brain has gradually shifted from irradiating the whole brain to irradiating a more specific site. Stereotactic radiosurgery has commonly been used as a primary radiation treatment among patients of this disease. Dosimetric analysis of each technique has encouraged physicians to select an appropriate radiation modality. The outcomes of this study indicate the best CGI in Cone-based planning, as has been supported by the findings of a study conducted in Taiwan (13). Hsu SM and colleagues have evaluated the availability of SRS for spherical tumors using different radiation techniques. It was found that the Cone-based approach, in which cone-diameter matched the tumor size, offered the best CI and CGI values (13). On the other hand, according to our results, the Cone-based approach exhibited poor CI and HI values when compared to the HT and VMAT approaches. The possible factors that were related to the worsening dosimetric data were tumor size, non-spherical shape, and the number of intracranial lesions. A larger tumor size would directly impact heterogenous radiation painting in the Cone-based approach. In this study, 11 out of 21 patients exhibited multiple brain metastases. Radiation homogeneity and conformality were found to be better in solitary brain lesions when compared to the multiple lesions observed in the Cone-based technique. These factors were associated with complex radiation planning through the use of multiple isocenters. Furthermore, the limitation of small-sized pencil beams resulted in multiple radiation beam directions.

VMAT displayed relatively excellent radiation output dose characteristics for SRS. This technique delivered a very steep radiation dose gradient as it had exhibited the best CI50 value when compared to the other two techniques. Moreover, VMAT exhibited the lowest normal brain parenchymal volume, which was received radiation dose more than 5 Gy for multiple lesions, and the shortest estimated BoT. Reducing the radiation delivery duration decreased the intra-fractional motion and technically promoted the degree of personal comfort. In our center, these points are considered advantages of appropriate radiation techniques where it is characterized by a rather massive workload that is constrained by a proportionally insufficient availability of radiation equipment. However, the result of BoT estimation in the Elekta machine (including in the VMAT and Cone-based techniques) had minimal degree of deviation from the re-calculating process while the BoT in the HT approach exhibited an even greater level of preciseness.

HT had identical Dmax, HI, and CI values but longer estimated BoT values when compared to VMAT. Among the three techniques, HT delivered the poorest CGI value. This outcome is related to the ordinarily helical coplanar beam direction employed in the HT technique. This factor restricts the steep radiation dose gradient, especially in the lateral dimension. However, HT can produce stereotactic radiation delivery at an acceptable radiation dose characteristic and at a passable level of toxicity. According to the results of a study conducted in Italy, 68 patients receiving a median radiation dose of 18 Gy were studied. The outcomes supported the feasibility and tolerance for SRS using the HT technique (14).

Decision Score analysis clearly revealed a better degree of performance in the VMAT technique. On the other hand, HT exhibited an identical performance in dosimetric domain for single lesion compared to Cone-based technique. The outcomes of these reports emphasize the usability of SRS by the IMRT technique over the Cone-based technique. There has been limited published data on the delivery of SRS using HT. Our study has confirmed the feasibility of this procedure in our facility and encourages SRS by HT in radiotherapy centers that have limited access to radiation modalities.

Conclusions

Many radiotherapy modalities were used to create SRS in the treatment of limited-number intracranial dissemination. Each technique is associated with a unique radiation beam characteristic. Dosimetric comparison analysis permitted physicians to choose an appropriate radiation technique that is compatible with their facilities. Our data indicates the dosimetric comparison between three radiation techniques for single and multiple lesions. The Cone-based technique revealed the poorest HI value. On the other hand, VMAT exhibited the best estimated BoT value. Moreover, we have reported the feasibility of SRS using a helical coplanar radiation machine that was associated with an acceptable degree of radiation output characteristic and well tolerability. This result was encouraged physicians to apply SRS using HT machine in radiotherapy centers that have limited access to other radiation modalities.

Declarations

Ethics Board approval

This study was approved by Research Ethics Committee of Faculty of Medicine Chiang Mai University, grant no.176/2017.

Consent for publication

Applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

BJ was first and corresponding author who was a major contribution in writing the manuscript.

CM performed the MRI reports of all patients in this study.

