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Clinical implementation of a PRIMO Monte Carlo-based dose verification and quality assurance model for stereotactic body radiotherapy (SBRT) treatment plans of the lung

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► ***Original article***

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ABSTRACT

***Background*:** Natural The validation and clinical implementation of the PRIMO Monte Carlo (MC) model of Clinac® iX Linear accelerator as an independent dose verification and quality assurance (QA) tool for the SBRT lung treatment plans. ***Materials and Methods*:** An independent MC based dose verification was performed for ten volumetric modulated arc therapy (VMAT) SBRT treatment plans.The plans generated in the Varian Eclipse treatment planning system (TPS) were recalculated with a PRIMO MC system for identical beam parameters.The log file-based QA was performed by comparing the TPS dose against the dose reconstructed from machine log files and the results were cross-verified with the Mobius3D® verification system. The dose-volume histogram (DVH) based plan comparison and 3D global gamma analysis were carried out. The statistical significance of the differences was tested with the Wilcoxon signed-rank test with a significance level of $P < 0.05$. ***Results*:** No statistically significant differences were observed in PTV and organs at risk (OARs) DVH parameters except for the PTVmax dose for both TPS vs PRIMO independent dose check and TPS vs PRIMO dynalog based QA. The 3D gamma analysis results show a minimum pass rate of 95% between TPS and PRIMO. Mobius3D® results showed a slightly higher percentage variation in the mean dose to PTV and OARs and a slightly lower gamma pass than TPS vs PRIMO results. ***Conclusion*:** This study showed that a validated MC model of PRIMO could be used as an effective tool for independent dose verification and machine log-files-based quality assurance of VMAT SBRT plans.

INTRODUCTION

Stereotactic body radiotherapy (SBRT) is increasingly used to treat non-small cell lung cancer (NSCLC) patients. The SBRT principle is to deliver large doses to the tumour volume in a few fractions. This results in a higher level of biological effect compared to conventional radiotherapy fractionation schemes. SBRT is applied only to small-sized tumours to minimize the normal tissue toxicity associated with high doses per fraction. Targets surrounded by low-density heterogeneity and the plans with many highly modulated small-field segments are the main challenges associated with the dose calculation of lung SBRT plans [1,2]. The high degree of modulation in SBRT plans can lead to deviation in the dose delivery due to multi-leaf collimator (MLC) leaf position errors and gantry rotational instability. The increased complexity of the VMAT SBRT plan necessitates implementing a rigorous patient-specific quality assurance (PSQA).

Independent validation of dose calculation is an essential part of PSQA for every intensity-modulated radiation therapy (IMRT|) and VMAT plan. Most independent verification systems can only be used for single-point dose calculations under homogeneous conditions [3]. The PSQA methods like monitor unit (MU) verification and gamma analysis alone are insufficient to validate the SBRT plans due to their increased complexity. Sun *et al.*[4] demonstrated that phantom-based PSQA might not be sensitive enough to detect gantry angle and MLC positioning errors during beam delivery. Many studies conclude that delivery log-file (dynalog file) based plan verification is an effective tool for verifying calculation inaccuracies, data transfer, and the MLC delivery performance, which cannot be easily detected in a phantom measurement-based QA [4–9]. In its Report 83,[10] the International Commission on Radiation Units and Measurements (ICRU) proposed a validated MC algorithm for independent dose verification, especially for analyzing the absorbed doses in heterogeneous tissues. The effectiveness of using a machine delivery log file for VMAT PSQA has been demonstrated previously [6,8,11]. Teke *et al.* [7] showed that MC-based

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RapidArc QA using linac log files assesses the physical delivery and dose calculation accuracy of RapidArc treatments. In a study by Hernandez *et al.* [12], Varian Trilogy and Clinac log files with plans delivered using a single TPS were examined to determine the optimal MLC tolerances for IMRT and VMAT. McGarry et al.[8] conducted a multi-institutional study to assess the delivery accuracy of VMAT plans for different Varian linear accelerator models using log file-derived MLC root mean square (RMS) values and concluded that log-file based QA could differentiate between the TPS errors and errors based on delivery.

The treatment planning system (TPS) dose calculation algorithms used in this study, Acuros®XB (Varian Medical Systems, Palo Alto, USA), implemented in the Varian Eclipse® (Varian Oncology Systems, Palo Alto, CA), is a fast and accurate alternative to MC for patient dose calculations [1,13].Mobius3D® (Varian Medical Systems, Palo Alto, USA) used in this study is a software package for calculating 3D dose distribution in the patient computed tomography (CT) using machine log files. Mobius3D®calculates the 3D dose received by the patient using independently verified beam models and a collapsed-cone algorithm. Studies that investigated the dosimetric accuracy of Mobius3D® and concluded that it could be used as a reliable secondary dose verification system[14,15].

