Technical Note

Dosimetric Evaluation of Radiation Treatment Planning for Simultaneous Integrated Boost Technique Using Monte Carlo Simulation

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Abstract

Monte Carlo (MC) techniques have been recognized as the gold standard for the simulation of radiation transport in radiotherapy. The aim of the study is to perform dosimetric evaluation of Simultaneous Integrated Boost (SIB) radiation treatment planning using MC simulation approach. The geometrical source modeling and simulation of 6 MV Flattening Filter Free (FFF)beam from TrueBeam linear accelerator have been carried out to simulate Volumetric Modulated Arc Therapy (VMAT) plans using MC simulation software PRIMO. All the SIB plans have been generated using VMAT techniques for patients with locally advanced postoperative head-and-neck squamous cell carcinoma in Eclipse Treatment Planning System (TPS) retrospectively. TPS plans have been compared against their respective MC-simulated plans in PRIMO. The quality assessments of plans have been performed using several dose volume parameters, plan quality indices, and methods of gamma analysis. D_{mean}, $D_{50\%}$, and $D_{2\%}$ received by planning target volume (PTV), PTV_{60}, and PTV_{52} have been found significantly lower in TPS-generated plans compared to MC-simulated plans. $D_{100\%}$, $D_{98\%}$, and $D_{95\%}$ received by PTV_{60} exhibit good agreement. However, PTV_{52} shows a significant deviation between TPS and MC plans. The mean organ-at-risk doses have been found significantly lower in TPS plans compared to MC plans. TPS and MC plans have been found in close agreement within gamma acceptance criteria of 3% Dose Difference (DD) and 3 mm Distance to Agreement (DTA). Dose distributions computed using MC simulation techniques are reliable, accurate, and consistent with analytical anisotropic algorithm. Plan quality indices have been found slightly compromised in MC-simulated plans compared with TPS-generated plans appeared to be a true representation of real dose distribution obtained from MC simulation technique. Validation using MC simulation approach provides an independent secondary check for ensuring accuracy of TPS-generated plan.

Keywords: Dosimetric evaluation, Monte Carlo, PRIMO simulation, radiation planning

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Introduction

The main advantage of simultaneous integrated boost (SIB) is that it delivers differential radiation doses to different targets of interest and reduces overall treatment time in a single sitting. The SIB technique may increase local tumor control and patient survival without adding an expected risk of normal tissue toxicity.[1] The complex differential dose distributions are achieved through intensity modulation, which generates nonuniform fluence maps obtained using the optimization process. Advanced Intensity Modulated Radiation Therapy (IMRT) or Volumetric Modulated Radiation Therapy (VMAT) demands accurate modeling of the radiotherapy beam to account for dose through a miniaturized field created during optimization. Besides, effects due to loss of lateral electronic equilibrium appeared in the small field, air cavity, tissue–air interface, and inhomogeneity required to be considered in an algorithm used for accurate beam modeling. These factors are still a concern for accurate dose calculation algorithms used in many commercially available Radiation Therapy (RT) Treatment Planning Systems (TPSs).[2,3] Most of the present commercial TPSs use empirical correction and

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model-based algorithms. In addition, some of the TPSs still utilize a water-based dose calculation instead of a medium based. Most of the Eclipse TPS (Varian Medical Systems, Palo Alto, CA, USA) users are still using the analytical anisotropic algorithm (AAA) for IMRT final dose calculation. Over a period of time, significant developments have been achieved in many aspects of AAA such as tissue heterogeneity modeling and accounting for dose from scattered radiation. However, dose calculation uncertainties with AAA cannot be eliminated completely, especially in the buildup region, low-density region, air–tissue interface, and heterogeneous media, and to account for dose due to lateral electron transport. There are available studies that have shown the limitations of AAA against Monte Carlo (MC).[4,5]

MC has played a very vital role in several aspects of radiotherapy. MC techniques were found to be most accurate in simulating phenomena of radiation transport and predicting accurate dose calculation for radiotherapy.[5,6] In addition, the Association of Physicists in Medicine Report-106 recommends MC simulation approach for validation of photon and electron beam commissioning that can serve as reference data for dosimetry. Over the last two decades, several MC packages and codes were developed in areas of RT medical physics involving PENELOPE, FLUKA, GEANT-4, EGSnrc, and PRIMO.[7-10] The PRIMO provides a user-friendly and most elegant way of simulation of geometrical source modeling for linear accelerators (linacs). PRIMO is layered software that combines PENGEOM, PENEASY, PENVOX, and PENELOPE to simulate a transport of radiation through linac geometry and calculation of dose distributions.[11] The recent version of PRIMO also supports the simulation of radiation treatment planning and facilitates the estimation of absorbed dose distribution in virtual phantom as well as on real patients' Computed Tomography (CT).[11]

Dosimetric investigation of contemporary AAA dose calculation algorithms is necessary to ensure the overall accuracy of delivered absorbed dose within ≤5% for the SIB-IMRT treatment plan.[12] This study is an extension of our previous study,[13] where the geometrical source modeling and commissioning validation of 6 MV Flattening Filter Free (FFF) beam have been performed using MC. This study has been carried out using the same MC source model. The objective of this study is to evaluate the accuracy and dosimetric performance of AAA against MC in patients undergoing SIB radiotherapy for treatment of head-and-neck cancer (Ca buccal mucosa and Ca tongue).