PS was responsible for statistical analysis

IC, ET, SC, PK, and WO were collected the data of patients.

All authors read and approved the final manuscript.

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Figures

Figure 1

This figure showed the non-invasive immobilization Stereotactic Radiosurgery (SRS)-system mask (R406-1 SRS mask, Klarity, China).

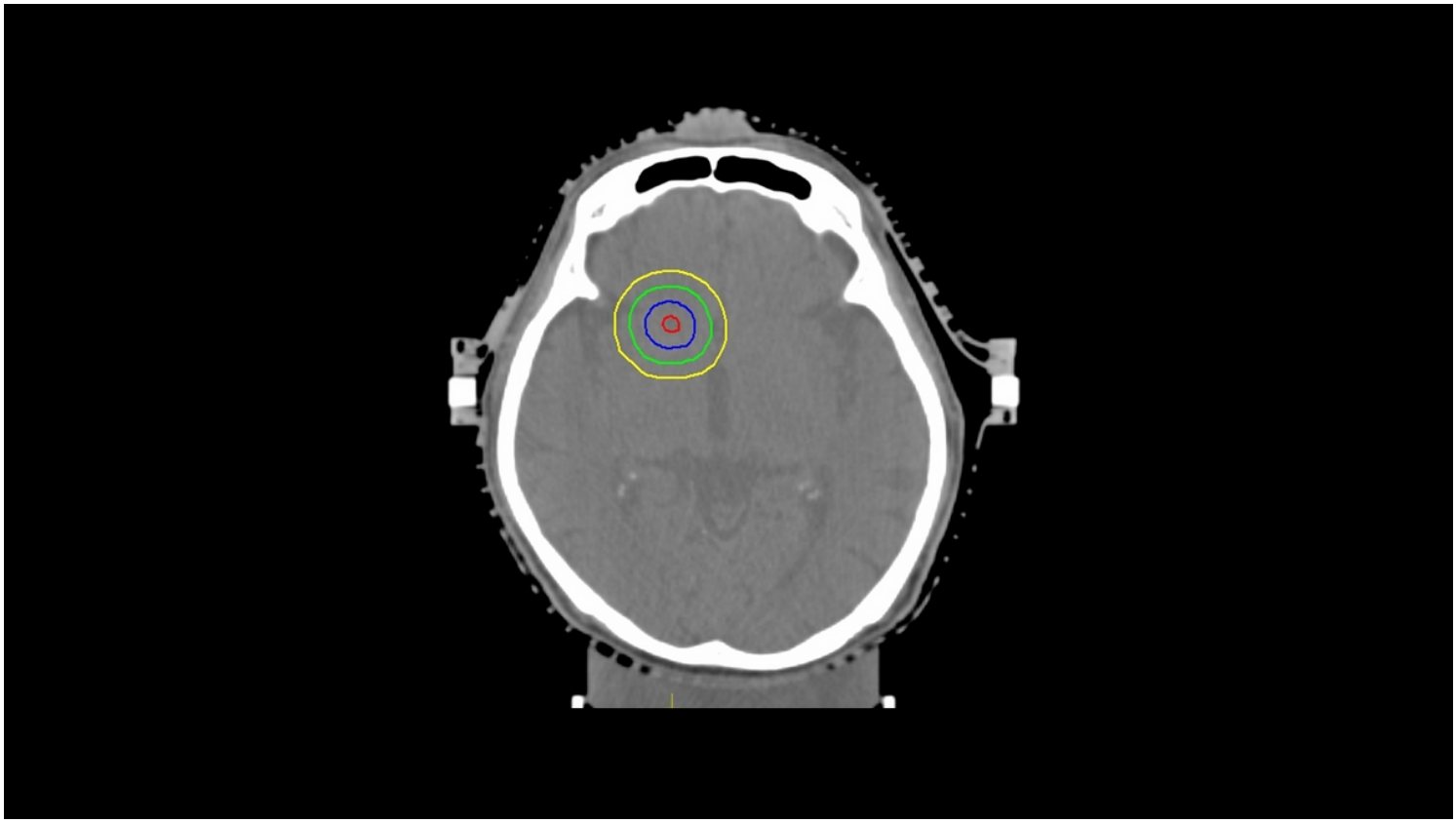

Figure 2

This figure exhibited the virtual structures to create SRS in inverse treatment planning, which included Helical Tomotherapy and Volumetric Modulated Arc Therapy. The blue line was the planning treatment volume (PTV). The red line represented the clinical sub-volume (CSV). The green and yellow lines were ring structures which expanded by 5 mm and 10 mm from PTV, respectively.

