DOSIMETRIC COMPARISON BETWEEN GATED AND UNGATED SBRT PLANS USING VMAT WITH FFF BEAMS

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Abstract— Repeated stop-and-go beams and interplay effect during gated and ungated treatment can have an impact on dose accuracy. We compared the dosimetric impact between gated and ungated SBRT using 6 MV FFF with maximum dose rate (DRmax) of 1400 MU/min and 10MV FFF beams with DR_{max} of 2400 MU/min and analyzed factors that would correlate with the dosimetric deviation. Fifteen SBRT lung clinical cases using 6 MV FFF RapidArc with DR_{max} of 1400 MU/min were chosen. 10 MV FFF SBRT plans were then generated by re-optimizing the 6 MV FFF plans with 10 MV FFF beams and 2400 MU/min DR_{max}. CIRS Dynamic Thorax Phantom with a lung equivalent rod and PTW 3D pinpoint detector were used in the verification plans. The target moved sinusoidally with 2 cm amplitude and 4 s period. The verification plan for each case was calculated on average intensity projection computed tomography volume across all phases and across 40% - 60% phases of the breathing cycle for the gated and ungated plans respectively using AcurosXB (AXB) and Anisotropic Analytical Algorithm (AAA). Wilcoxon signed-rank tests were performed on the absolute dose deviation (ADD; measured versus calculated dose in the planning system) between gated and ungated cases. Correlation tests between ADD and the dose coefficient of variation (CV) among the voxels inside the internal target volume of the active volume of the chamber (ITV_{acv}), beam on time/MU and number of cycles of stop-and-go motion were conducted. A significant difference was found on ADD between gated and ungated 10 MV FFF beams with 2400 MU/min DR_{max} (Wilcoxon signed-rank test; p≤0.015), but not the 6 MV FFF beams with 1400 MU/min DR_{max}. It also revealed that there were significant correlation coefficients r of 0.5947 (AAA) and 0.5470 (AXB) between the ungated 10 MV FFF ADD and the dose CV among the voxels inside ITV_{acv}.

Keywords-gating, ungating, VMAT, FFF, SBRT

I. INTRODUCTION

Some previous studies [1, 2, 3, 4, 5] had investigated dosimetric deviation caused by interplay and stop-and-go effects for gated and ungated radiotherapy. It was noted that the dosimetric impact were dependent on the machine models and delivery methods. Kanai *et al.* [1] studied the mechanism regarding respiratory gated volumetric modulated arc therapy (VMAT) using 6MV beams with Clinac iX (Varian Medical Systems, Palo Alto, CA, USA). They found that the passing rate of gamma analysis for the gated and ungated plans were comparable. In their study, the rotation speed of gated VMAT was decreased by 30% in comparison with that of the ungated VMAT. The reduced dose rate led to decreased multi-leaf collimator (MLC) leaf speed, which then reduced the MLC positioning error and gap size error. However, Yoon et al. [2] found that the dosimetric error was greater in gated RapidArc delivery than continuous RapidArc delivery by using Novlis Tx linear accelerator (Varian Medical Systems, Palo Alto, CA, USA). This was due to the stop-and-go motion of the heavy gantry which would offset the gantry restart position due to momentum effects. This also reduced the accuracy of the MLC position and dose rate in RapidArc delivery. Wiersma et al. [3] also found that gating was inferior to ungating in dosimetric precision in step-and-shoot intensity-modulated radiation therapy (IMRT) plans, because dosimetric errors would be induced by interruption of the "overshoot phenomena" [4, 5], which was an overshoot of the initial segment dose of each beam on. The average timing deviation for intermediate segments was longer for gating when compared with non-gating.

The study presented in this paper used a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA) with two different beams, 6 MV Flattening Filter Free (FFF) with 1400 MU/min maximum dose rate (DR_{max}) and 10MV FFF with 2400 MU/min DR_{max} . This study aims at comparing the absolute dose deviation (ADD) between gated and ungated beams and investigating any unexplored factors that might correlate with the ADD. Another purpose of this study is to find out if the stop-and-go effect would have a prominent role affecting accuracy of gated radiotherapy by using number of cycles of beam on-and-off ($NC_{stop-and-go}$) to quantify the stop-and-go effect suggested by Yoon *et al.* [2]. Preliminary results have been reported in the form of conference publication. [6]