Materials and Methods

MC simulation software PRIMO version 0.3.64.1814 was used to simulate RT treatment plans for retrospective patients who underwent RT. This study has been conducted in two separate phases. Initially, retrospective RT treatment plans have been made for selected patients in Eclipse version 15.5 TPS. In the second half of the study, all those treatment plans have been imported individually into the PRIMO software to simulate using the MC technique. Every individual patient has been simulated using MC simulation technique. Eventually, RT dose files of each individual patient plan have been imported from TPS into PRIMO to compare against the simulated dose distribution tallied using MC technique. Both qualitative and quantitative investigations of the TPS-generated and MC-simulated plans have been accomplished by several plan quality parameters. Besides this, comparisons of TPS and MC-simulated plans have been carried out by the method of gamma analysis using the plan evaluation module available in PRIMO. All the treatment plans made using TPS have been compared against their respective MC-simulated plans in PRIMO. Chi-square analysis test has been used to perform plan comparison. The results obtained using MC simulation techniques are considered a reference baseline for plan comparison.

Patient selection and treatment planning

The radiotherapy treatment plan of 25 postoperative patients of locally advanced (Ca buccal mucosa and Ca tongue) head-and-neck squamous cell carcinoma (HNSCC) treated during the years 2019–2022 has been selected for retrospective dosimetric evaluation. All the selected patients were diagnosed with TNM stage T2 or T3, N0SCC underwent radiation therapy for 60 Gy dose at primary site and 52 Gy dose for prophylactic nodal irradiation in 30 fractions treated using SIB VMAT. All the VMAT treatment plans were generated using 6 MV FFF beam to deliver on TrueBeam linac. The plans have been made using dual arc (CW and CCW) with a full gantry rotation of 360˚.The photon optimizer (PO) has been used to optimize arc-segmented fluence and the final dose calculation was carried out using AAA algorithm version 15.5 with a grid size of 0.25 mm. All those clinical plans were made to satisfy the minimum dose to target volume with an acceptance criterion of $D_{95\%} \geq$ prescription dose and organ-at-risk (OAR) doses under clinical acceptance criteria (As per QUANTEC).

PRIMO setup and Monte Carlo simulation

PRIMO simulates geometric source modeling of linac and estimates absorbed dose distribution through three consecutive segments (S1, S2, and S3), as shown in Figure 1. Primarily, source modeling and its commissioning validation of 6 MV FFF beam for TrueBeam linac were performed during the first phase of the study cited above.[13] Initial beam parameters for modeling TrueBeam 6 MV FFF include an initial beam energy of 5.85 MeV with an energy full width half maximum (FWHM) of 0.05 MeV, FWHM of focal spot size 0.8 mm, and beam divergence of 1 degree. Table 1 lists all the major and minor simulation parameters used during MC simulation of RT treatment plans. The TrueBeam 6 MV FFF beam has been modeled using the modeled phase-space file created at the downstream end of the upper half of the linac while simulating segment S1 in PRIMO during the first phase of the study. Hereafter, all the plans have been imported into PRIMO from Eclipse TPS to run MC simulation. These treatment plans have been simulated in PRIMO with the combination

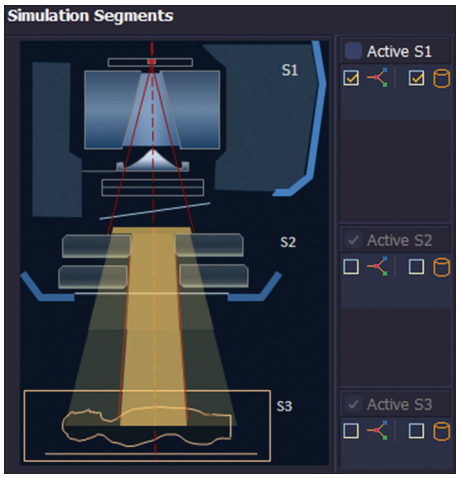

Figure 1: Pictorial representation of different segments of PRIMO simulation software

Table 1: List of simulation parameters

Parameters	Description
Processing unit and processor	Dell precision T7810 Tower Desktop, 32 GB Ram, 2.4 GHz processor
Program/code/version	PRIMO/MC- PENELOPE/0.3.64.1814
Transport parameters	Initial beam energy: 5.85 MeV, FWHM of energy: 0.05 MeV
	FWHM of focal size: 0.8 mm, beam divergence: 1°
	C1: Average angular deflection between consecutive hard events
	C2: Limit maximum average fractional energy loss between consecutive hard events
	C1=C2=1
	WCC: Energy cutoff for bremsstrahlung collision=200 KeV
	WCR: Energy cutoff for bremsstrahlung emission=50KeV
	E_{abs}: Absorption emission
	$E_{abs}(e^-)=E_{Abs}(e^+)$=200 KeV, E_{abs}(Ph)=50 KeV
VRT	Particle splitting and Russian roulette techniques
	Forcing factor: 16
	CT splitting factor=100
Histories, statistical uncertainties (σ), and time (T)	Total number of primary particle histories (segment: S1)=1.56×10^8
	Size 100 Gb
	Simulation statistical uncertainties ≤0.64%
	Simulation time for segment S1: 190 h, segment 2: 10 h–15 h

