RESEARCH ARTICLE

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Evaluation of Patient-Specific Quality Assurance in Single Isocenter Multitarget Stereotactic Radiosurgery of Brain Metastases Using Octavius 4D for Flattening Filter Free Beams

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Abstract

Aim: To evaluate the patient-specific quality assurance (PSQA) in Single Isocenter Multitarget (SIMT) Stereotactic Radiosurgery (SRS) of brain metastases using Octavius 4D for flattening filter free (FFF) X-ray beams. **Materials and Methods:** Octavius 4D with 1000 SRS detector array was used for doing PSQA in fifteen patients planned using volumetric modulated arc therapy (VMAT) based stereotactic radiosurgery (SRS) of SIMT technique for treating multiple brain metastases. Measurements were made both in standard setup as well as in special setup through which the region of measurement is increased. The obtained results are compared with TPS reference doses at different dose grid sizes and minimum dose cutoff thresholds for both 6X-FFF and 10X-FFF energies. **Results:** The percentages of measurable targets were 83.34% and 93.54% in standard and special set respectively. In standard set, the average gamma passing rate was 97.63±1.26% and 97.78±1.09% for 6X-FFF and 10X-FFF respectively. The mean gamma passing rates was 97.97±0.99% and 97.85±1.13% for 6X-FFF and 10X-FFF in special set respectively. PSQA passing rate decreases with increasing TPS grid size in both the energies. The mean gamma passing rate for 6X-FFF was 97.97±0.99% and 96.94±1.11% at 10% and 25% cutoff dose respectively. The mean gamma passing rate for 10X-FFF at 10% and 25% dose cutoff was 97.85±1.13% and 97.12±1.29% respectively. Low-dose masking effect was more in 6X-FFF than observed with 10X-FFF energy. **Conclusion:** The performance of Octavius 1000 SRS for PSQA of VMAT based SRS were evaluated and found satisfactory at 6X-FFF and 10X-FFF energies in SIMT of brain metastases.

Keywords: SRS QA- SIMT- brain metastases- FFF beams- Octavius 4D- 1000 SRS

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Introduction

Stereotactic Radiosurgery (SRS) for the treatment of multiple brain metastases has increased in recent years owing to the technological advancements and increased accuracy in pre-treatment image verification and treatment delivery. Different methods of planning strategies were continuously developed and employed in clinics which includes HyperArc VMAT by Varian Medical Systems, Elements Multiple Brain Mets SRS by BrainLab and High definition dynamic radiosurgery by Elekta which enabled the precise delivery of very high doses of radiation (>15Gy) to sparsely separated multiple (>6) small intracranial lesions (Vergalasova et al., 2019). One such novel concept of SRS treatment planning is the use of Single Isocenter Multitarget (SIMT) technique for the irradiation of multiple brain metastases planned using Volumetric Modulation Arc Therapy (VMAT) (Clark et al., 2010).

VMAT based SIMT for multiple brain metastases is an attractive alternative to multi-isocenter radiosurgery because of clinically equivalent dose conformity, dose falloff, 12Gy isodose volume and low-dose spillage along with reduced treatment time (Thomas et al., 2014; Morrison et al., 2016). SRS using single isocenter VMAT for multiple brain lesions has shown good local metastases control rate irrespective of distance of targets from isocenter illustrating the superior efficacy of SIMT technique (Kraft et al., 2021; Aoki et al., 2021). Also the elimination of multiple isocenter allows the treatment to be completed within a reasonable time frame without the need for extensive pre-treatment verification of each target. Instead the single treatment isocenter is volumetrically verified using kilo-voltage cone beam computed tomography (kV-CBCT) and the position of all target lesions relative to their planned positions is confirmed by radiographic verification of the skull bony anatomy. In recent decade, there has been a lot of interest in using flattening filter-free (FFF) X-ray beams in VMAT for SRS of brain metastases as it delivers the dose faster than flattened beams because of increased dose rate which leads to a significant reduction in treatment delivery time

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with benefit in both patient discomfort and better target localization due to reduced opportunity for intra-fraction motion (Lai et al., 2017; Prendergast et al., 2011). Also in addition, the out-of-field dose is shown to reduce in FFF beams because the removal of flattening filter results in the reduction of head scatter and residual electron contamination which directly minimizes radiation induced Secondary Cancer Risk (SCR) in healthy irradiated tissues surrounding the tumor (Louise et al., 2015).