II. METHODOLOGY

Fifteen Stereotactic Body Radiotherapy (SBRT) lung clinical cases using RapidArc were chosen for retrospective analysis. The age of the patients in these fifteen cases ranged from 47 to 82. More than 70% of them were confirmed to have adenocarcinoma of lung. All patient information was anonymized in this study and ethic approval was granted. The fractionated scheme for the patients varied from 6 to 18 Gy/fraction with 3 to 10 treatment fractions. The radiotherapy plans consisted of either 2 or 3 half arcs (half gantry rotation) or 2 partial arcs with 200 degrees at 6 MV FFF energy and a DR_{max} of 1400 MU/min in the TrueBeam linear accelerator (version 2.7, Varian Medical Systems, Palo Alto, CA, USA) equipped with a 120 leaf Millennium MLC. 10 MV FFF SBRT plans were generated by re-optimizing the fifteen 6 MV FFF plans using 10 MV FFF beams with 2400 MU/min DR_{max} keeping the same objective functions in the plan optimization using Eclipse treatment planning system (version 15.5, Varian Medical System, Palo Alto, CA, USA).

The Dynamic Thorax Phantom (model 008A, CIRS, Norfolk, VA, USA) in Fig. 1 representing an average human thorax in shape, proportion and composition was used for the verification plans. A lung equivalent rod (0.21 g/cc) containing a spherical 20 mm target and a PinPoint 3D ion chamber (PTW, Freiberg, Germany) with sensitive volume of 0.016 cm3 was inserted for integrated dose measurement. The target in the lung equivalent rod was programmed to move in a sinusoidal fashion of ± 2 cm in the inferior/superior direction with a period of 4s while a surrogate (marker block) was moved ±1cm in the anterior/posterior direction with a period of 4s. Acquisition of the four-dimensional computed tomography (4DCT) of the phantom was performed using computed tomography (CT) scanner (SOMATOM Definition Flash, Siemens Healthineers, Erlangen, Germany).



Fig. 1 The Dynamic Thorax Phantom for point dose measurements

The verification plans for each treatment plan were then calculated on the average intensity projection CT volume across all the phases (for ungated cases) and across 40%-60% phases (for gated cases) of the sinusoidal cycle of the phantom using AcurosXB (AXB, version 15.5) and Anisotropic Analytical Algorithm (AAA, version 15.5), where the peak of inhalation is defined as 0% (Fig. 2). All calculations were based on dose to water.

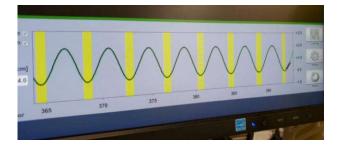


Fig. 2 Sinusoidal cycle of the phantom (green) and the planned phases 40-60% (yellow)

The ITV_{acv} is defined as a single volume encompassing all the active volumes of the chamber across all the phases (Fig. 3) and 40%-60% exhalation breathing phases of the sinusoidal cycle for ungated and gated cases respectively. The voxel-average doses of the ITV_{acv} were compared with the measured values, namely dose deviation. The Hounsfield units (HU) of the ITV_{acv} as well as the stems in both CTs were overridden to 0 HU.

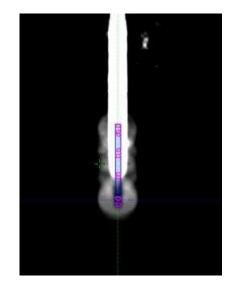


Fig. 3 The chamber is shown in the average CT set. The pink small volumes are the active volumes of the chamber in ten phases of the 4DCT. The blue volume is a single volume encompassing all the pink volumes, namely Internal Target Volume (ITV) of the active chamber volume (ITV_{avv}) for the ungated cases.

The inclusion criteria of the SBRT cases were that: 1) The superior-inferior dimension of the PTV was larger than 4.1 cm to fit the phantom motion. 2) The Internal Target Volume (ITV) encompassing the active volumes of the chamber in different phases did not fall into the penumbra region of the verification plan. (Fig. 4)

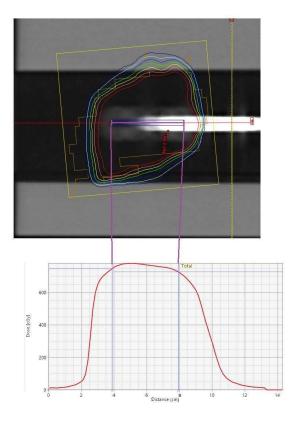


Fig. 4 Example of dose profile of the ungated $\mathrm{ITV}_{\mathrm{acv}}$ with the penumbra region avoided

Interplay effect is the potential deterioration in dose distribution that results from the simultaneous movement of internal structures and targets and dynamic MLCs motion. It leads to either underdosage or overdosage of the organs-at-risk or target. Therefore, this study only focuses on the magnitude of the dose deviation – absolute dose deviation (ADD). ADD is defined as | measured dose – calculated dose | / calculated dose. Friedman test and Wilcoxon signed-rank test were performed for the ADD of both the 6 MV FFF and 10 MV FFF beams to see if there was any significant dosimetric difference on ADD.