VRT: Variance reduction techniques, FWHM: Full width half maximum, WCC: Energy cutoff that separates hard and soft interactions for inelastic collisions with atomic electrons, WCR: Energy cutoff for bremsstrahlung emission, CT: Computed tomography

of segments S2 and S3 for downstream end of linac and absorbed dose distribution, respectively. The simulation of segment S2 takes into account the plan geometry parameters of secondary jaws and tertiary multileaf collimator settings imported from the plan. However, segment S3 handles dose parameters and simulation of absorbed dose distribution tallied on actual CT of the patient. PRIMO is a free and non-open source computational simulation program based on the MC PENELOPE radiation transport code for calculation of absorbed dose distribution released in 2011 Salvat *et al*.[14] PRIMO code suggested using Russian roulette splitting technique is a Variance Reduction Technique (VRT) as most suitable for nominal energy below 15 MV, which has been applied during simulation.[15] In addition, interaction force in target as forcing factor and particle splitting defined as CT splitting factor was kept at 16 and 100, respectively.

Analytical anisotropic algorithm

AAA is a dose calculation algorithm incorporated by the Varian used in an Eclipse TPS originally developed by Ulmer and Kaissl.[16-18] The recent version of AAA is the 3D pencil beam convolution/superposition method (CSM) usually based on a MC-generated kernel used for energy deposition in an infinitesimal homogeneous medium. CSM uses a separate MC-derived model for the primary photon, extra-focal photon, and the scattered photon and electron from beam-limiting devices and the air (photon and electron contamination) coming of linear accelerator. In the contemporary AAA algorithm, the lateral scatter kernel is modeled using the sum of the six exponential functions. The initial photon fluence spectrum is determined just below the target from the Eclipse beam data configuration that was prevalidated by MC simulation. Significant improvements have been made in AAA, especially in the areas of treatment unit, tissue heterogeneity modeling, and correction for lateral scatter dose calculation.[19]

AAA accounts for three-dimensional tissue heterogeneity anisotropically for neighboring interaction sites using photon scatter kernels. The final dose distribution is obtained by superposition of dose calculated with photon and electron convolution. The clinical applications of AAA are categorized into photon source modeling and dose calculation. Primarily, photon source modeling determines fundamental physical parameters for dose calculation that includes modeling of primary source and secondary scatter. Secondly, AAA calculates the dose deposition using fundamental physical parameters. These parameters characterize the particle fluence and energy spectra of the photons and electrons in the clinical beam.[19,20]

Plan evaluation

The quality assessment of both the TPS-generated and MC-simulated RT treatment plans was carried out qualitatively and quantitatively. Qualitative evaluations of the treatment plan were assessed by evaluating slice-by-slice isodose or color wash distribution within the target and its surrounding. The dose–volume estimation is a measure of quantitative evaluation that determines the quality of target coverage.The dose received by percentage of target volume is a evaluation metric; D_{mean}, $D_{100\%}$, $D_{98\%}$, $D_{95\%}$, $D_{50\%}$, $D_{20\%}$ were estimated to evaluate all the TPS and MC simulated plan. In addition, quantitative evaluation of treatment plans was assessed using method of gamma analysis,

dose–volume histogram (DVH), and RT indices proposed in the International Commission on Radiation Units and Measurements (ICRU) Report-83.[19]

Plan quality coverage index

This determines the coverage quality of radiotherapy treatment plan proposed by RT Oncology Group defined as.[20]

$$Quality\ Coverage\ Index\ (QI) = \frac{D_{Min}}{D_{RI}} \qquad \text{.....(1)}$$

where D_{min} is minimum isodose cover around the target and D_{RI} is reference isodose. In this study, 98% of prescription isodose was chosen as reference isodose line.

Heterogeneity index

Homogeneous dose distribution throughout the target is highly desirable in radiotherapy; however, dose heterogeneity increases with the complexity of plan and constraint used, especially in IMRT or VMAT SIB plan. ICRU defines the heterogeneity index (HI) for dosimetric analysis of IMRT treatment plan as follows,[21]

$$Heterogeneity\ Index\ (HI) = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \qquad \text{..... (2)}$$

where $D_{2\%}$ is dose received by 2% target volume, $D_{98\%}$ is dose received by 98% target volume, and $D_{50\%}$ is dose received by 50% target volume. The ideal value of HI in the above expression is indicated as zero. The value of HI increases as heterogeneity increases.

Conformity index

ICRU-83 recommends the use of a conformity index for analyzing the dose conformity of routine IMRT treatment plans. Lomax and Scheib proposed the most accepted conformity index, which exclusively takes into account irradiation of healthy tissue.[21]

$$Conformity\ Index\ (CI) = \frac{TV_{RI}}{V_{RI}} \qquad \text{.....(3)}$$

where TV is target volume, TV_{RI} is target volume covered by reference isodose, and V_{RI} is volume of reference isodose. Ideal value of CI is considered to be one. However, the above expression of CI does not take into account the part of target volume not covered by prescription isodose.

Conformation number

The alternative CI proposed by Van't Riet *et al*.[22] and Paddick[23] know as conformation number (CN) takes into account the measure of target coverage and normal tissue overdose defined as,

$$Conformation\ Number\ (CN) = \left(\frac{TV_{RI}}{TV}\right) * \left(\frac{TV_{RI}}{V_{RI}}\right) \qquad \text{.....(4)}$$

The ideal value of $CN = 1$ indicates complete target coverage and complete normal tissue sparing. The assessment of degree of conformity of IMRT treatment plans was analyzed based on values of both CI and CN.