The SIMT technique of VMAT based SRS along with FFF beams however poses some challenges and has several complicating factors. Translational and rotational error uncertainties during setup and intra-fractional treatment can have serious dosimetric impacts and increased risk of geometrical miss of the target lesions (Tsui et al., 2022; Prentou et al., 2020). By design, SIMT technique involves multiple highly modulated beams which demands for pre-treatment patient-specific quality assurance (PSQA) for verification of delivered dose as recommended (Miften et al., 2018; Moran et al., 2011). Conventionally, patient-specific validation of dose is usually performed by recalculating the planned dose onto a phantom in which a measurement is then made. In SIMT, during treatment planning the treatment isocenter is normally placed in a location central to all the sparsely separated treating target lesions and not inside of any specific target, hence complicates the measurement of dose distribution during PSQA. Typical dose distribution of SRS in multiple brain metastases is characterized by low volume of high-dose regions and high volumes of low-dose regions. The high-dose target regions are relatively quite small in size, small field dosimetry concerns are heightened and appropriate dosimeters as well as chambers are indicated for this type of measurements (Duggan and Coffey, 1998). There are multiple PSQA techniques which could be applied to VMAT based SIMT. The use of film and chamber for measuring relative dose distribution and absolute dose assessment respectively can be useful but the choice of measuring plane (sagittal or axial or coronal) can be focused only onto limited lesions and thus unable to capture the dose delivered to all targets. To maximize the number of targets covered in a single plane, a novel spherical radiotherapy phantom was designed and developed specifically for doing PSQA of mono-isocentric multiple metastases SRS (McKenna, 2021) but the phantom is not commercialized yet. Detector arrays cast in various 2D and 3D shapes are also widespread in use which can facilitate PSQA in SRS (Bruschi et al., 2018; Rose et al., 2020; Ahmed et al., 2019) but studies are limited validating their use to VMAT based SIMT technique in treating multiple brain metastases. The main purpose of this study is to check the feasibility of Octavius 4D (PTW, Freiburg, Germany) phantom in conjunction with Octavius 1000 SRS detector array in doing PSQA for multiple brain metastases planned with SIMT technique. In addition, the performance results of Octavius 1000 SRS in pre-treatment plan verification of multiple brain metastases is evaluated for different influential parameters such as dose grid calculation size used in Treatment planning System (TPS) and beam energy used for planning because by virtue of its nature, the volume of treating lesions tends to be relatively small in sizes and the amount of low-dose spillage outside the targets tends to be larger in volume respectively. Since the ratio of treating target volume to the normal brain tissue volume is relatively small in SRS treatment of multiple brain metastases and also in combination with VMAT based treatment delivery technique, the volume of low dose spillage and spread in normal tissues is increased and hence the effect of low-dose masking on the resultant area gamma needs further evaluation by varying the cutoff dose threshold included in the gamma evaluation criteria.

Materials and Methods

The PTW Octavius 4D phantom (PTW, Freiberg, Germany) is a cylindrical phantom with a diameter of 32cm, length of 34.3cm and weights 29kg. It is made up of water equivalent polystyrene material of density 1.05g/cm3. The phantom has an insert in the center for a detector array. The entire cylindrical phantom is mounted on a rotating platform controlled by a motor. The built in mechanics allows the cylindrical phantom to rotate synchronously with gantry ensuring perpendicular incidence of the radiation beam on the detector array at all times with the data aid from an wireless inclinometer attached to the treatment machine gantry. The PTW Octavius 1000 SRS detector array consists of 977 liquid-filled ionization chambers arranged in a grid fashion span over a square area of 11 cm × 11 cm. Each detector has a size of 2.3 mm × 2.3 mm × 0.5 mm (volume = 2.65 mm3). In the inner high-resolution area of 5.5 cm × 5.5 cm, the center-to-center spacing of the detectors is 2.5 mm, whereas the center-to-center spacing of the detectors in the outer area is 5 mm. On the main axes, the detector distance is 2.5 mm while on the diagonals it is 3.5 mm. The detector size is consistent throughout the array and the detectors on the outer periphery are the same as those on the inner area. The reference point of measurement of detectors is located at 9 mm below the surface of the detector array and placed at 16cm depth from the surface of the rotation unit. The Octavius 1000 SRS uses PTW's VeriSoft software (PTW, Freiburg, Germany) for measurement data acquisition and data analysis. In the Verisoft, the users has multiple tools to analyze and compare the measured dose against the reference dose exported from Treatment Planning System (TPS) through profiles (horizontal, vertical, and diagonal), planar isodose overlay, and gamma index calculation. Figure 1 shows the setup of Octavius 4D dosimetric system used for measurements along with 1000 SRS detector array in place.

