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The impacts of dose rate in sliding window intensity modulated radiation therapy quality assurance

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► ***Original article***

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ABSTRACT

Background: The present study aims to compare the impacts of dose rate in intensity-modulated radiation therapy (IMRT) plan delivery by using the gamma agreement between the calculated and measured doses by pretreatment quality assurance (QA). ***Materials and Methods:*** Ten nasopharynx cancer patients who underwent IMRT treatment were included in this study. The treatment plans were performed using Varian DHX eclipse treatment planning system (TPS) version 15.1. and the QA plans were generated for the dose rates of 300, 400, 500 and 600 MU/min. All measurements were performed by aS1000 Electronic Portal Imaging Device (Epid) integrated into Varian DHX linear accelerator and 2D array detector. The dose distribution was evaluated with gamma area histograms (GAHs) generated using different γ criteria (2%/2 mm and 3%/3 mm) for dose agreement and distance to agreement parameters. Statistical analyses were evaluated by using Mann-Whitney Test and a p-value of $p < 0.05$ was considered to be significant. ***Results:*** There was a significant decrease in the percentage gamma pass rate when the dose rate was increased from 300 MU/min to 600 MU/min ($p<0.05$). There was a significant difference between Epid and Epiqa for all dose rates ($p<0.05$). The total number of MU was correlated to the dose rate. When comparing MU from 300 MU/min to 600 MU/min dose rate, it was observed that the MU of IMRT plans increaed as the dose rate was increased. ***Conclusion:*** In this study, we have demonstrated that IMRT delivery using sliding window method is affected by the dose rate.

Keywords: *Dose rate, epid, epiqa, 2D array, IMRT.*

INTRODUCTION

The aim of radiotherapy treatment planning is to create the best dose conformation to the target volume while sparing critical organs and healthy tissues. IMRT is an attractive technique that provides highly precise dose around the target volume to treat head and neck cancer [1]. Several critical organs in the brain and head and neck regions are usually in close proximity to the tumor. The simultaneous integrated-boost IMRT (SIB IMRT) technique is favored over the sequential IMRT technique, electively increase dose per fraction to the target site SIB IMRT, also known as a dose painting technique, is used [2,3]. IMRT is delivered with a multileaf collimator (MLC) either in segmental mode (SMLC or step-and-shoot) or dynamic mode (DMLC or sliding window) [4]. In segmental MLC (SMLC) technique delivery, the treatment plan is performed by multiple fields and each field is subdivided into a set of subfields irradiated with uniform beam intensity levels. The subfields are created by the MLC and the accelerator is turned off while the leaves move to create the next subfield. This technique of IMRT delivery is known as step -and-shoot [5].

Dynamic MLC method the corresponding leaves sweep simultaneously and unidirection-ally, each with a varied velocity as a function of time. Unlike SMLC delivery, the accelerator beam is on while the leaves are

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moving [6]. The method is called as dynamic MLC (DMLC) or "sliding window. Patient-specific quality assurance (QA) in IMRT is important to verify the accuracy of dose calculation and delivery. IMRT QA is commonly accomplished by comparing a calculated dose distribution with an actually measured dose distribution [7,8]. Various methods, including the use of electronic portal imaging device (EPID), Epiqa software using GLAaS algorithm and 2D Array detectors have been employed during patient-specific QA in pretreatment verification to detect possible errors between the dose calculated by the TPS and the measured dose [9,10,11]. IMRT programs today almost universally use some method of quantitative comparison between TPS planar dose and measured dose, generating statistics of calculations such as percentage difference, distance to agreement (DTA), and gamma analysis [12].

There are several dosimetric studies on the impact of dose rate in IMRT plan delivery using the gamma agreement. Moreover, from 300 MU/min to 600 MU/min the verification of dose distribution for treatment plans using tighteningevaluation criteria of 2%/2 are rare.