Dose Coefficient of Variation (CV) of ITV_{acv} , depicts the ratio of the dose standard deviation among the voxels inside the ITV_{acv} to the mean dose of the ITV_{acv} in the treatment planning system, was studied to see if there was correlation with ADD. Correlation between the ADD and beam on time/MU was also studied.

 $NC_{stop-and-go}$ is defined as the beam on time divided by the period of a sinusoidal cycle, which was 4 seconds in our study. $NC_{stop-and-go}$ of the gated cases with two energies were compared to study the contribution of stop-and-go effect to the ADD, so as to find out if the stop-and-go effect would have a significant role affecting the accuracy of the gated radiotherapy. Paired t-tests and correlation tests were

conducted to see how $NC_{stop-and-go}$ would correlate with the ADD.

Plan complexity in terms of number of MU / prescribed dose was also investigated to see if there was a statistically significant difference in plan complexity between the 10 MV FFF and 6 MV FFF treatment plans.

Normality tests for all the data were conducted before the analysis. All the tests were performed by SPSS Statistics (version 25, International Business Machines Corporation, Armonk NY, USA).

III. RESULTS

Absolute Dose Deviation (ADD)

All the data were put into eight groups. It consisted of two main groups, 6MV FFF and 10MV FFF. Each energy beams had two subgroups: gated and ungated, which were further broken down into two calculation algorithms. Fig. 5 illustrates the ADD of all the groups. It was noted that the mean ADD in the ungated cases were higher than that of the gated cases in both energies, 3.16% vs 2.50% for 6MV FFF and 4.43% vs 2.59% for 10 MV FFF. The ADD of the AXB cases were found always less than that of the AAA cases. All data groups passed the Shapiro-Wilk Normality Test, i.e. their p-values were larger than 0.05. However, Mauchly's test of sphericity for 10 MV FFF group was violated (p<0.05). As such, Friedman tests (non-parametric alternative to one-way ANOVA with repeated measures) and Wilcoxon signed-rank test were conducted for both 10 MV FFF and 6 MV FFF groups.

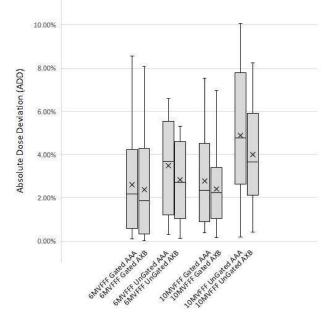


Fig. 5 ADD of the eight groups

Table 1 illustrates the results of Friedman test and Wilcoxon signed-rank test. For the Friedman tests, significant difference was observed in 10 MV FFF group with 2400 MU/min DR_{max} , but not in 6 MV FFF group with 1400 MU/min DR_{max} . For the Wilcoxon signed-rank tests, significant difference in ADD was shown between 10MV FFF gated and ungated cases but not in 6 MV FFF. Significant differences in ADD between AAA and AXB were also observed in ungated cases in both energies.

Table 1 Results of Friedman test and Wilcoxon signed-rank test
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		p-value of Wilcoxon signed-ranks test			
	Friedman Test	Gated vs UnGated		AAA vs AXB	
Energy	P-value	AAA	AXB	Gated	Ungated
10MV FFF	0.020*	0.011*	0.015*	0.088	0.023*
6MV FFF	0.184	0.256	0.551	0.363	0.036*

Dose Coefficient of Variation (CV) of ITVacv

Pearson correlations among ADD and dose CV of ITV_{acv} were performed. All the groups of ADD and dose CV passed the Shapiro-Wilk Normality Test, i.e. larger than 0.05. Table 2 shows the results of the correlation tests between ADD and dose CV of ITV_{acv} . It proved that the dose CV of ITV_{acv} significantly correlated with ADD in ungated 10 MV FFF cases with 2400 MU/min DR_{max} for both AAA and AXB, but not gated cases and in 6 MV FFF cases with 1400 MU/min DR_{max}. Fig. 6 shows the trend of the correlation. The Pearson correlation coefficient for AAA was 0.5947, and for AXB was 0.5470, of which the p values were less than 0.05.