Fifteen patients of multiple brain metastases treated with varying number of target lesions (3 to 12 target lesions per patient) and target size (0.12cc to 14.91cc) were chosen retrospectively for this study. The details of treating target lesions were shown in Table 1. Treatment plans were generated in Eclipse TPS version 13.0 (Varian Medical Systems, Palo Alto, CA, USA) for VMAT based delivery in Truebeam STx linear accelerator equipped with 120 High Definition Multileaf Collimator (HDMLC) system having central 32 leaf pairs of 2.5mm leaf width and peripheral 28 leaf pairs of 5.0mm leaf width defined

at isocenter distance. SIMT treatment plans were designed by placing single isocenter at the geometric centre of the treating targets. For planning, a total of 7 beam arcs were used which was placed in a standard configuration including two full coplanar arcs (360° each) and rest five semi arcs (≤180°) equally distributed in non-coplanar fashion around the head as shown in Figure 2. Treatment plans were generated using FFF beams for both 6X and 10X energies with same planning parameters and optimization objectives to compare the effect of beam energy on PSQA. Volume dose was calculated using Anisotropic Analytical dose calculation Algorithm (AAA) with 1mm dose calculation grid size and a dose of 18Gy in 1 fraction was prescribed to the target volumes.

For the execution of PSQA of the SIMT plans, the generated patient treatment plans were transferred to the Octavius 4D phantom and the dose was recalculated onto the phantom by maintaining the actual geometry of beams (coplanar and non-coplanar) with various dose grid sizes (1mm, 1.5mm, 2.0mm and 2.5mm). The recalculated doses onto the Octavius 4D phantom is shown in Figure 3. During measurements with the Octavius 4D phantom at the machine, all beams were delivered at coplanar setup (couch 0 degree) to ensure the rotation of the phantom and the detector array stays always perpendicular to the gantry rotation. Although for all the coplanar and non-coplanar beams, measurements were done with couch 0 degree, the Verisoft software during dose reconstruction process, accounts for the actual non-coplanar angles with our couch angle inputs thus reflecting the correct position of the target lesions with respect to the location of the treatment plan isocenter.

Standard set of PSQA measurements include setting up of the Octavius 4D phantom at the isocenter of the machine, delivery of the treatment plan and acquisition of dose. Since the size of the 1000 SRS detector array is 11 cm × 11 cm, the maximum space available for measurements is limited to target lesions falling outside the cylindrical volume of diameter 11cm and length 11 cm centered at isocenter, thus unable to capture and verify the dose delivered to those target lesions. To include and evaluate the accuracy of dose delivered to distant lesions located distal to the isocenter of SIMT plans, non-standard (special) set of PSQA measurements were required. To acquire special set of data, the treatment plans were delivered twice, one set with the Octavius 4D in 0 degree and the other set with 180 degree phantom setup coupled through a desired translational shift of the entire rotation unit along the Gun – Target direction. The two sets of measurement data were then composed and the final measured dose was reconstructed to larger lengths (>11cm upto 20cm) than the active length of the 1000 SRS detector array (11cm). In this way, the fraction of measurable target lesions in the PSQA of SIMT plans was maximized and provides reliable comprehensive PSQA results encompassing as many number of treating target lesions as possible in the analysis.