The present study aims to compare the impacts of dose rate of sliding window IMRT dose delivery, as measured using Epid, Epiqa and 2D array using four dose rates: 300 MU/min, 400 MU/min, 500 MU/min and 600 MU/min. The dose distributions were analysed using gamma area histograms (GAHs) generated using different γ criteria (2% / 2mm and 3% / 3mm).

MATERIALS AND METHODS

Patient selection and positioning

Computed tomography (CT) images for a group of 10 randomly selected anonymous nasopharynx cancer who underwent IMRT treatment using Clinac iX Linear Accelerator (Varian Medical Systems, Palo Alto, CA, USA) in our clinic were enrolled for this dosimetric study. Ethics committee approval was not required since this was not a clinical study performed on patients, but a dosimetric simulation study. Informed consent was not required since the dosimetric simulation study was performed on anonymous patient data. All patients were immobilized in a supine position using a thermoplastic head cast, neck support. The patients were transferred to the image TPS (Eclipse, version 15.1; Varian Medical System Inc, Palo Alto, CA, USA) after a CT scan with a 3 mm cross-sectional range.

Contouring and treatment planning

All clinical target volumes (CTVs) were contoured, according to the International Commission on Radiation Units and Measurements (ICRU) Report 50. Four planning target volumes (PTV) and critical organs were generated: PTV70, PTV59.4, PTV66 and PTV54. The organs at risk (OAR) that were contoured included the spinal cord, brainstem, optic nerves, optic chiasm, parotid glands, temporomandibular joints, temporal lobes eyes, lens, cochlea, temporomandibular joints. The prescribed dose, which was defined as the mean dose in the PTV, was 69.96 Gy in 33 fractions at 212 cGy per day using the Simultane Integrated Boost (SIB) technique. For the SIB technique, we used seven fields (gantry angles: 0°, 52°, 104°, 156°, 204°, 256° and 308°) around each patient. IMRT treatment plans were generated using 6-MV photons designed to treat.

The MLC motion was optimized using the sliding window technique. The dosimetric accuracy of the SW-IMRT deliveries was evaluated for four dose rates: 300 MU/min, 400 MU/min, 500 MU/min and 600 MU/min. Anisotropic Analytical Algorism (AAA) dose distributions were calculated after optimization with reverse planning. Calculations were applied possible minimum doses to critical organs to obtain PTV coverage of at least 95% dose to 95% of PTV volume. Treatment was conducted using a linear accelerator with the Millennium 80 MLC system (Clinac iX; Varian Medical Systems Inc.).

Quality assurance for linear accelerator

Mechanical test measured by the idealized intersection of collimator, gantry and couch rotation axes were performed before dose measurement. And also, light field system,

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collimator, and gantry readout calibration were controlled. The measured values were found to be within values provided by the acceptance test of machine. Build-up Depth, Photon Beam Flatness and Photon Beam Symmetry were checked. The measured values were found to be within values provided by the acceptance test of Varian Clinac IX Linac machine.

Dose meaurements

Portal dosimetry

All EPID images were with an aSi-1000 imaging device mounted on a linear accelerator. The calibration of EPID is performed, where the radiation beam is linked to calibration units (CU). The calibration is generated with an open field of 10 × 10 cm^2 and 100 Monitor Unit (MU). The EPID is graded to the extent that 1 CU is matched to 1 MU delivered. Quality assurance plans were created for portal dosimetry. Portal dosimetry system is based on the methods described by Van Esch *et al.* [13]. Portal dosimetry is developed for non-transmission pre -treatment verification of IMRT. A single pencil beam dose calculation algorithm is applied to TPS to predict portal dose images for the planned fluence of the delivered beam. After that, the predicted portal dose image is compared to the measured EPID images [14]. Comparison of gamma analysis of treatment plan for EPID is shown in figure 1.

Epiqa

Epiqa is software which has been developed based on the work of Nicolini *et al.* [9]. Epiqa is used for pre-treatment verification for IMRT plans. This system converts EPID images to an absolute dose map at a depth of maximum dose in water, and compared to dose calculated with TPS. Comparison of gamma analysis of treatment plan for EPID is shown in figure 2.