Gamma analysis

Gamma analysis is a method of composite dose analysis that comprises Dose Difference (DD) and Distance to Agreement (DTA) proposed by Low *et al*.[24] The method of gamma evaluation compares two dose distributions obtained using different modes. In this study, gamma analysis was performed to determine agreement between the dose distribution obtained using MC-simulated dose in PRIMO and TPS-calculated dose. The calculated dose at each point is evaluated to determine DD and DTA with respect to MC-simulated dose point. For the simulated point P_i, TPS-calculated dose (d_c) was compared against MC-simulated dose (d_s) at the same point. The expression for gamma index (Γ) is defined as,

$$\Gamma = \min\left\{\sqrt{\left(\frac{\Delta d_i}{\Delta D}\right)^2 + \left(\frac{\Delta s_i}{\Delta S}\right)^2}\right\} \qquad \text{.....(5)}$$

where ΔD and ΔS are levels of acceptance criteria for DD and DTA respectively. Δd_i is the DD between MC-simulated dose d_s (p) and TPS-calculated dose d_c (p_i) at certain points of interest. Similarly, Δs_i is the distance between p and p_i. The acceptance criteria of 3% DD, 3 mm DTA; 2% DD, 2 mm DTA; and 1% DD, 1 mm DTA were used during gamma analysis of TPS calculated against MC-simulated dose distribution. Besides, the percentage of plan passing criteria was set at ≥95%.

Results

In order to reduce the amount of numerical data produced in a study, the mean values of quantitative parameters are taken. These mean values are averaged over all the treatment plans made for all 25 retrospective patients studied. The results of TPS plans calculated by AAA were compared against their respective MC-simulated plans from PRIMO. The statistical data were summarized using mean ± standard deviation and P values computed for $\alpha = 0.01$ at 99% confidence level (CL).

Dose distribution analysis

Table 2 summarizes the results for the mean dose received by percentage of target volume of planning target volume (PTV) $_{60}$ and PTV_{52}. The estimated P value ($P \leq 0.01$) indicates that D_{mean}, $D_{50\%}$, and $D_{2\%}$ received by PTV_{60} and PTV_{52} were found to be significantly lower in TPS plans than their respective MC plans. Dose–volume parameters such as $D_{100\%}$, $D_{98\%}$, and $D_{95\%}$ were found negligibly higher in TPS plans compared to MC plans for PTV_{60}. Moreover, the P value ($P \geq 0.01$) indicates insignificant change, which exhibited good agreement between the TPS and MC plans for $D_{100\%}$, $D_{98\%}$, and $D_{95\%}$ received by PTV_{60}. However, substantial deviations between TPS and MC plans were found in $D_{100\%}$, $D_{98\%}$, and $D_{95\%}$ received by PTV_{52} indicated by estimated P value ($P \leq 0.01$). The estimated Pearson correlation coefficient between TPS and MC plans for D_{mean} received by PTV_{60} and PTV_{52} was found to be $r = 0.86$ and $r = 0.923$, respectively, that established strong existence of positive linear correlation. In addition, Figures 2 and 3

Table 2: Comparison of mean dose received by percentage of target volume and plan quality indices between treatment planning system-generated and Monte Carlo-simulated plan

Parameters	PTV60			PTV52		
	TPS (Gy), mean±SD	PRIMO MC (Gy), mean±SD	*r* (*F*)=*X*, *P*	TPS (Gy), mean±SD	PRIMO MC (Gy), mean±SD	*r* (*F*)=*X*, *P*
D_{mean}	61.45±0.33	62.45±0.35	0.86, 0.00	53.36±0.44	54.41±0.44	0.923, 0.001
$D_{100\%}$	57.41±0.94	56.76±1.03	0.50, 0.01	49.68±1.21	49.40±0.97	0.721, 0.002
$D_{98\%}$	59.32±0.29	58.12±0.66	0.338, 0.098	51.56±0.47	50.67±0.83	0.871, 0.001
$D_{95\%}$	60.13±0.09	59.66±0.21	0.285, 0.167	52.16±0.35	51.81±0.44	0.869, 0.002
$D_{50\%}$	61.53±0.35	62.66±0.44	0.799, 0.00	53.43±0.38	54.37±0.49	0.802, 0.002
$D_{2\%}$	62.73±0.57	65.28±0.75	0.697, 0.00	54.76±0.54	57.16±0.71	0.875, 0.001
QI	0.976±0.016	0.965±0.017	0.502, 0.012	0.974±0.023	0.969±0.019	0.721, 0.001
HI	0.056±0.011	0.096±0.016	0.553, 0.004	0.058±0.010	0.102±0.010	0.834, 0.001
CI	0.846±0.033	0.785±0.041	0.839, 0.001	-	-	-
CN	0.838±0.031	0.763±0.038	0.822, 0.002	-	-	-

$D_{X\%}$ represents dose to X % volume. *r* (*F*)=X is correlation coefficient, where *F*=(*n*-2)=23 represents degree of freedom and *n* is sample size. Chi-square analysis test performed using criteria of *P*=0.01 within 99% confidence level. PTV: Planning target volume, TPS: Treatment planning system, MC: Monte Carlo, SD: Standard deviation, HI: Heterogeneity index, CI: Conformity index, CN: Conformation number, QI: Quality coverage index