The measured and reconstructed dose were analyzed and compared against the reference dose exported from TPS using a method of Gamma Evaluation (Low et al., 1998) in Verisoft. The Verisoft does gamma calculation by interpolating doses between points just in case if a reference dose point has no measured dose point near it. Stringent gamma criteria of 1mm Distance to Agreement (DTA) and 3% Dose Difference (DD) were used to evaluate the PSQA of SRS plans in global gamma mode analysis. To analyze the delivery accuracy of SIMT plans, the agreement of measured dose with reference dose were evaluated for different combinations of DTA (3mm, 2mm, 1mm) and DD (3%, 2%, 1%). The QA pass acceptance criteria were set as area gamma (γ) <1 should be ≥ 95% of the total evaluated points falling within the measurement volume with a minimum dose threshold of 10% and normalization of global maximum dose. Typical dose distributions of multiple brain metastases presents with small volumes of high-dose regions and larger volumes of low-dose regions. Though the accuracy of delivered dose is equally important both at high-dose and low-dose regions, in SRS treatment plans which involves delivering a very high dose of radiation to the targets in contrast to surrounding normal tissue, a dose threshold of 10% cutoff included in gamma analysis may not be appropriate enough to evaluate delivery accuracy at target lesions and has greater chances for misjudging the resultant area gamma. The effect of low-dose masking on the overall passing criteria was thus investigated by varying minimum dose cutoff values in the gamma analysis criteria.

Results

The results of gamma passing rates for the comparison made between the measured and calculated dose as evaluated in Verisoft at the criteria of 1mm/3% were shown in Table 2 for both the energies. The average gamma passing rate was 97.65±1.67% and 97.82±1.50% for 6X-FFF and 10X-FFF beams respectively in standard measurement set. Targets visible in the measurement were considered as measurable targets and the percentages of measurable targets were 83.34% and 93.54% in standard and special set of measurements respectively. The percentage of measurable targets increased in 53.33% of total evaluated patients during special set of measurements. In rest of the 46.67% patients, either the targets were completely covered initially in the standard measurements or some of the targets were lying outside the measurement purview in the anterio-posterior and left-right directions. Since the special set of measurements expands the range of

Figure 1. Setup of Octavius 4D with 1000 SRS Detector

Table 1. Details of Treating Target Lesions

Patient	Number of Targets	Total Volume of Targets (cc)	Range of Target Volumes (cc)	Mean Volume of Targets and SD (cc)
1	3	3.32	0.26 - 2.35	1.11 ± 1.10
2	6	19.57	0.22 - 14.91	3.26 ± 5.73
3	7	14.37	0.12 - 5.98	2.05 ± 2.07
4	3	4.77	0.86 - 2.92	1.59 ± 1.15
5	5	5.46	0.63 - 1.66	1.09 ± 0.39
6	5	18.18	0.15 - 7.63	3.64 ± 3.41
7	5	12.71	0.19 - 9.38	2.54 ± 3.87
8	12	24.05	0.74 - 4.59	2.00 ± 1.12
9	9	30.33	0.33 - 9.91	3.37 ± 3.56
10	8	18.84	1.56 - 3.22	2.36 ± 0.58
11	6	14.62	0.84 - 7.62	2.44 ± 2.57
12	4	9.56	0.12 - 3.99	2.39 ± 1.63
13	4	16.18	0.65 - 8.50	4.05 ± 3.54
14	8	18.3	0.20 - 5.45	2.29 ± 2.13
15	7	26.77	2.28 - 6.74	3.82 ± 1.45

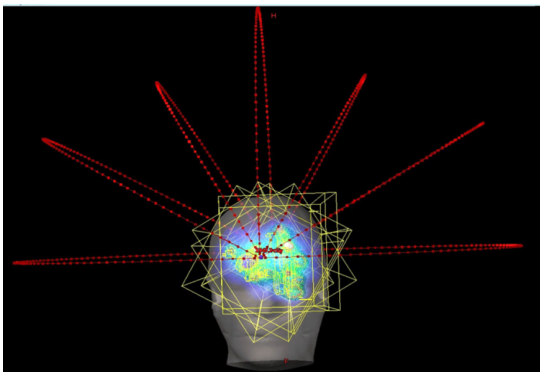

Figure 2. Arc Arrangement Used for SRS Planning

measurement only in the superior-inferior (cranio-caudal) direction, the targets situated far away from the isocenter in other directions can possibly be included for evaluation only by using a larger detector array than Octavius 1000 SRS. The mean gamma passing rate of measurements made in special set were 98.00±1.42% and 97.87±1.57% for 6X-FFF and 10X-FFF energies respectively. The comparison of gamma passing rates between standard and special set of measurements at different dose calculation grid sizes were shown in figure 4 and 5 for 6X-FFF and 10X-FFF beams respectively. It had been observed from