The 729 2D array

The 729 ion chamber array (PTW, Freiburg, Germany) consists of 27x27 vented cubic ion chambers each with dimensions 0.5 × 0.5 × 0.5 cm^3, with a center to center spacing of 1 cm. The Verisoft software enables comparision of the radiation dose distributions in IMRT verification plan with calculated using TPS. The software subtracts matrices of measured and calculated points of an IMRT beam and visualizes the results. Software benefits the method of gamma evaluation and describes variation between a measured and calculated plan. In this study, the measured dose was compared with the dose calculated using TPS and imported into VeriSoft.

The gamma index evaluation is used to evaluate measured distributions in detector systems against the dose distribution predicted by TPS. The QA plans for absolute point dose measurements were performed for the planar dose distributions computed using TPS. The verification of dose distribution for all treatment plans was performed using 2%/2 mm and 3%/3 mm γ evaluation criteria. The criteria validation was accepted as a section with $\gamma \leq 1$ to be 95%. In this study, we also compared the total monitor units (MUs) and delivery treatment time from the obtained various dose rate. Comparison of gamma analysis of treatment plan for 2D Array is shown in figure 3.

Statistical analysis

All statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 25.1. (SPSS, Ilinoisi Chicago, USA). Mann- Whitney U test was used for comparisons. A p value of <0.05 was considered to be significant.

RESULTS

To give the intended dose to a moving target, the velocities of the DMLC leafs in the original IMRT plans were modified from 300MU/min to 600MU/min. The velocities of DMLC leaves are increased as the dose rate was increased. The percentage of values that passed the gamma criteria of 2% dose difference and 2 mm distance to agreement is given in table 1. It was observed from these results that the differences between the mean values of gamma pass rates determined were statistically examined and there was a significant difference between Epid and Epiqa for all dose rates. (p=0.002 for 300MU/min, p=0.001 for 400MU/min, p=0.000

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for 500MU/min and p=0.000 for 600MU/min) and Epiqa and 2 D array concerning mean values of gamma pass rates for 600MU/min (p=0.000). There was no significant difference between the Epid and 2D array concerning mean values of gamma pass rates that were determined as a result of the gamma analysis performed for all dose rates.

The percentage of values that passed the gamma criteria of 3% dose difference and 3 mm distance to the agreement is given in table 2. It was observed from these results that the differences between the mean values of gamma pass rates determined were statistically examined and there were significant differences between Epid and Epiqa for all dose rate. (p=0.001 for 300MU/min, p=0.001 for 400MU/min, p=0.001 for 500MU/min and p=0.000 for 600MU/min). That was statistically supported that there were significant differences between Epiqa and 2D array concerningmean values of gamma pass rates for all dose rates. (p=0.000 for 300MU/min, 400MU/min, 500MU/min and 600MU/min).There was a statistically significant difference between Epid and Epiqa for only 600MU/min dose rate (p=0.000). The mean MU counts required for 300MU/min, 400MU/min, 500MU/min and 600MU/min dose rate were 1425.60±152.22, 1509.10±1744, 1587.40±111.32 and 1649.90±120.31 (table 3).

The MU of IMRT plans increased as the dose rate was increased. When comparing the delivery time for 300MU/min, 400MU/min, 500MU/min and 600MU/min dose rate, it was observed that the delivery time of IMRT plans decreased as the dose rate was increased. The mean delivery time for 300MU/min, 400MU/min, 500MU/min and 600MU/min dose rate were 5.90±0.65, 4.61±0.38, 3.85±0.26 and 3.31±0.22, respectively. The total numbers of MU for all patients are shown in figure 4. As the dose rate increases from 300 to 600, the number of MU in the plans also increases. The evaluation of the mean irradiation times of the individual patient for different dose rates is shown in figure 5.

Table 1. The comparison of gamma analysis percentage pass using gamma criteria of 2 mm DTA and 2% dose difference.