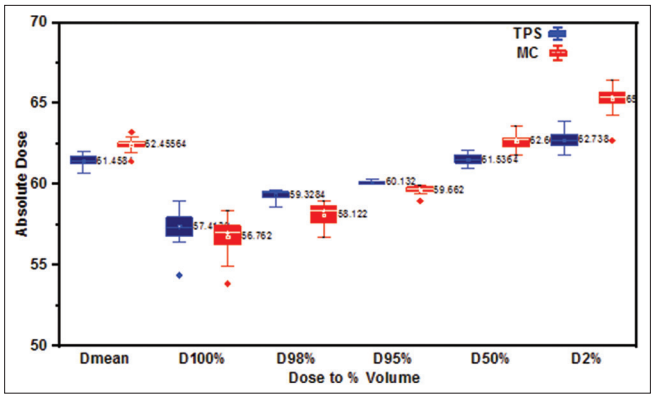

Figure 2: Comparison of absolute dose received by percentage of target volume planning target volume$_{60}$ in treatment planning system-generated and Monte Carlo-simulated plan. TPS: Treatment planning system, MC: Monte Carlo

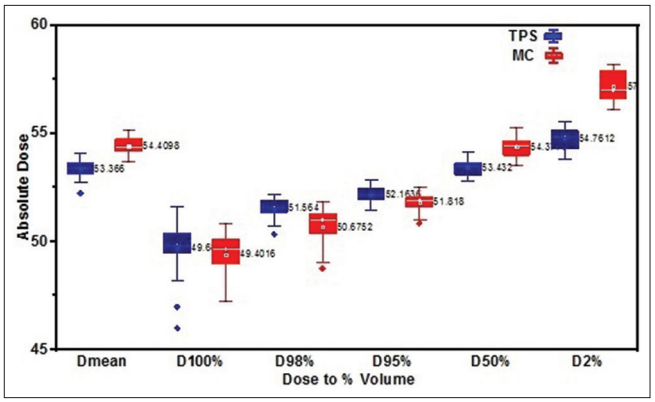

Figure 3: Comparison of absolute dose received by percentage of target volume planning target volume$_{52}$ in treatment planning system-generated and Monte Carlo-simulated plan. TPS: Treatment planning system, MC: Monte Carlo

depict the variation for absolute dose received by percentage target volume of PTV_{60} and PTV_{52} in a TPS against MC plans. Dose coverage and quality of plans were investigated based on several indices such as QI, HI, CI, and CN. The statistical comparison of plan quality indices between TPS and MC plans is summarized in Table 2 and their graphical illustrations are shown in Figure 4. The mean value of QI for TPS and MC plans was found comparable for both PTV_{60} and PTV_{52}. However, *P* values for QI were found significantly different. The mean and estimated *P* values of HI, CI, and CN were found significantly different in TPS-generated plan compared to MC-simulated plan. HI found differences by 41% and 43% between TPS plans compared to MC plans for PTV_{60} and PTV_{52}, respectively, whereas the mean values of CI and CN were found significantly higher by 7.77% and 9.82% in TPS plans than MC plans for PTV_{60}, respectively.

Table 3 summarizes the results for maximum and mean doses received by serial and parallel organs in TPS and MC plans, respectively. The box plot in Figure 5 depicts the variation of OARs mean doses received in TPS plan compared against MC plan. The doses received by all the OARs were found significantly different in TPS-generated plan compared to MC plan. The estimated mean dose indicates that the dose received by both the serial and parallel organs was significantly lower in the TPS-generated plans compared to their respective MC-simulated plans. The computed *P* value ($P \leq 0.01$) shows a significant difference between OARs doses received from TPS and MC plans. Furthermore, Pearson correlation coefficient found for all the OAR ($r \geq 0.87$) shows a strong positive correlation between OARs doses from TPS and MC-simulated plans.

Gamma analysis results

Table 4 summarizes the gamma analysis results as the mean result obtained from comparison of TPS-generated and MC-simulated plans for a variety of retrospective patients studied. This comprises the average, maximum,

Table 3: Comparison of dose received by organ at risk between treatment planning system-generated and Monte Carlo-simulated plan

OAR	Dose received			
	TPS (Gy), mean±SD	MC (Gy), mean±SD	TPS and MC % mean difference	*r* (*F*)=X, *P*
Maximum dose (Gy)				
Spinal cord	35.71±1.94	37.62±2.35	5.02	0.919, 0.001
SCPRV	39.79±2.24	42.35±2.88	5.93	0.871, 0.001
Brainstem	29.62±4.21	31.89±4.16	10.19	0.996, 0.002
BSPRV	32.93±6.56	34.93±6.78	10.38	0.986, 0.001
Chiasm	4.91±2.36	6.11±2.83	23.04	0.986, 0.001
Right optic nerve	3.25±0.861	3.59±1.098	11.97	0.938, 0.001
Left optic nerve	3.68±1.82	4.36±2.24	13.48	0.938, 0.002
Right eye	7.023±3.81	8.635±4.84	17.16	0.939, 0.001
Left eye	10.82±8.61	12.76±10.78	20.53	0.989, 0.003
Mean dose (Gy)				
Right parotid	28.18±4.32	32.53±5.67	13.34	0.823, 0.003
Left parotid	32.74±8.94	35.803±9.45	10.63	0.966, 0.002
Larynx	43.52±4.22	44.96±4.61	3.20	0.930, 0.002
Right cochlea	12.48±8.95	14.67±10.23	16.93	0.997, 0.002
Left cochlea	8.67±4.22	9.96±4.61	16.33	0.930, 0.001

r (*F*)=X is correlation coefficient, where *F*=(*n*-2)=23, where f represents degree of freedom and *n* is sample size. Chi-square analysis test performed using criteria of *P*=0.01 within 99% confidence level. OAR: Organ at risk, TPS: Treatment planning system, MC: Monte Carlo, SCPRV: Spinal cord planning at risk volume, BSPRV: Brainstem planning at risk volume