Table 2. Gamma Passing Rate (%) at 1mm/3% Criteria with 10% Dose Cutoff for 1mm TPS Dose Grid Size

Patient	Gamma Passing Rate (%)	
	6X-FFF	10X-FFF
1	99.5	99.2
2	98.9	98.5
3	96.2	97.4
4	99.1	99.8
5	97.3	96.5
6	99.7	98.9
7	95.6	95.1
8	98	99.3
9	95.1	96.2
10	96.4	95.8
11	99.2	98.7
12	99.9	99.6
13	97.7	98.4
14	96.8	97.3
15	95.4	96.6
Mean	97.65	97.82
Standard Deviation	1.67	1.5
Range	95.1-99.9	95.1-99.8

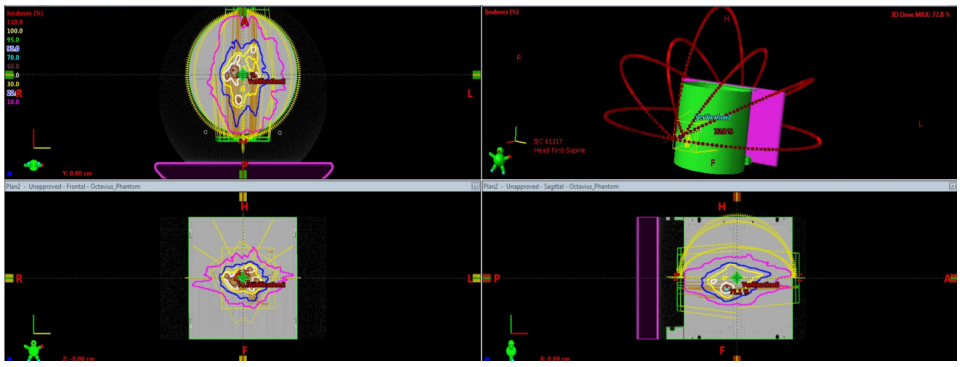