Parameters	EPID	EPIQA	2D-ARRAY	p		
				EPID/EPIQA	EPID/2D-ARRAY	EPIQA/2D-ARRAY
300	98.32 ± 0.71 [96.90 99.11]	97.90 ± 0.79 [96.58 99.02]	95.90 ± 2.11 [93.50 98.90]	**0.002***	0.10	0.677
400	97.41 ± 0.76 [95.99 98.40]	94.91 ± 1.02 [93.50 97.06]	95.39 ± 2.08 [92.60 98.80]	**0.001***	0.034	0.596
500	96.44 ± 1.29 [94.10 97.99]	92.78 ± 1.23 [90.77 94.54]	95.07 ± 2.00 [92.50 98.60]	**0.000***	0.075	0.016
600	91.54 ± 3.24 [87.12 99.47]	66.81 ± 5.73 [56.51 73.48]	94.34 ± 2.12 [91.20 98.10]	**0.000***	0.080	**0.000***

Table 2. The comparison of gamma analysis percentage pass using gamma criteria of 3 mm DTA and 3% dose difference.

Parameters	EPID	EPIQA	2D-ARRAY	p		
				EPID/EPIQA	EPID/2D-ARRAY	EPIQA/2D-ARRAY
300	99.51 ± 0.54 [98.11 99.94]	98.42 ± 0.42 [97.96 99.12]	99.78 ± 0.27 [99.30 100.00]	**0.001***	0.111	**0.000***
400	99.29 ± 0.61 [97.99 99.91]	97.76 ± 0.48 [96.98 98.36]	99.73 ± 0.29 [99.20 100.00]	**0.001***	0.030	**0.000***
500	99.04 ± 0.76 [97.25 99.79]	97.34 ± 0.63 [99.01 98.11]	99.65 ± 0.37 [99.10 100.00]	**0.001***	0.023	**0.000***
600	97.90 ± 0.79 [96.58 99.02]	83.07 ± 4.08 [78.08 89.11]	99.46 ± 0.40 [99.00 100.00]	**0.000***	**0.000***	**0.000***

Table 3. Comparison of MUs and delivery time between different dose rates.

Parameters	300	400	500	600
MU	1425.60 ± 152.22 [1266 1738]	1509.10 ± 131.41 [1335 1744]	1587 ± 111.32 [1408 1720]	1649.90 ± 120.31 [1439 1804]
Delivery Time	5.90 ± 0.65 [5.06 6.96]	4.61 ± 0.38 [4.02 5.14]	3.85 ± 0.26 [3.42 4.18]	3.31 ± 0.22 [3.01 3.66]

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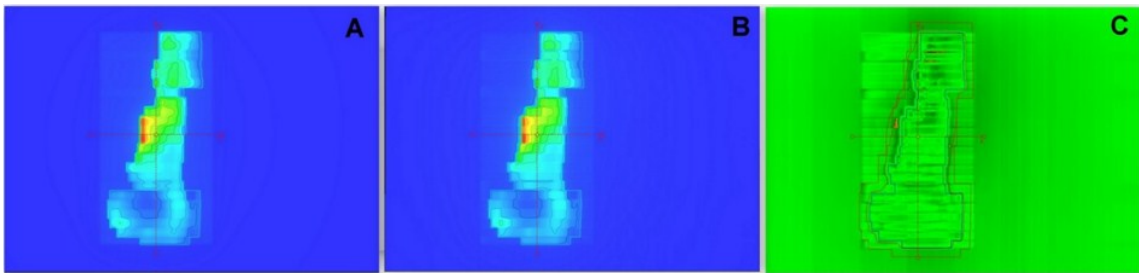

Figure 1. Comparison of gamma analysis of treatment plan for EPID **(A)** Predicted Dose, **(B)** Portal Dose and **(C)** Dose Difference.

