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ORIGINAL ARTICLE

Effects of varying statistical uncertainty using a Monte Carlo based treatment planning system for VMAT

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Summary

Purpose: *To determine the severity of the effects on VMAT dose calculations caused by varying statistical uncertainties (SU) per control point in a Monte Carlo based treatment planning system (TPS) and to assess the impact of the uncertainty during dose volume histogram (DVH) evaluation.*

Methods: *For this study, 13 archived patient plans were selected for recalculation. Treatment sites included prostate, lung, and head and neck. These plans were each recalculated five times with varying uncertainty levels using Elekta's Monaco Version 5.11.00 Monte Carlo Gold Standard XVMC dose calculation algorithm. The statistical uncertainty per control point ranged from 2 to 10% at intervals of 2%, while the grid spacing was set at 3 mm for all calculations. Indices defined by the RTOG describing conformity, coverage, and homogeneity were recorded for each recalculation.*

Results: *For all indices tested, one-way ANOVA tests failed to reject the null hypothesis that there is no significant difference between SU levels ($p>0.05$). Using the Bland-Altman analysis method, it was determined that we can expect the indices (with the exception of CI_{RTOG}) to be within 1% of the lowest uncertainty calculation when calculating at 4% SU per control point. Beyond that, we can expect the indices to be within 3% of the lowest uncertainty calculation.*

Conclusion: *Increasing the SU per control point exponentially decreased the amount of time required for dose calculations, while creating minimal observable differences in DVHs and isodose lines.*

Key words: *Monte Carlo, dose calculation, statistical uncertainty, treatment planning*

Introduction

Since its introduction in 1982, intensity modulated radiation therapy (IMRT) has continued to develop and has become one of the most used modalities for radiation therapy [1]. One such development of IMRT is volumetric modulated arc therapy (VMAT). This treatment method allows for variation in gantry rotation speed, dose rate, and field shape through the use of MLCs [2]. Varying these parameters allows for modulation of beam intensity according to the location of the target and surrounding organs at risk (OARs) to provide highly conformal dose delivery.

There are many treatment planning systems (TPS) which can be used to develop VMAT plans, each utilizing its own dose calculation algorithm. Of the various dose calculation algorithms, Monte Carlo dose calculation algorithms are considered to be the benchmark for analytic calculation [3]. However, Monte Carlo dose calculation algorithms have historically been considered as computationally demanding and time consuming to the point of being impractical for use. One method for decreasing the computation time is to increase the statistical uncertainty (SU) of the calculations, but

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this will inherently lower the accuracy of the final dose calculation. Other studies have previously evaluated the overall effects of SU on dose calculations [4-7], however, the purpose of this study is to specifically evaluate the clinical impact on VMAT plans of altering the SU using Elekta's Monaco Version 5.11.00 Monte Carlo Gold Standard XVMC dose calculation algorithm. A previous study conducted by Palanisamy et al [8] also explored the dosimetric impact of varying SU when calculating the dose of VMAT plans, however, their analysis was performed on the SU per plan, whereas ours was on SU per control point which is a significant difference as explained later in the discussion section of this article.

Methods

For this study, 13 non-site-specific VMAT patient plans were selected from our clinical archives. Each plan had been previously optimized and approved prior to performing the dose recalculations using Elekta's Monaco Version 5.11.00 Monte Carlo Gold Standard XVMC dose calculation algorithm. For the calculations, a Hewlett-Packard Z820 workstation with 128GB RAM, Intel Xeon CPU E5-2695 @ 2.40 GHz (2-Processor), and the 64-bit operating system was used. For each patient, five dose calculations were performed with varying statistical uncertainty per control point. The degree of uncertainty per control point ranged from 2.00% to 10.00% at intervals of 2.00%, and the grid spacing was set at 3 mm for all calculations. The lower and upper bounds used for SU per control point in this study were the minimum and maximum allowable in Monaco. For a standard dual-arc VMAT plan, an entire-plan SU of less than 2% can be expected even when calculating at the maximum SU of 10% per control point.

The dose volume histogram (DVH) statistics tool within Monaco was used to retrieve relevant data regarding the planning target volume (PTV) from the recalculated plans. The parameters recorded for each plan along with their definitions can be found in Table 1. Using the parameters from Table 1, the coverage (Q), conformity index (CI_{RTOG}), and homogeneity index (HI) were calculated as a measure of plan quality. These plan quality metrics are all defined by the Radiation Therapy Oncology Group and are calculated using the equations in Table 2 [9].