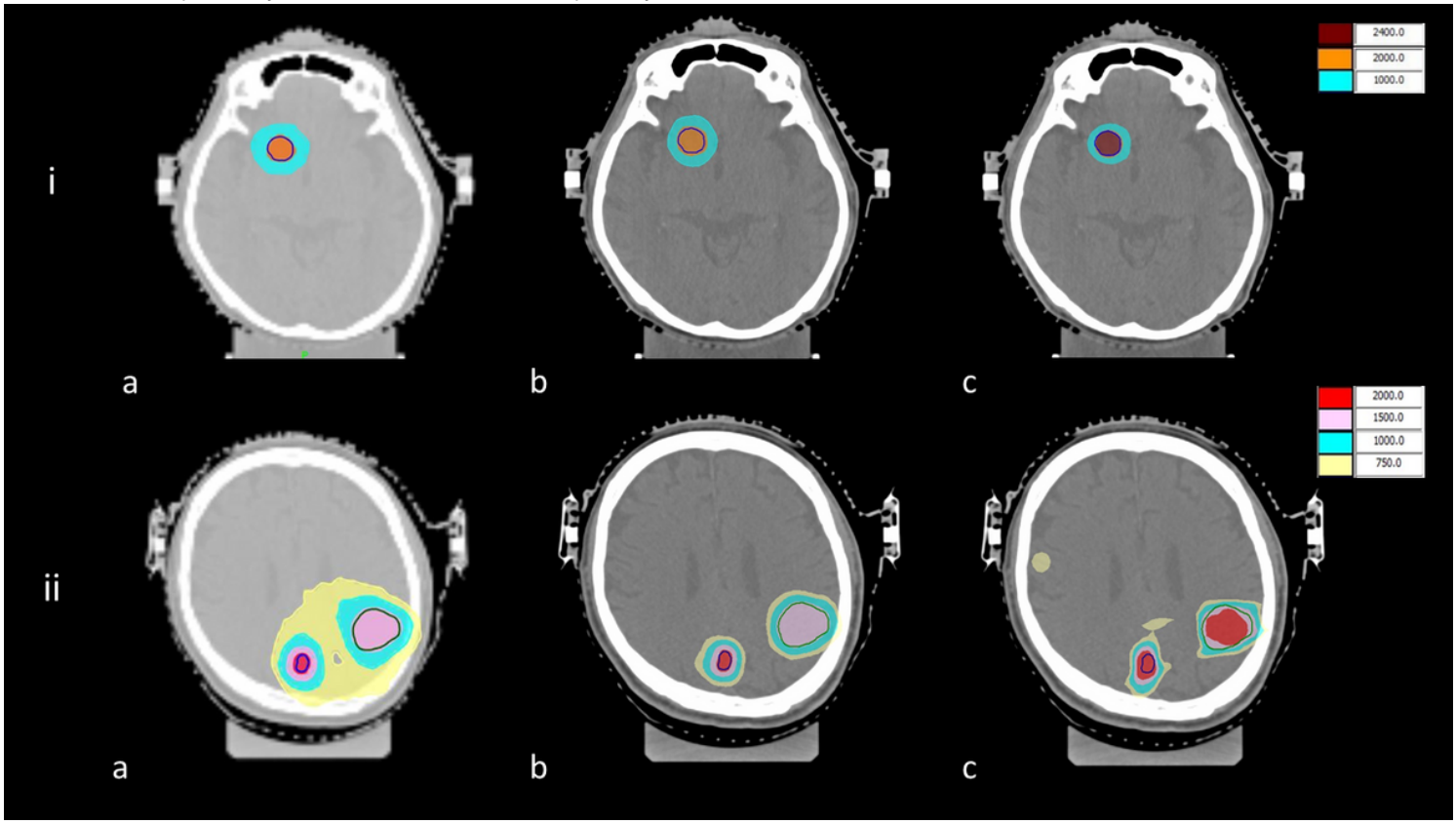

Figure 3

This figure demonstrated an isodose distribution for single and multiple metastatic lesions. Comparing between three radiation techniques; Helical Tomotherapy (a), Volumetric Modulated Arc Therapy (b), and Cone-based (c). i : single lesion at left temporal region (20 Gy). PTV was presented in blue line. ii : multiple lesions. This patient had three lesions located at right temporal (20 Gy), left occipital (20 Gy), and left parietal (15 Gy) regions. PTV of left occipital and parietal were presented in blue and green line, respectively .

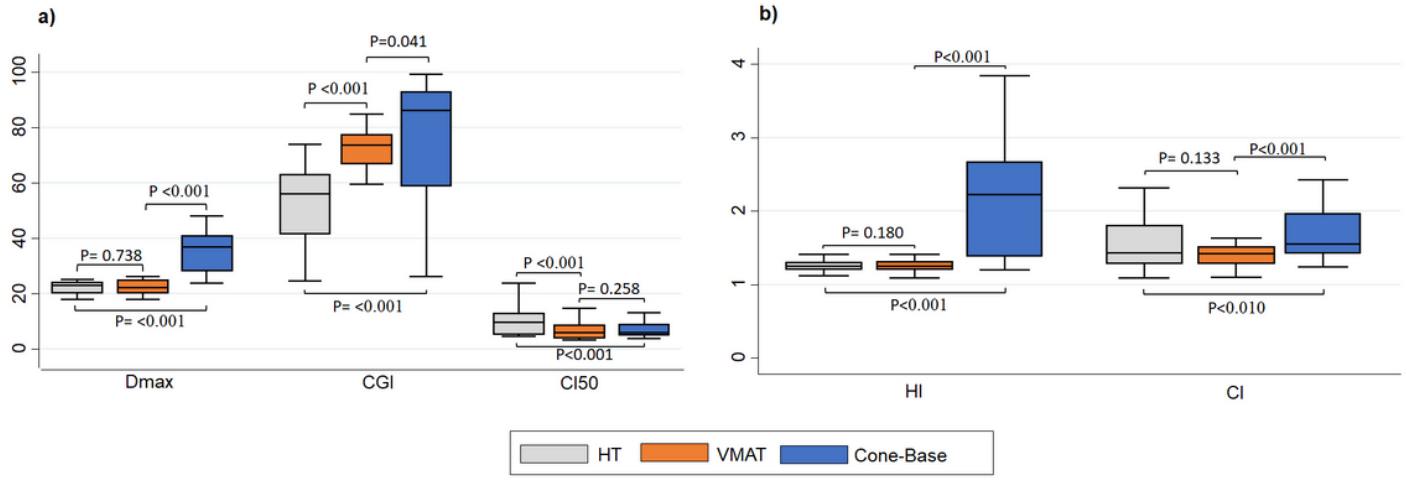

Figure 4

This figure displayed the dosimetric comparison between three radiation techniques in the whole cohort. To compare between each technique, p-value was calculated by pair-wise comparison. Dmax = maximal dose. CGI = gradient index. HI = homogeneity index. CI = conformity index.