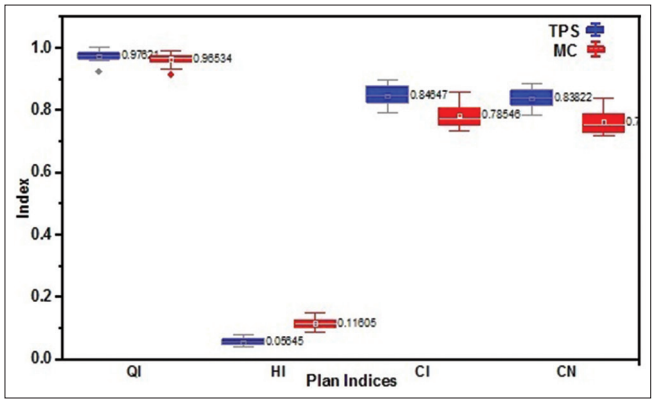

Figure 4: Comparison of absolute dose received by percentage of target volume planning target volume$_{60}$ in treatment planning system-generated and Monte Carlo-simulated plan. TPS: Treatment planning system, MC: Monte Carlo

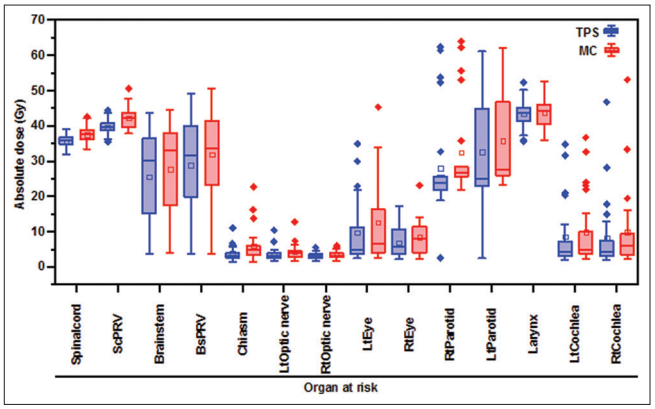

Figure 5: Comparison organ-at-risk (OAR) dose received by treatment planning system-generated and Monte Carlo-simulated plan. In a figure, box plot represents the maximum and mean dose for serial and parallel OARs, respectively. TPS: Treatment planning system, MC: Monte Carlo

and minimum percentages of gamma passing obtained from the comparison of TPS and MC plans. Figure 6 depicts a graphical representation of the percentage of gamma passing rate for comparison of TPS plans against their respective MC plans. All the TPS plans compared against the MC plans were analyzed with gamma criteria of 3% DD, 3 mm DTA and closely matched within the minimum gamma passing rate of 98.49%. The gamma analysis performed using 2% DD, 2 mm DTA shows a minimum plan passing rate of 94.24% obtained slightly below the plan passing criteria of ≥95% for few patients, as shown in Figure 6. However, gamma analysis performed using 1% DD and 1 mm DTA badly fails with a minimum plan passing rate between 89.12% and 85.45%.

Discussion

The present study provided an evaluation of SIB VMAT plans calculated by AAA generated in TPS against MC plans simulated using PRIMO. The significant deviations for D_{mean}, $D_{50\%}$, and $D_{2\%}$ of the target volumes and doses to the OARs were observed between TPS and MC plans during this study. Statistically, it is evident that insignificant differences were noticed for $D_{100\%}$, $D_{98\%}$, and $D_{95\%}$ received by the primary target PTV_{60}. However, secondary target PTV_{52} shows considerable deviation between TPS and MC plans. These differences can be appreciated from numerical data presented in Table 2. Figures 2-5 provide the graphical illustrations of D_{volume}, various plan quality indices, and OAR doses obtained from TPS and MC plans. The box plot depicted in figures shows

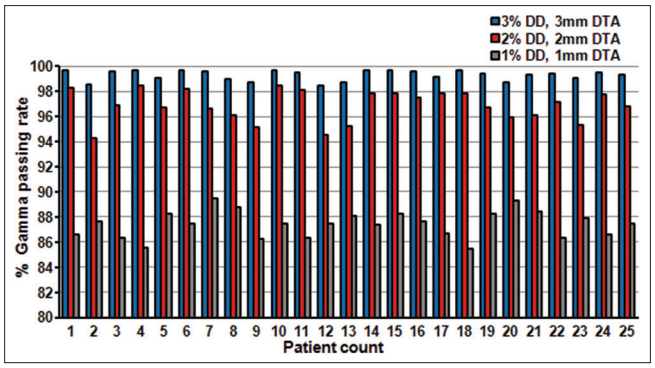

Figure 6: The gamma analysis result comparison of treatment planning system against Monte Carlo plan for all patients studied using three different gamma passing criteria. DTA: Distance to agreement