Coverage, Q, describes the minimum isodose line that fully captures the target and is given as a percentage. Full coverage (Q=100%) is desired to ensure that the intended prescription is being achieved. The CI_{RTOG} is a conformity index defined as the ratio of the total volume receiving the prescription dose (PI) to the volume of the target (TV). For an ideal plan, the value would be equal to unity. If the value is less than unity, then the target is not being fully covered by the prescribed dose. If the value is greater than unity, then normal tissue outside of the target is being irradiated. The homogeneity index, HI, provides information about the intensity of a hotspot and the homogeneity of dose within the target. It is a ratio of the maximum dose delivered to the target (MD) to the prescription dose.

Table 1. Metrics collected from DVH statistics

Parameter	*Definition*
TV	Target volume (cm^3)
TVPI	Volume of target receiving prescription dose (cm^3)
MIN	Minimum dose to target, defined as dose covering 98% of target (cGy)
MAX	Maximum dose to target, defined as dose covering 2% of target (cGy)
MEAN	Mean dose to target (cGy)
PI	Total volume in patient receiving prescription dose (cm^3)
$PI_{50\%}$	Total volume in patient receiving 50% of the prescription dose (cm^3)

Results

There was little visual difference observed among the dose distributions between each level of statistical uncertainty. Figure 1 shows the PI (74 Gy) and the $PI_{50\%}$ (37 Gy) isodose lines for each SU level for a prostate plan. Upon visualization, only slight differences in the noise of the lines

Table 2. Plan quality metrics used to compare plans between SU levels

Metric	*Definition*	*Equation*
Q	Coverage, Q, describes the minimum isodose line that fully captures the target and is given as a percentage.	$Q=\left(\frac{MIN}{PD}\right)\times 100$
HI	Homogeneity index, HI, is a ratio of the maximum dose delivered to the target to the prescription dose	$HI=\left(\frac{MAX}{PD}\right)$
CI_{RTOG}	Conformity index, CI_{RTOG}, is a ratio of the total volume receiving the prescription dose (PI) to the volume of the target (TV).	$CIR_{TOG}=\frac{PI}{TV}$

can be observed as the SU level increases. Figure 2 shows the overlapping DVHs for the same prostate plan. When comparing the OARs, the DVHs are nearly indistinguishable. For the PTVs and CTVs, very slight differences can be visually observed between each SU level. Figure 3 shows the Q, HI, and CI_{RTOG} values at each SU level for every patient included in the study. Apart from a few outliers, there is little noticeable change between SU levels and no apparent correlations.

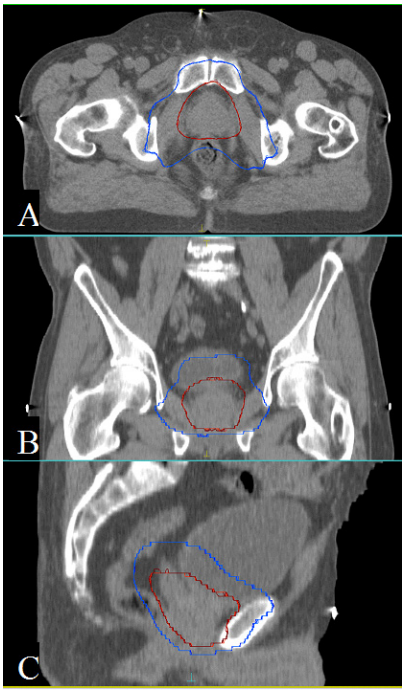

Figure 1. Transverse **(A)**, coronal **(B)**, and sagittal **(C)** views of the 74 Gy (RX dose) and 36 Gy isodose lines from each level of statistical uncertainty per control point for a recalculated prostate plan. There is little distinguishable difference between the 5 isodose lines (1 for each SU value) for the 100 and 50% isodose levels.

To determine if there were any significant differences that were too small to be recognized through a visual analysis, one-way ANOVA tests were performed for each of the plan quality metrics described in the methods section. The null hypothesis of the one-way ANOVA test was that there is no significant difference in means between the tested uncertainty levels [10]. The results for all metrics indicated that we failed to reject the null hypothesis ($p>0.05$) that there is no significant difference among the SU levels. While the results of the one-way ANOVA tests fail to prove a significant difference in means between each uncertainty level, they also do not guarantee agreement between the groups as we do not accept the null hypothesis, only fail to reject it.