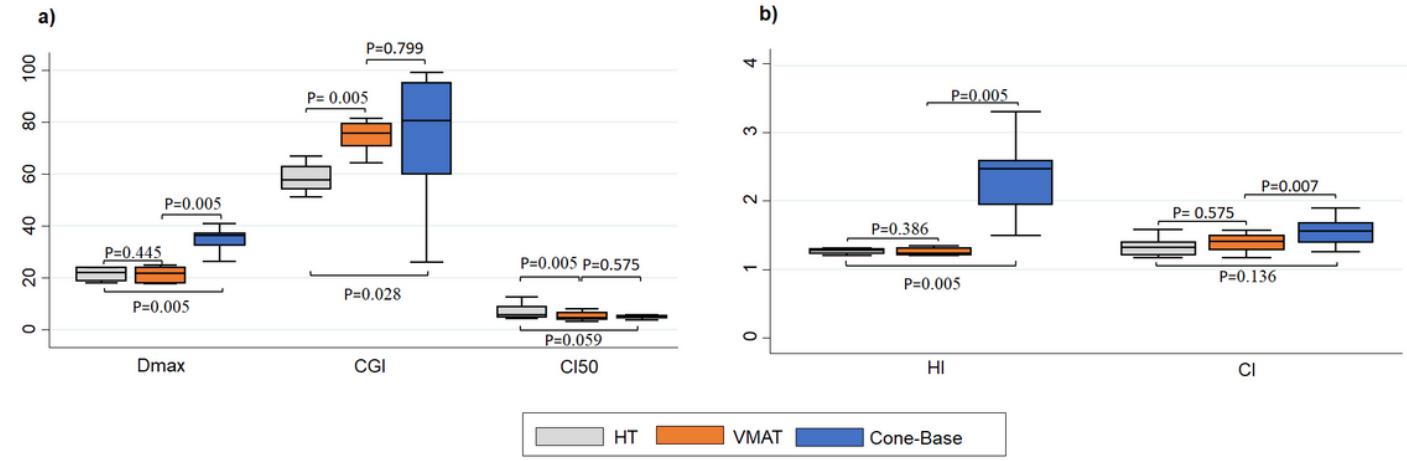

Figure 5

This figure showed the dosimetric comparison between three radiation techniques for single lesion. To compare between each technique, p-value was calculated by pair-wise comparison. Dmax = maximal dose. CGI = gradient index. HI = homogeneity index. CI = conformity index.

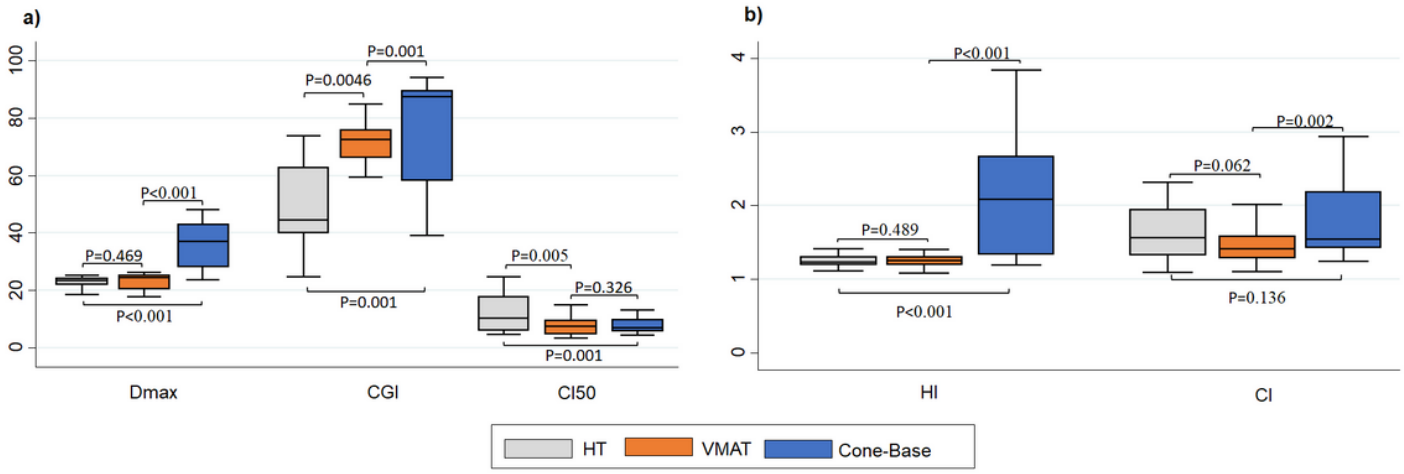

Figure 6

This figure demonstrated the dosimetric comparison between three radiation techniques for multiple lesions. To compare between each technique, p-value was calculated by pair-wise comparison. Dmax = maximal dose. CGI = gradient index. HI = homogeneity index. CI = conformity index.