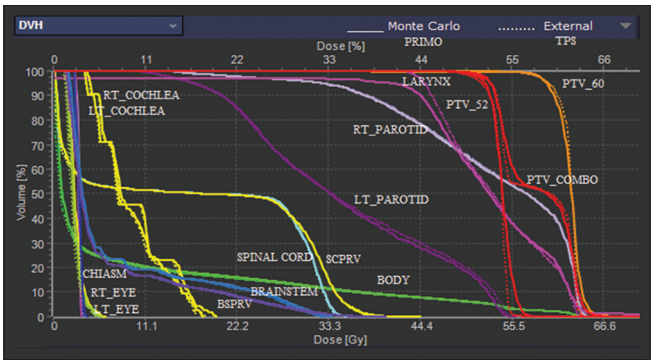

Figure 7: Comparison of dose–volume histogram obtained from treatment planning system-generated and Monte Carlo-simulated plan for one of the retrospective patients studied. PTV: Planning target volume, TPS: Treatment planning system

Table 4: The gamma analysis results over range of patients studied using three different gamma acceptance criteria

Gamma analysis	Gamma acceptance criteria		
	3% DD and 3 mm DTA	2% DD and 2 mm DTA	1% DD and 1 mm DTA
Average gamma passing rate	99.31	96.87	87.41
Maximum gamma passing rate	99.73	98.50	89.45
Minimum gamma passing rate	98.49	94.24	85.45

DTA: Distance to agreement, DD: Dose difference

the distribution of numerical data obtained from sample patients. The estimated *P* value for QI was $P \geq 0.01$ showing an insignificant deviation that exhibits concurrence between the target coverage quality of PTV_{60} in TPS and MC plans. On the other hand, outcomes of P value ($P \leq 0.01$) suggest a significant deviation between TPS and MC plans target coverage quality for PTV_{52}. The differences can be noticed from Figure 7 which illustrates the comparison of DVH between TPS and MC plans for one of the patients studied. Pertaining to heterogeneity, $D_{2\%}$ and $D_{98\%}$ represent the maximum and minimum dose received by target volume significantly higher and lower in MC-simulated plan compared to TPS-generated plan respectively. This confirmed that MC plans tend to be more heterogeneous than TPS plans. All the plan quality indices were observed to be better in AAA-calculated plans than MC plans. However, fundamental approaches utilized in the dose calculation algorithm AAA and MC are entirely different.

The dose discrepancies in AAA over MC have been illustrated by several studies, especially in regions of air cavities, lung, high-density bone, heterogeneous medium, and tissue–bone interface.[25] Several studies have shown the range of deviation between AAA and MC dose distributions. The patients head-and-neck site is especially full of heterogeneities. This involves lots of air cavities, large number of different tissue-air and tissue-bone interfaces known as inherent Dose perturbation elements (DPEs) are involved. The modeling of AAA does not fully account for these DPEs. In addition, AAA does not account for real tissue density properties and computes the dose to water followed by rescaling as per Hounsfield unit (HU) that corresponds to CT electron density.[26] The OARs with relatively small volumes and low-density regions have shown a large deviation between TPS and MC plans. AAA tends to overestimate dose at air cavities and soft tissue interfaces, which is considerably more pronounced in case of larynx can be perceived from DVH shown in Figure 7. The volumetric dose calculation is affected by the variation of voxel grid size used during dose computation in TPS and MC simulation. The fixed grid size of 2 mm was used for volumetric dose computation in TPS, while PRIMO had set it by default according to the size of patient CT. Consequently, variation of voxel size and number of dose matrices within the structure of interest could affect quality of dose distribution predominantly in small volume structures. The maximum dose for a serial organ is greatly influenced by the size of voxel and dose matrix in TPS and PRIMO. Similarly, dose per matrix affects the mean dose of the target structure. The variation of dose matrix can cause variation in dose distribution calculated using AAA and MC algorithms. However, its quantitative assessment is difficult and beyond scope of this study.

Figure 8 shows the comparison of dose distributions between TPS and MC plans in an isocenter plane on different sections of the CT (axial, sagittal, and coronal) for one of the retrospective patients studied. Similarly, the comparisons of depth dose profiles at the plane from the geometric center of TPV_{60} for TPS and MC plans are shown in Figure 9. The depth dose uncertainties are found to be higher at the edges of the target volume in the gradient region than within the target. AAA has a tendency to show dose inconsistency away from the central axis in the high-dose region as well as underestimate the dose in the high-gradient region. The minimum to maximum dose disagreement in the high- and low-dose gradient regions of the target lies within 1.5%–2.5% with 1 mm to 4 mm shifts in isodose profiles can be appreciated from Figure 9. The PRIMO enables the composite plan comparison and gamma analysis of two different dose distributions. The overall gamma analysis for the comparison of TPS and MC plans was determined using three different