To explore the agreement between the groups, a Bland-Altman Analysis was performed [11,12]. This analysis plots the percent differences between corresponding points from a comparison group and a reference group along the y-axis, and the mean of the two corresponding points along the x-axis. The dose calculation at 2.00% statistical uncertainty was used as the reference, as this is the most precise level we can compute within Monaco. The mean percent difference between the two groups being compared is plotted along the y-axis along with its 95% confidence interval. In addition to the

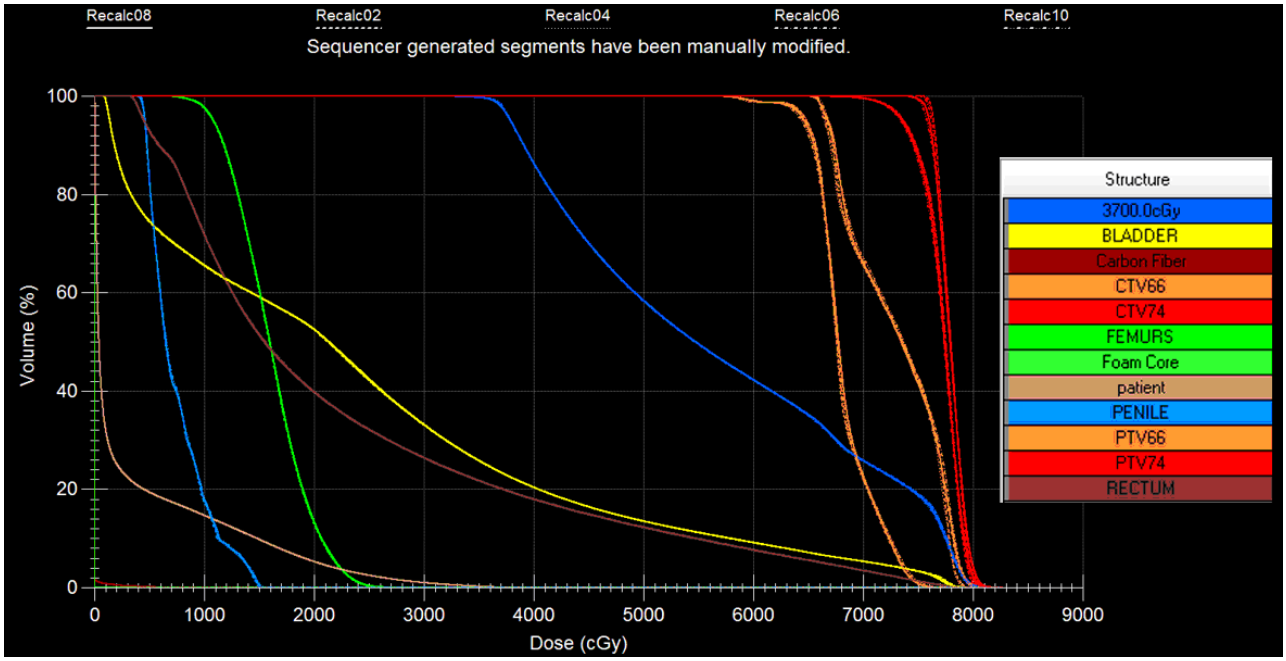

Figure 2. Overlapping DVHs from each level of statistical uncertainty per control point for a recalculated prostate plan.

mean percent difference, the upper and lower limits of agreement are plotted along the y-axis with their respective 95% confidence intervals. An example of the Bland Altman analysis between HI at the 4.00% and 2.00% statistical uncertainty levels can be seen in Figure 4. Table 3 shows the individual calculations performed to plot this figure. This same analysis was performed for each plan quality metric, and the upper and lower limits of agreement at each SU level can be seen in Table 4. Except for CI_{RTOG}, we can expect agreement within 3% from all SU levels to the set reference level of 2.00%.

Additionally, the computation time was recorded for each recalculation. A plot of the average calculation time at each SU level can be seen in Figure 5. The time required for calculation decreases significantly as the SU level increases. This is expected as the number of histories used for dose calculation decreases as the inverse of the squared statistical uncertainty.