Table 2 Correlation Test between ADD and dose CV of ITV_{acv}

			Pearson Correlation Coefficient r	p value
6XFFF -	Gated	AAA	0.2983	0.2801
		AXB	0.3398	0.2153
	UnGated	AAA	0.2102	0.4520
		AXB	0.0531	0.8510
10XFFF -	Gated	AAA	-0.1605	0.5678
		AXB	-0.0259	0.9269
	UnGated	AAA	0.5947	0.0194*
		AXB	0.5470	0.0348*

*significantly correlated, p<0.05

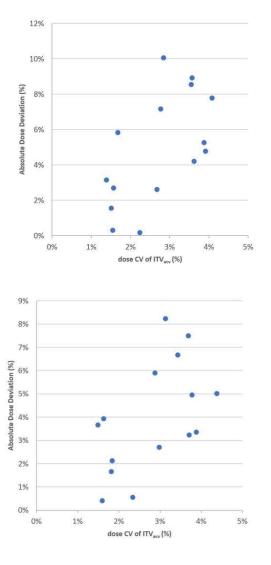


Fig. 6 ADD vs dose CV of ITV_{acv} in 10MV FFF ungated beams using AAA algorithm (upper) and AXB algorithm (lower)

Beam On Time per MU

Fig. 7 shows the beam on time per MU for both gated and ungated cases of both energies. Three groups, namely the 6 MV FFF gated and ungated and the 10 MV FFF ungated, failed the Shapiro-Wilk Normality Test, i.e. less than 0.05, thus a non-parametric equivalent for paired t-test, Wilcoxon signed-rank test, was used. Table 3 illustrates the results of the Wilcoxon signed-rank tests with one-tailed and two-tailed hypothesis. Significant differences were observed among 10 MV FFF and 6 MV FFF for ungated and gated cases with one-tailed hypothesis. Spearman's Rho correlation (non-parametric alternative to Pearson correlation) was also conducted between the ADD and beam on time per MU, however no significant correlation was found.

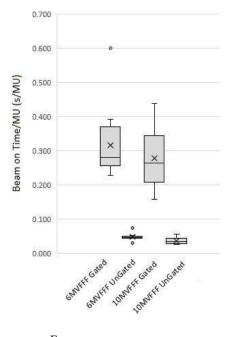


Fig. 7 Beam on time per MU

Table 3 Wilcoxon signed-rank test for Beam On Time/MU

			p-value of Wilcoxon signed-ranks test		
		mean of beam on Time / MU (s/MU)	One-tailed Hypothesis	Two-tailed Hypothesi	
6MV FFF	Gated	0.317	0.037*	0.071	
10MV FFF		0.278	0.037*	0.074	
6MV FFF	UnGated	0.047	0.0018	0.0028	
10MV FFF	UnGated	0.036	0.001*	0.003*	
Prio.	Same differ	rence, n<0.05			

*significant difference, p<0.05</p>

Number of cycles of stop-and-go motions (NC_{stop-and-go})

The ADD and $NC_{stop-and-go}$ of the gated cases were studied for the stop-and-go effect. All the groups passed the normality test, i.e. their p-value were larger than 0.05. Thus, paired t-test for ADD and $NC_{stop-and-go}$ comparison, and also Pearson correlation were conducted.

Fig. 8 summarizes the NC_{stop-and-go} for the gated cases of both energies. Table 4 shows the results of the ADD comparison and NC_{stop-and-go} comparison between 6 MV FFF and 10 MV FFF in gated cases. Significant difference in NC_{stop-and-go} was observed between the two energies with different DR_{max} but it showed no significant difference in ADD in AAA and AXB. Also, no significant correlation was found in Pearson correlation between ADD and NC_{stop-} and-go.

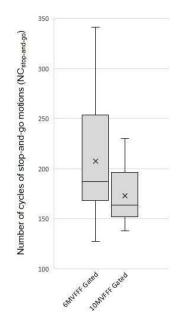


Fig. 8 NC_{stop-and-go} for the gated cases of 6MV FFF and 10MV FFF

Table 4 Results of paired t-test of ADD and NCstop-and-go

ADD Comparison			mean ADD	p-value of paired t-test	
6MV FFF		1370	2.39%		
10MV FFF	Gated	AXB	2.40%	0.97	
6MV FFF	0.4.1		2.61%	0.77	
10MV FFF	Gated	Gated AAA	2.77%	0.77	
NC _{stop-and-go} Compa	rison		mean NC _{stop-and-go}		
6MV FFF			207.7	0.03*	
10MV FFF	Gated		173.2	0.03*	

*significant difference, p<0.05

Plan complexity

The number of MU per prescribed dose (Gy) was used for evaluating the plan complexity. Both groups, 6 MV FFF and 10 MV FFF, passed the normality test. Paired t- test in plan complexity was conducted for the two energies. It was found that no statistically significant difference was observed in the test (p=0.699).