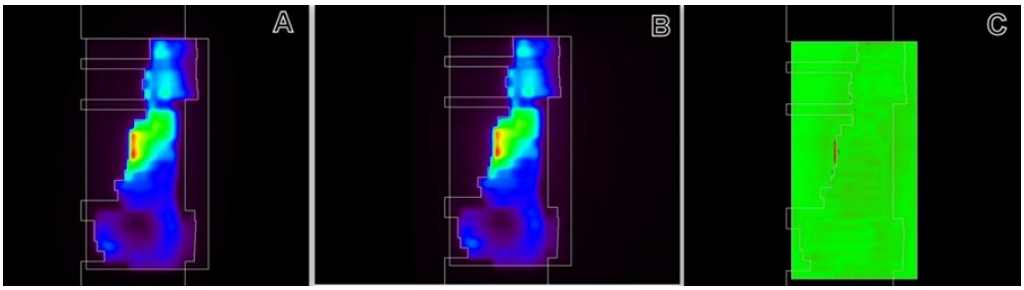

Figure 2. Comparison of gamma analysis of treatment plan for Epiqa **(A)** Predicted Dose, **(B)** Portal Dose and **(C)** Dose Difference.

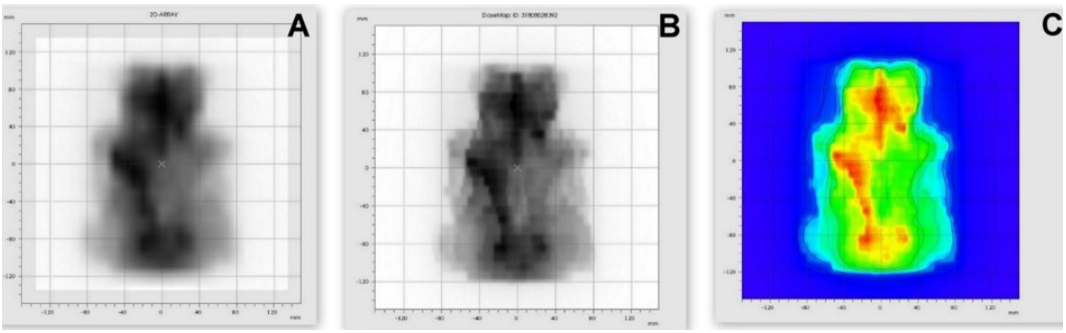

Figure 3. Comparison of gamma analysis of treatment plan for 2D Array **(A)** Predicted Dose, **(B)** Portal Dose and **(C)** Dose Difference.

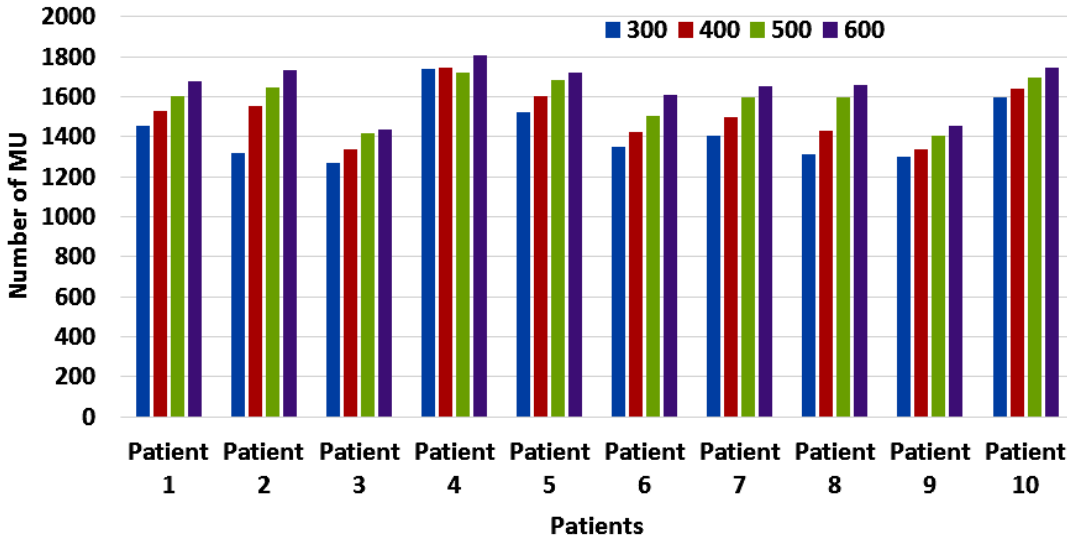

Figure 4. Average MU assessment of individual patient for different dose rate.