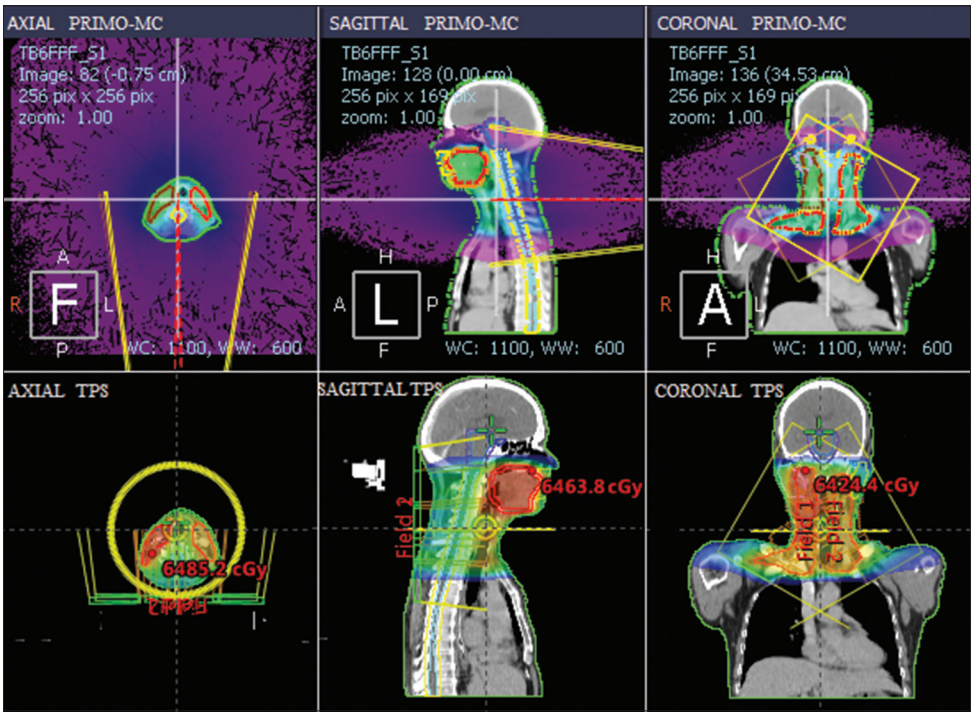

Figure 8: Comparison of dose distributions between treatment planning system-generated and Monte Carlo-simulated plan for one of the retrospective patients studied. PTV: Planning target volume, TPS: Treatment planning system, MC: Monte Carlo

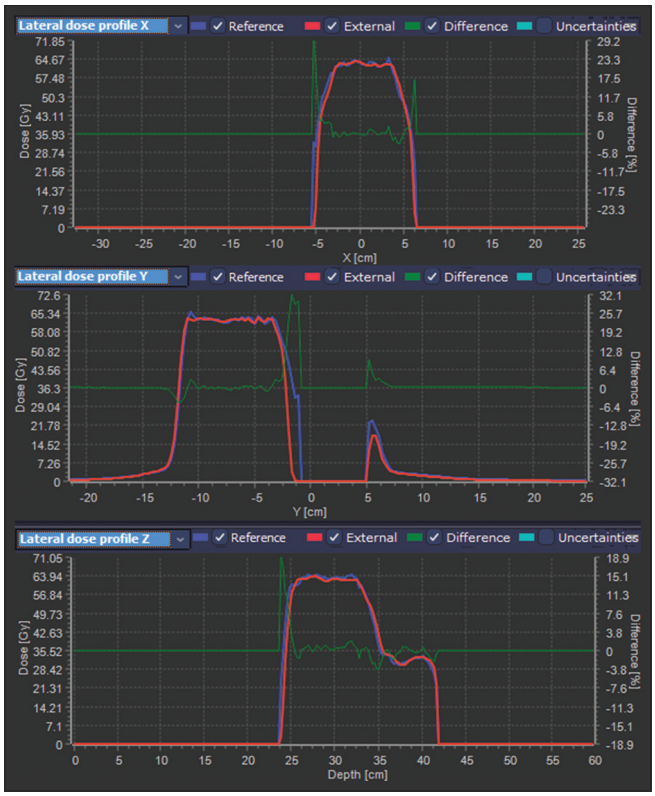

Figure 9: Comparison of depth dose profiles at plane from geometric center of planning target volume$_{60}$ between treatment planning system-generated and Monte Carlo-simulated plan for one of the retrospective patients studied

DD and DTA acceptance criteria. All the plans passed within 98.49% gamma with acceptance criteria of 3% DD and 3 mm DTA establishing close agreement between TPS-calculated and MC-simulated plans. However, the percentage of gamma passing decreased as plan acceptance criteria became more stringent to 2% DD, 2 mm DTA and 1% DD, 1 mm DTA, as shown in Table 4.

Conclusion

The accuracy of TPS-generated VMAT-SIB treatment plans was validated against MC simulation techniques using PRIMO. The resultant gamma analysis showed the dose distribution simulated using MC establishing closed agreement with AAA calculated dose distribution found within tolerance. However, this study also confirmed the known limitation of AAA and revealed the deviation of dose distribution for routine clinical treatment plans calculated using AAA with respect to MC algorithm.[26,27] Numerical statistics showed that the plan quality indices are little compromised in MC-simulated plans compared to TPS-generated plans appeared to be true representation of real dose distribution obtained from MC simulation technique. Recent version of PRIMO was found to be a more consistent, reliable tool for geometrical modeling and simulation of TrueBeam linear accelerator and dose computation in user-defined patient CT-based geometries. Validation using MC simulation approach provides an independent secondary check for ensuring the accuracy of TPS-generated plan.

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Conflicts of interest
There are no conflicts of interest.

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