IV. DISCCUSION

This study evaluated the dosimetric impact of the stopand-go effect and interplay effect between gated and ungated SBRT using 6MV FFF and 10MV FFF energy beams with targets motion ± 2 cm inferior/superior motion with period of 4s. According to Court *et al.* [12, 13] and Ong *et al.* [14, 15], greater target motion would lead to larger dose discrepancies, so a relatively large motion of ± 2 cm was used for amplifying the motion effect as well as the interplay effect. A relatively short period of 4s was chosen, so as to maximize the stop-and-go effect.

From the Friedman tests shown in table 1, statistically significant difference was shown in 10 MV FFF with 2400 MU/min DR_{max} (p value = 0.020), but not in 6 MV FFF with 1400MU/min DR_{max} (p value = 0.184). The difference of the mean ADD of AAA and AXB between gated and ungated cases for 10 MV FFF was 1.84%, compared with that 0.66% of 6 MV FFF. The difference was due to the higher dose rate used in the cases of 10MV FFF. High dose rate is more susceptible to interplay effects, leading to larger dose deviation [14, 16, 20]. The results of the Wilcoxon signed-ranks tests that the 10 MV FFF ungated ADD was significantly larger than the 10 MV FFF gated ADD means the 10 MV FFF with the ungated beams are more susceptible to interplay effect, compared with the gated beams to both interplay and stop-and-go effect.

It was known that there were several proposed solutions to reduce the dosimetric impact due to interplay effect, for example, using lower dose rate [11, 13, 14, 20], avoiding highly modulated plans [12, 15, 20] or providing sufficient target margin [23]. In this study, less target dose inhomogeneity is also proved to be one of the solutions for reducing ADD in ungated 10 MV FFF with 2400 MU/min DR_{max} cases. It was found that the dose CV of ITV_{acv} statistically correlated with the ADD in ungated 10MV FFF cases. Again, this did not happen in the 10MV FFF gated cases, 6 MV FFF gated and ungated cases. The positive correlation between the ADD and dose CV of ITV_{acv} in ungated 10 MV FFF with 2400 MU/min DR_{max} implied that the ADD could be decreased by using a target dose with reduced dose inhomogeneity.

Due to the complicated technical nature of VMAT on gated radiation therapy, backlash of gantry rotation and MLC position may affect the precision of radiation dose delivery. Yoon et al. [5] reported that the more stop-and-go motions will result in more dosimetric errors. Since dose rate of 2400 MU/min was used for 10MV FFF and 1400 MU/min for 6 MV FFF, there was significant difference in NCstop-and-go between the two energies. NCstop-and-go of 10 MV FFF groups are much smaller than that of 6 MV FFF. Thereby significant difference in stop-and-go effect between 10 MV FFF and 6 MV FFF would be expected and could be reflected in the difference in ADD according to Yoon et al. [5]. However, the expected result did not appear in this study. It was observed from table 4 that there was significant difference in NCstop-and-go between 6 MV FFF and 10 MV FFF, but no significant difference in ADD between two energies implying that the stop-and-go effect was not significant in gated SBRT.

Jiang *et al.* [11] performed single point measurements on the IMRT plans with a 0.6cc Farmer chamber moving in a one-dimensional sinusoidal fashion. This study used similar setup to that of Jiang's. They had 30% variation for one IMRT field in one fraction and 18% for five IMRT fields over one fraction. When compared with Jiang *et al.* [11], the maximum ADD of this study was approximately 10% over two RapidArc fields. Some improvements were made in this study to reduce the dose deviation. (1) Instead of using a 0.6cc Farmer chamber, a 0.016cc PinPoint 3D ion chamber was used to avoid dose averaging. (2) The measured dose was compared with the planned dose of the ITV_{acv} instead of the corresponding static point dose. (3) The ITV_{acv} used for dose comparison did not fall into the penumbra region of the verification plan to avoid the dose blurring effect [11].