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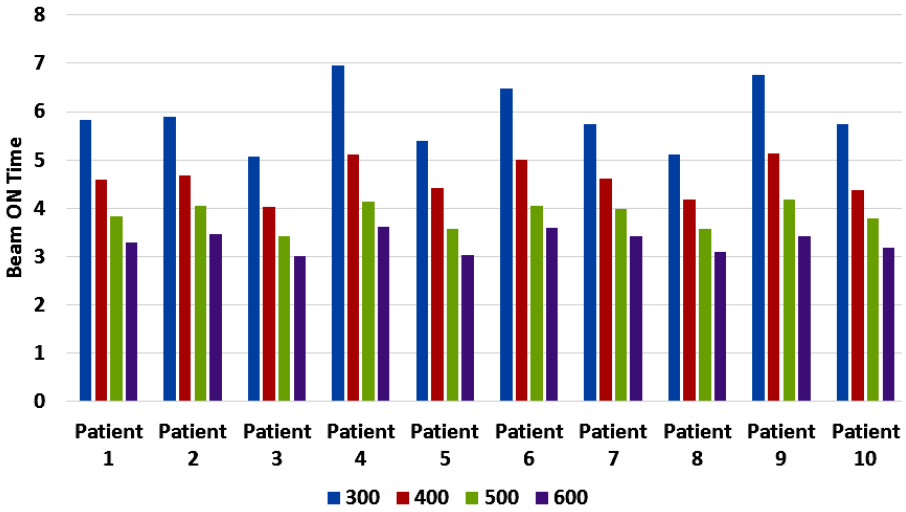

Figure 5. Average delivery time assessment of individual patient for different dose rate.

DISCUSSION

IMRT requires a complex treatment planning concerning QA and needs detailed two-dimensional dosimetric verification. The evaluation between the calculated and the measured doses plays a crucial role in the reliability of the results in the QA of IMRT. There are several methods to verify the dose distribution calculated. In the current study, the various QA systems including Epid, Epiqa, and 2D array were used to verify the delivery of IMRT treatment.In this study, the dose rate effects of using the 'γ evaluation method' which is composite analysis of 2 mm and 3 mm DTA and 2% and 3% dose difference (DD) were figured out regarding gamma passing rate. According to the results obtained from this study, it is revealed that Epid, Epiqa and 2Darray dosimetric systems are applicable for the measurements that are used to investigate the dosimetric accuracy of IMRT treatment plans and the quality accuracy data with dosimetric systems, it was statistically verified that there was a significant difference in gamma pass rate between the different dose rate. The effects of dose rate from 300MU/min to 500MU/min which is composite analysis of 2 mm DTA and 2% dose difference, gamma pass rate obtained from Epid that is used to treat 10 patients are higher than gamma pass obtained from Epiqa and 2D array method that is used to treatment of the same 10 patients.

For 600 MU/min, gamma pass obtained from the 2D array is higher than the gamma pass obtained from Epid and Epiqa. The effecst of dose rate from 300MU/min to 600MU/min which is composite analysis of 3 mm DTA and 3% dose difference, gamma pass rate obtained from 2D array that is used to treatment of 10 patients are higher than gamma pass obtained from Epid and Epiqa. As a consequence of the comparison of quality accuracy data with dosimetric systems, it was statistically confirmed that there was a significant difference in gamma pass rate between the Epid and Epiqa. According to the results obtained from this study that recalculating the plans at a lower dose rate (300 MU/min) decreased gamma values compared to the increased dose rate (600 MU/min).