Figure 3.Recalculated Dose on Octavius 4D Phantom

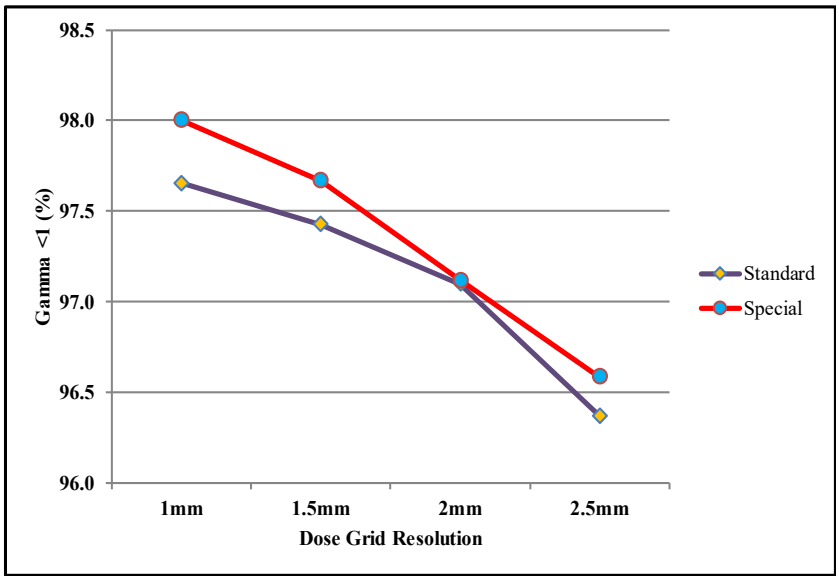

Figure 4. Area Gamma<1 for 6X-FFF at Different Fose Grid Resolution

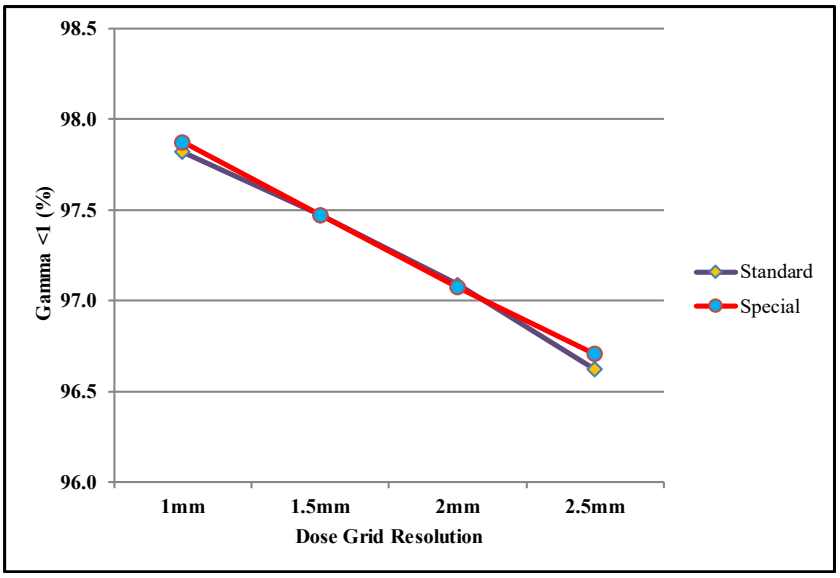

Figure 5. Area Gamma<1 for 10X-FFF at Different Dose Grid Resolution

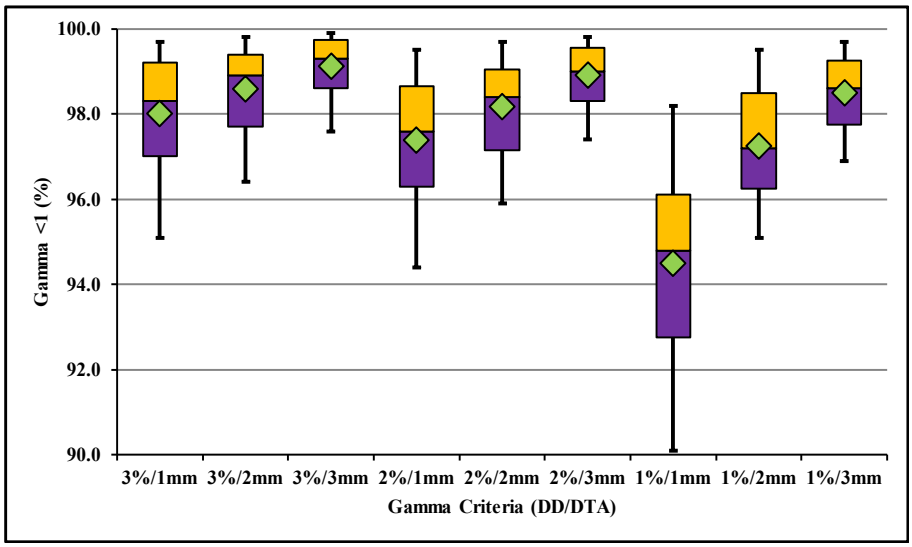

Figure 6. Area Gamma<1 in Special Measurement Setup for 6X-FFF at Different Gamma Criteria