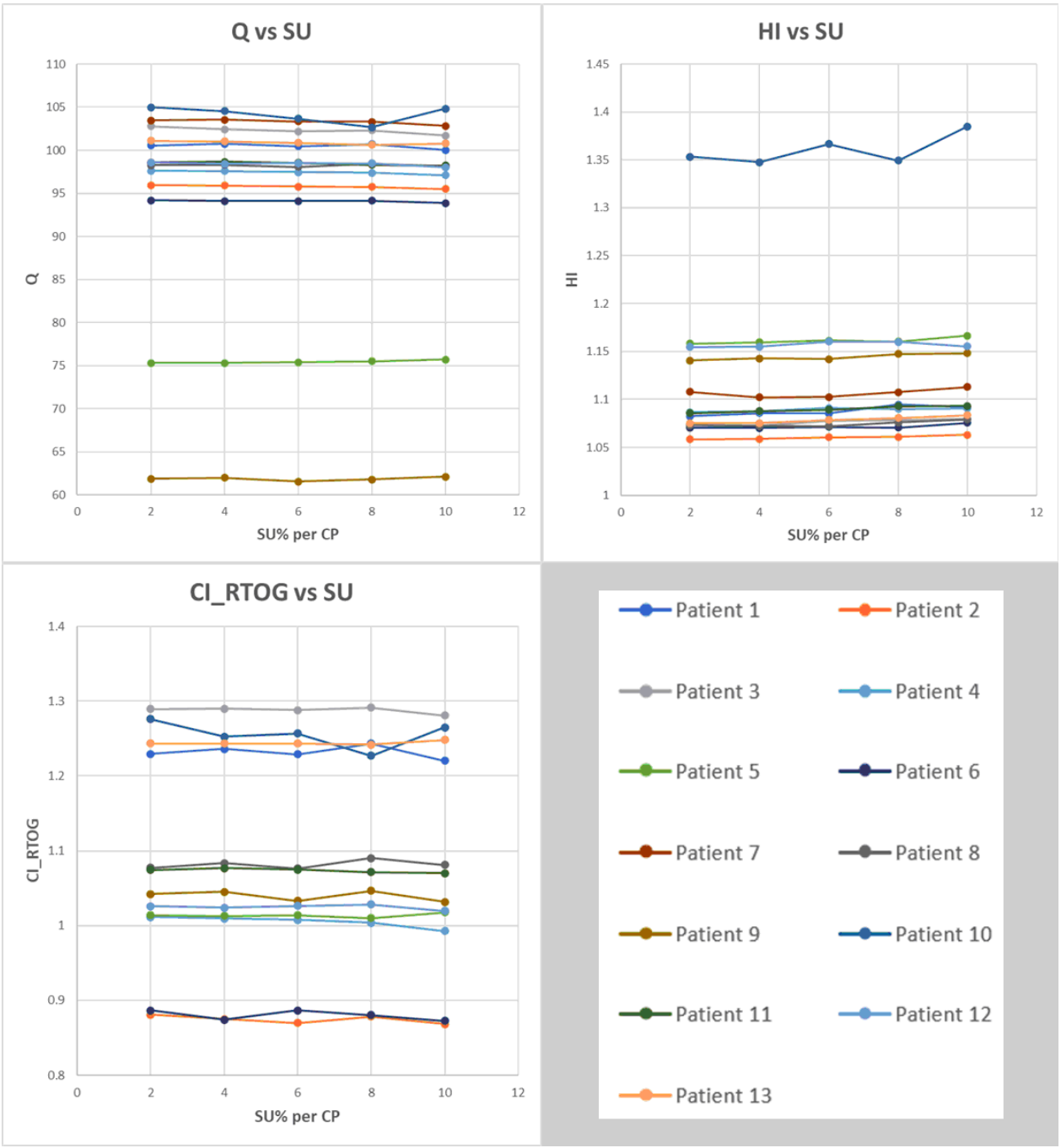

Figure 3. Scatter plots demonstrating the coverage (Q), homogeneity index (HI), and conformity index (CI_RTOG) for each patient plan calculated at every SU level tested.

Discussion

A previous work by Palanisamy et al also aimed to study the dosimetric impact of statistical uncertainty on Monte Carlo dose calculations for VMAT using Monaco. However, their study varied the SU per plan, unlike this study which varied the SU per control point. When performing dose calculations, Monaco has a limit for the maximum uncertainty per control point of 12%. If the user sets the SU for the overall plan too high, the uncertainty per CP will exceed this 12% and Monaco will ignore the user input and default to the set limit. Thus, the particle histories will remain the exact same even when the user continues to increase the SU per plan, and the calculations will yield identical dosimetric results. When reviewing the results from Palanisamy et al study, the repetition of values from their higher uncertainty calculations (SU per

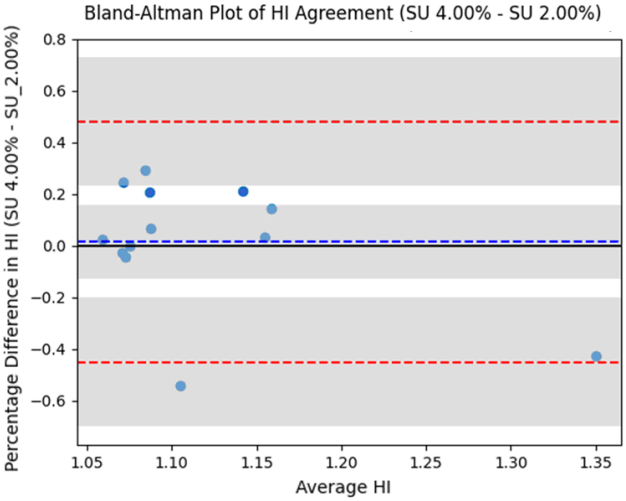

Figure 4. Bland Altman plot of agreement between the HI for the 4.00% and 2.00% SU levels.