Kaviarasu *et al.* examined the impacts of dose rate on accuracy of intensity modulated radiation therapy (IMRT) plan delivery by comparing the gamma agreement between the calculated and measured portal doses by pretreatment quality assurance (QA) using electronic portal imaging device dosimetry [15]. They showed that lower dose rate (300 MU/min) decreased gamma values compared to the increased dose rate (500 MU/min). They suggested that re-calculating the fields at lower dose rate (300 MU/min) was an effective strategy for decreasing gamma values, thereby

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improving the agreement between the measured portal dose and the calculated portal dose.

Njeh *et al.* researched the impacts of using two dose rates on plan quality assurance (QA) [16]. They found that the mean percentage gamma pass rate of 94.9% and 93.5% for 300 MU/min and 600 MU/min dose rate, respectively. There was a significant (p = 0.001) decrease in the percentage gamma pass rate when the dose rate was increased from 300 MU/min to 600 MU/min.

Yoganathan *et al.* researched the capabilities of DMLC to deliver the respiratory motion-synchronized dynamic IMRT (MS-IMRT) treatments under various dose rates [17]. The dosimetric accuracy of the MS-IMRT deliveries was evaluated for three dose rates: 100 MU/min, 400 MU/min, and 600 MU/min. They found that, the percentage of pixels passing the gamma test was in the range of 91.89 to 98.44 for 100 MU/min, 89.16 to 98.34 for 400 MU/min, and 77.73 to 96.48 for 600 MU/min. in the MS-IMRT delivery. They observed inferior dosimetric accuracy in MS-IMRT deliveries at the dose rate of 600 MU/min. In addition, the MS-IMRT deliveries at the dose rate of 600MU/min did not result in any additional benefit over corresponding gated deliveries in terms of dosimetric accuracy. Therefore they suggested that in order to have better dose delivery in MS-IMRT treatments, optimal dose rate should be used.

Vieillevigne *et al.* compared the gamma analyses using Epid and 2D array for 15 prostate patients, and they found that 97.2%±1.6 and 98.1%±1.7 for Epid and 2D array with 3%/3 mm criteria [18]. With the tightening criteria of 2%/2 mm the average pass rates were 99.5%±0.4 and 100±0.0 PD and 2D array, respectively. In the current study, we found that the 2%/2 mm and 3%/3 mm criteria, the passing rates of gamma analysis for the PD system were higher than those of Epiqa and 2D array. These results were in good agreement within our study.

Xu et al. investigated the dose rate response characteristics of the Digital Megavolt Imager (DMI) detector for flattening filter-free (FFF) beams [19]. They measured as a function of dose rate on a Varian TrueBeam machine. Images were acquired at dose rates ranging from 400 to 1400 MU/min for 6XFFF and 400 to 2400 MU/min for 10XFFF. They found that gamma agreement index was decreased from 100% to 97.8% when dose rate increased from 400 to 1400 MU/min for 6XFFF, and from 99.9% to 91.5% when dose rate increased from 400 to 2400 MU/min for 10XFFF.

These results suggest that lowering the dose rate can be effective for improving gamma agreement between the calculated and measured doses. This result can be associated with an increase in the time assigned for the delivery of each field segment. Lowering the dose rate reduces the number of segment points per minute, enabling smoother MLC delivery over time. Increasing the dose rate increases the number of segment points per min and increases the difficulty of the MLC delivery that increases the gamma index values. The higher dose rates may not be sufficiently compatible with the MLC motion and this may affect the accuracy of the dose delivery. This study analyzed the impacts of dose rate in the dynamic IMRT pretreatment verification QA fields using Epid, Epiqa and 2D array. In light of the data in this study, the findings suggest that 300 MU/min dose rate is optimum and lowering the dose rate provides to obtain an enhanced gamma agreement between the measured and calculated doses of complicated fields.

***Conflicts of interest*:** *Declared none.*

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