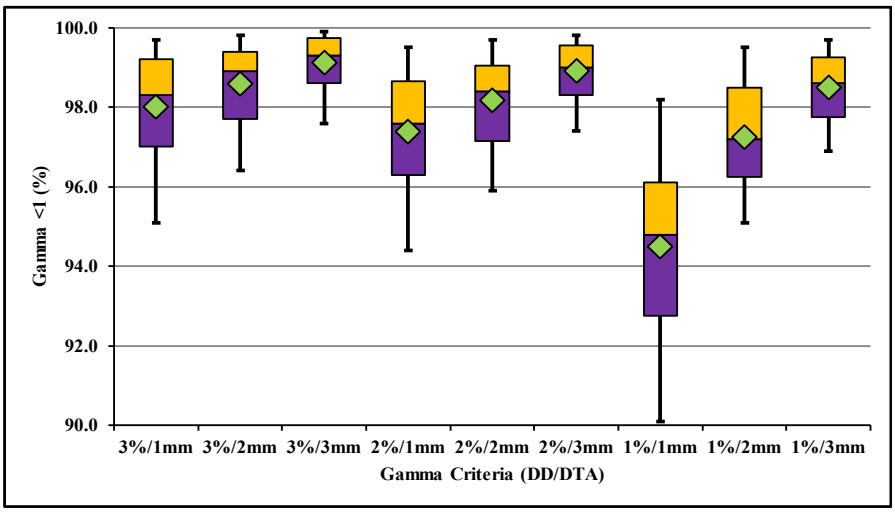

Figure 7. Area Gamma<1 in Special Measurement Setup for 10X-FFF at Different Gamma Criteria

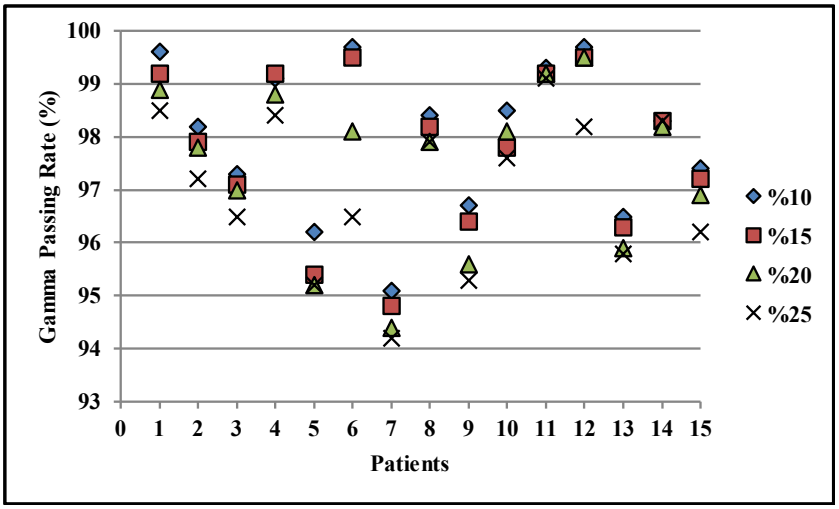

Figure 8. Area Gamma<1 in Special Measurement Setup for 6X-FFF at Different Cutoff Dose Thresholds

the results that the gamma passing rate increases in special set of measurement on comparison with standard set of measurements at all dose grid sizes and the increase was more pronounced in low energy than observed in higher energy. Also the gamma passing rate is sensitive to variation in dose grid sizes and the mean gamma passing rate decreases with increasing dose calculation grid size for both the energies. The change in calculation grid size in TPS had an impact in the distribution of calculated doses within the target lesions and the effect was seen

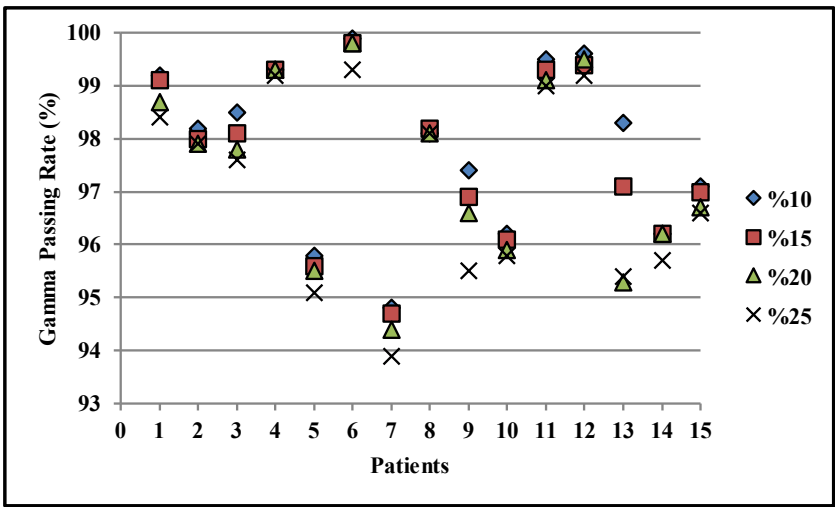

Figure 9. Area Gamma<1 in Special Measurement Setup for 10X-FFF at Different Cutoff Dose Thresholds