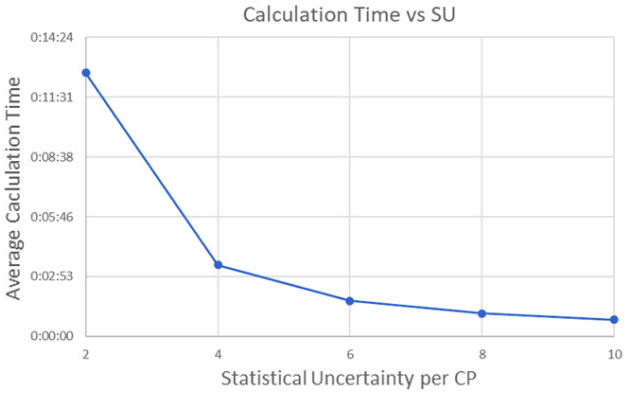

Figure 5. Average plan calculation time (H:MM:SS) for each level of SU.

Table 3. Test statistics used to create the Bland Altman plot for HI between 4.00% SU and 2.00% SU

Parameter	*Value*	*Standard Error Formula*	*Standard Error (se)*	*t value for 12 degrees of freedom*	*Confidence (se*t)*	*Confidence Interval Infimum*	*Confidence Interval Supremum*
number (n)	13						
degrees of freedom (n-1)	12						
mean difference (d)	0.014	$\sqrt{S^2/n}$	0.066	2.18	0.130	-0.130	0.158
standard deviation (s)	0.238						
Upper limit (d-1.96s)	-0.452	$\sqrt{3S^2/n}$	0.114	2.18	0.23328	-0.701	-0.203
Lower limit (d+1.96s)	0.480	$\sqrt{3S^2/n}$	0.114	2.18	0.23328	0.231	0.729

Table 4. Upper and lower bounds of agreement in percent difference from 2.00% SU for each metric at each SU level. Color scale is applied to each row, where values that are green are closest to 0, and values that are red are furthest from 0

	SU4		*SU6*		*SU8*		*SU10*	
	Lower	*Upper*	*Lower*	*Upper*	*Lower*	*Upper*	*Lower*	*Upper*
Q	-0.59	0.49	-1.29	0.75	-2.11	1.53	-1.53	0.88
CI_RTOG	-2.88	2.15	-2.34	1.45	-3.86	3.44	-3.16	2.11
HI	-0.70	0.73	-0.75	1.28	-0.73	1.46	-0.81	2.23
MIN	-0.59	0.49	-1.29	0.75	-2.11	1.53	-1.53	0.88
MAX	-0.70	0.73	-0.75	1.28	-0.73	1.46	-0.81	2.23

plan >3%) indicates that Monaco reverted to the default set value, which may have affected their findings. For this reason, we felt it was important to perform our own study which varied instead the SU per CP thus bypassing the Monaco inherent limitation and truly explore the effect of SU on plan quality.

The conclusions of our study were based solely upon plan quality metrics associated with the target and does not explore the consequences of varying SU levels on OARs. It should be noted that the SU for each voxel outside the high dose volume in the PTV has higher uncertainty than that achieved in the PTV, as fewer particles are simulated in these regions. Although the dose within each voxel is reported to be very close to that of the 2% SU calculation as seen in Figure 1 and Figure 2, the uncertainty of the dose is higher for the low dose voxels. This is outside of the scope of this study and has not been investigated. It is recommended that the SU of the irradiated volume is reviewed during planning prior to plan approval.

Conclusion

Increasing the SU per control point significantly decreased the amount of time required for dose calculations while creating minimal observable differences in DVHs and isodose lines. Values of Q, HI, MAX, and MIN are within 1% of agreement to the lowest possible SU level (2.00% per control point) when calculating at 4.00% SU per control point. Even when the uncertainty reaches the highest level of 10%, all plan quality metrics are expected to be within 4% agreement of the lowest possible SU level (2.00% per control point).

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Conflict of interests

The authors declare no conflict of interests.

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