Despite considerable evidence demonstrating the dosimetric effects of interplay averaging out for multiple fractions [11, 12, 14, 21, 22], the effects for individual fractions is still of importance and a topic of interest due to the unknown biological effect applied to this averaging. Moreover, hypofractionation is becoming increasingly popular, in which radiotherapy is delivered in fewer fractions. This will inevitably result in the averaging effect being reduced. Likewise, it is well known that the dosimetric effects of interplay are of little significance to the gross tumor volume (GTV) coverage as long as a sufficient margin is given [23]. However, the effects for ITV dose deviation is still important due to the tighter margins afforded by the increased availability of image-guided radiotherapy (IGRT) and improved machine accuracy and precision.

The pre-set maximum dose rate in 10 MV FFF was higher than that of 6 MV FFF for both gated and ungated cases, thus one-tailed hypothesis of Wilcoxon signed-rank test was used for the beam-on time/MU comparison. For ungated SBRT, the beam-on time/MU of 10 MV FFF was, as expected, significantly shorter than that of 6 MV FFF. Whereas in gated SBRT, a certain amount of time was required for ramping up the dose rate. Combined with the short gating window, the dose rate for the gated cases might not reach its maximum (1400 MU/min for 6 MV FFF and 2400 MU/min for 10 MV FFF) before the gated period was over. However, our results showed that 10 MV FFF had significantly shorter beam on time/MU than 6 MV FFF for the 40%-60% gating window. This implied that the 10 MV FFF still had a higher average dose rate within the gating window than 6 MV FFF beams in gated cases.

Since the dosimetric accuracy affected by the interplay effect would be decreased by increasing the dose rate [14, 16, 20], it was therefore thought that there would also be correlation between the ADD and the beam on time/MU for ungated 10 MV FFF. However, no significant correlation was found. It was then proposed that instead of studying the

beam on time/MU alone, the effect by instantaneous dose rate can be further studied.

With the re-optimization of the 6 MV FFF treatment plans to be 10 MV FFF treatment plans, different MLC patterns were used in the 6 MV FFF and 10 MV FFF plans. Plan complexity of the two energies plans was of concern whether this would have partially accounted for the differences in ADD, beam on time/MU and NC_{stop-and-go}, as well as correlation tests, since multiple proof of dosimetric effects of interplay generally increased with the plan complexity [10, 15, 20]. The plan complexity in terms of number of MU/Gy among the groups of two energies was compared. No significant difference was found. Therefore, it is interpreted as plan complexity having no significant impact on the results in this study.

A significant difference of ADD was observed between AAA and AXB in ungated cases for 10MV FFF and 6 MV FFF (table 1). Although there was no significant difference for the gated groups, Fig. 1 shows the ADD of AXB cases were always lower than that of AAA cases in all groups. Our findings therefore agreed with the results reported by previous studies on the superiority of AXB over AAA in dose calculation in heterogeneous media [17, 18, 19].

Limitations and improvements

The influence of the interplay effect on dosimetric accuracy and the delivery accuracy of respiratory gating was evaluated only in the superior-inferior direction, where the tumor motion was the most significant. Secondly, the analysis encompassed only the target area. Thirdly, the analysis was conducted by using a phantom with regular simulated motion, which could not accurately represent true motion of a human patient motion. Fourthly, due to the reoptimization in the 10 MV FFF plans, different MLC patterns were used for the 6 MV FFF and 10 MV FFF ADD comparison though there was no significant difference in plan complexity. Moreover, as only single point measurements were made, there was no multi-dimensional measurement results. Shift and change in the shape of the dose distribution caused by interplay effect were not accounted in this study. Finally, the limited sample size led to only the ungated data showing a significant difference between AAA and AXB. Therefore, false negative error would be reduced, if the sample size could be increased.

V. CONCLUSIONS

This study found that the interplay effect had a statistically significant adverse dosimetric impact in 10MV FFF ungated SBRT due to the high DR_{max} 2400MU/min.

This adverse impact on ADD could be decreased by using a target dose with reduced dose inhomogeneity due to the significant correlation found between ADD and dose CV of ITV_{acv} . On the other hand, the stop-and-go effect showed no significant effect to the ADD. To conclude, the interplay effect outweighed the stop-and-go effect for the TrueBeam linear accelerator. Lastly, SBRT using 10 MV FFF with DR_{max} 2400 MU/min had significantly shorter beam-on time/MU than that when using 6 MV FFF with DR_{max} 1400 MU/min in both gated and ungated cases.

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