MC simulation techniques are the gold standard to calculate radiation absorbed dose [16,17]. Several publications have extensively validated MC simulation for complex techniques such as IMRT and VMAT [7,13,18,19]. The utilization of MC systems as a secondary check makes the verification process fully independent from the TPS. PRIMO [20] is an MC simulation package that facilitates medical linac simulations and estimates dose distribution in water phantoms and CT. It is a program based on the codes PENELOPE [21], PENEASY [22], and PENEASYLINAC [22]. The fast MC simulation algorithm for electron and photon transport inside the patient geometry DPM[23] is also incorporated in PRIMO. Since most of the varian linac geometries are included in the PRIMO package, the user does not need to enter details about the geometry or materials of the linac head. PRIMO provides default initial simulation parameters that can be finetuned until the best agreement between simulations and measurements is achieved. The parallel processing capability and the variance reduction techniques available in PRIMO can reduce the simulation time and the associated statistical uncertainties [24]. PRIMO allows the import of a treatment plan from an external TPS in the DICOM (Digital Imaging and Communications in Medicine) format. Graphical and numerical tools for the analysis of dose distributions are incorporated in PRIMO. Moreover, PRIMO can reconstruct a treatment plan from varian's treatment log files (dynalog files) and estimate the actual dose delivered to the patient during the treatment.

The present study aimed to demonstrate the clinical implementation of the PRIMO MC model of Clinac® iX as an independent MC-based PSQA tool for lung SBRT. In this study, PRIMO log-file-based plan reconstruction was validated for the complex SBRT plans. Also, the PRIMO log-file-based plan reconstruction results were cross verified against the Mobius3D® commercial dose verification system, to our knowledge for the first time, against a full MC simulation.

MATERIALS AND METHODS

PRIMO simulation software Version 0.3.64 (https://www.primoproject.net) was used in this study. A validated MC model of a linac was required for the simulation of clinical treatment plans. The full MC simulation of Clinac®iX (Varian Medical Systems, Palo Alto, USA) linac was performed using PRIMO, and the phase-space data (PSFs) were generated. The simulated Varian Clinac®iX linear accelerator model was validated by comparing the simulated percentage depth dose (PDD) and beam profile curves against the measured data. The tuning of simulation parameters for the 6MV photon beam model of Clinac® iX and its validation under homogeneous and heterogeneous conditions has been described previously [25]. The resulting PSFs file thus generated was used for all SBRT plan simulations performed in this study. In order to reduce the calculation time, the simulations were divided into two parts. First, the PSFs of the patient independent part above moveable jaws were linked to each SBRT plan simulation, avoiding repeating the patient-independent part of the simulation above the movable jaws. Subsequently, the simulation of the patient-dependent part of the linac (movable jaws, MLC) and the voxelized geometries was carried out using the above phase-space file as the radiation source. The fast MC algorithm DPM was used for the simulation inside the patient geometry. The default values of transport parameters [26] provided by PRIMO have been used for simulation. The particle splitting variance-reduction technique was applied in the simulation of patient geometries, and a splitting factor of 300 was found adequate to obtain a statistical uncertainty of around 1%. The simulations were performed using a Dell T5600 workstation with 32 GB of RAM and 24 CPU cores with 2.0 GHz speed.

Clinical plans

Ten SBRT NSCLC cases previously treated with VMAT at our center were included in this retrospective study. The study was approved by the Institutional Review Board (IRB:03/2019/03, Dated: 22/03/2019). Patient treatment plans with tumour volume less than 60 cm^3 were selected for simulation.

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The CT images of the ten patients were acquired in a General Electric (GE) Optima™ CT scanner (GE Healthcare, Waukesha, WI) with 512 × 512 pixels at 0.25 cm slice spacing. Clinically acceptable VMAT SBRT plans were planned and delivered using the Clinac iX linac with Millennium 120-leaf MLC (Varian Medical Systems, Palo Alto, CA, USA). The plans of four arcs (two coplanar and two non-coplanar) of 6 MV photons were generated in Eclipse® TPS (Version 15.6). The dose prescription was 48 Gy in four fractions as per the Radiation Therapy Oncology Group (RTOG) 0915 Protocol[27] followed in our institution for non-small cell lung tumours. Acuros®XB algorithm (Version15.6) was used for dose calculation with the photon optimization algorithm (PO, version 15.6, Varian Medical Systems, Palo Alto, CA, USA) for plan optimization. A grid size of 2.5 mm was selected for dose calculation, and the dose report mode chosen in this study was dose to medium. The absolute dose (D) in Gray (Gy) conversion was performed in PRIMO according to equation 1.

$$D = \frac{D_{exp}^{ref}}{MU^{ref}} \frac{D_{MC}}{D_{MC}^{ref}} MU \quad (1)$$

Where D_{exp}^{ref} is the dose in Gy measured in reference conditions (100cm SSD, 10 × 10cm^2 field size, 10cm depth) in a water tank phantom. D_{MC}^{ref} is the dose estimated by a MC simulation (in eV/g per history) in reference conditions. MU^{ref} is the reference monitor units used to obtain the measured reference dose. D_{MC} is the simulated dose (in eV/g per history) for the treatment plan, and MU is the monitor unit of the plan.