huge especially in the presence of very small target lesions. As the size of the dose grid decreases especially ≤ 1.5mm, the dose coverage in small targets increases which further translates improvement in the comparison against measured dose and the gamma passing rate increases. The accuracy of gamma evaluation increases with decreasing dose grid sizes.

Figures 6 and 7 shows the results of gamma passing rates evaluated at different gamma criterias for 6X-FFF and 10X-FFF beams respectively for special set of measurements compared against the calculated dose at a grid size of 1mm. The mean gamma passing rate results was acceptable (>95%) for both the energies at all the gamma criterias evaluated except at 1%/1mm. The results of passing gamma were 94.55±1.71% and 93.50±1.81 for 6X-FFF and 10X-FFF at 1%/1mm evaluation criteria. The results have shown no difference been observed between the energies in terms of gamma passing rates. The observed superiority in gamma passing rates from this initial study results were clear indicative of combined accuracy of delivery and measuring systems together .

Figures 8 and 9 shows the effects of change in low dose threshold on the gamma passing rates for 6X-FFF and 10X-FFF energies respectively. A variation spread of more than 1% in gamma passing rate across the cutoff dose limits studied were considered as an impact of low-dose masking. The mean gamma passing rate for 6X-FFF was 97.97±0.99% and 96.94±1.11% at 10% and 25% cutoff dose respectively. Similarly, the mean gamma passing rate for 10X-FFF at 10% and 25% dose cutoff was 97.85±1.13% and 97.12±1.29% respectively. The effects of low-dose masking were more in low energy than observed in high energy. As the cutoff dose threshold is increased, the mean gamma passing rate decreases in both the energies which indicates that the fraction of failing points at high dose regions lying within the treating target lesions and its vicinity is clearly masked because of the inclusion of low dose points in the gamma evaluation.

Discussion

A major limitation of this study is the PSQA execution time at the machine is doubled to acquire the special set of measurement data which demands the same treatment plan to be delivered twice with a change of Octavius 4D phantom setup required in-between the two measurements. Another drawback of the study is the region of measurement using Octavius 1000 SRS can be extended only in the cranio-caudal direction using special set of measurements and hence for lesions falling outside the cylindrical volume of diameter 11cm from cannot be included in PSQA evaluation. It is better suggested to perform the PSQA in special setup mode when the treating lesions are far away from the isocenter only in the Superior-Inferior direction.

In conclusion, the performance of Octavius 1000 SRS at FFF beams for PSQA of VMAT based SRS were studied at 6X and 10X energies. Detailed analysis of the effect of dose grid size and cutoff dose on measurement results was performed. Based on the results from this initial study for evaluating the accuracy of Octavius 4D with SRS 1000 detector to perform the PSQA of VMAT based SRS of multiple brain metastases, we recommend to use an optimal gamma evaluation criteria of 1mm DTA and 3% DD with 25% cutoff dose threshold to be compared against the reference dose from TPS calculated at the dose grid size of 1.0mm. Overall results demonstrate the capability of the Octavius 4D measuring system coupled along with Octavius 1000 SRS detector array to perform PSQA in SRS of brain metastases using SIMT technique.

Author Contribution Statement

Study concept, data collection, analysis, interpretation of results and draft manuscript preparation done by the first author. All authors reviewed the results and approved the final version of the manuscript.

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Declaration

This article is not been previously submitted in whole or part of an approved student thesis and it was not approved by any scientific body.

Ethical Declaration

This article does not contain any studies with human participants or animals. Ethical committee approval is not required.

Availability of data

Data sharing is not applicable to this article

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