Independent dose verification

The TPS independent dose calculation was performed in PRIMO. The VMAT SBRT plans and CT images and structures were exported from Eclipse TPS in DICOM format and imported in PRIMO for MC calculations. It is necessary to generate a voxelized simulation geometry composed of a set of material and mass density value pairs before any simulation can begin [26]. The voxelized simulation geometry was generated after importing the CT volume. Each voxel's material type and mass density were defined using PRIMO's CT number-to-mass density conversion curve and material assignment library. Figure 1 shows the CT number to mass density conversion curve used to assign mass densities to CT numbers and the materials used from the material assignment library to generate the voxelized simulation geometry. A set of six materials, air, lung ICRP, adipose tissue, muscle-skeletal, cartilage and compact bone, are assigned to the voxels according to their density and the CT calibration curve to create a voxelized geometry. The composite image of a CT slice after generating the voxelized geometry is also shown in figure 1. The plans were simulated using the same beam settings and MU of the TPS plan.

The Eclipse® calculated 3d dose in RT Dose format was imported into PRIMO for comparison. The DVH parameters for planning target volume (PTV) and OARs were compared for all SBRT plans. The dose distributions were compared using the gamma evaluation method [28] with a 2% dose difference and 2 mm distance-to-agreement as acceptance criteria. The dose distribution obtained from TPS was used as a reference. The percentage of the difference between TPS and PRIMO was calculated using equation 2.

$$\% \text{ Difference} = \frac{(TPS\ dose - PRIMO\ dose)\ X\ 100\%}{TPS\ dose} \quad (2)$$

TPS dose > TPS calculated dose
PRIMO dose = PRIMO MC calculated dose

Pretreatment quality assurance

Pretreatment quality assurance for all SBRT plans was performed using ArcCHECK™ (Sun Nuclear Corporation, Melbourne, FL, USA) cylindrical phantom. Gamma analysis (2%,2mm) was performed using SNC Patient™ software version 6.6 (Sun Nuclear Corporation, Melbourne, FL, USA). A cavity plug holding an ion chamber was used to measure the dose at the centre of the ArcCHECK™ phantom. The absolute dose at the isocenter was verified using CC-13™ (IBA Dosimetry, Schwarzenbruck, Germany) 0.13cc ion chamber.

Plan reconstruction from dynalog files

The Varian linac's MLC controller creates a set of dynalog files (one for each MLC bank; A and B) for each VMAT field delivered. The dynalog data were recorded every 50 ms by the MLC controller unit. The most relevant data included in the dynalog files are the gantry angle, the jaws position, the expected and actual positions of each MLC leaf, the fractional MU delivered, and the segment number. PRIMO can reconstruct a treatment plan from the data extracted from the dynalog files. In the present study, the machine log file was acquired during the delivery of the original plan without the patient in the QA mode. The original plan from TPS was imported into PRIMO before importing the dynalog files. During plan reconstruction, the couch rotation and the isocenter position data were extracted from the original plan. The reconstructed dose was generated from the actual MLC positions recorded in the dynalog files. The Uniform Reconstruction (UR) [26] method coded in PRIMO was used for plan reconstruction. The plans were reconstructed by uniformly sampling the records in the dynalog files at a specific time interval. The maximum number of control points allowed in a plan reconstruction is 3000. The minimum value of time resolution of uniform sampling was chosen for

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each plan by keeping the number of control points in the reconstruction < 3000.PRIMO reported the maximum leaf error found in any leaf and the overall RMS. The reconstructed dose was estimated in the patient's geometry created from the CT image exported by the TPS. The reconstructed dose was compared to the TPS dose.

Mobius3D®verification

To compare the performance of PRIMO against Mobius3D®, all VMAT plans generated in TPS were recalculated using the Mobius3D® software. Also, the treatment plans were reconstructed from dynalog files using the Mobius FX® (Varian Medical Systems, Palo Alto, USA) module incorporated in the Mobius3D® for all plans. The dynalog files were imported, and dose distributions were calculated on each patient's CT dataset by Mobius3D®. The mean dose to PTV and OARs were compared to that of TPS. The 3D dose distributions were compared using the gamma analysis method with 2%, 2mm acceptance criteria. The gamma evaluation was performed for two structural volumes, PTV and the entire body corresponding to the irradiated volume within the dose calculation region. The percentage difference between TPS and Mobius was calculated using equation 3.

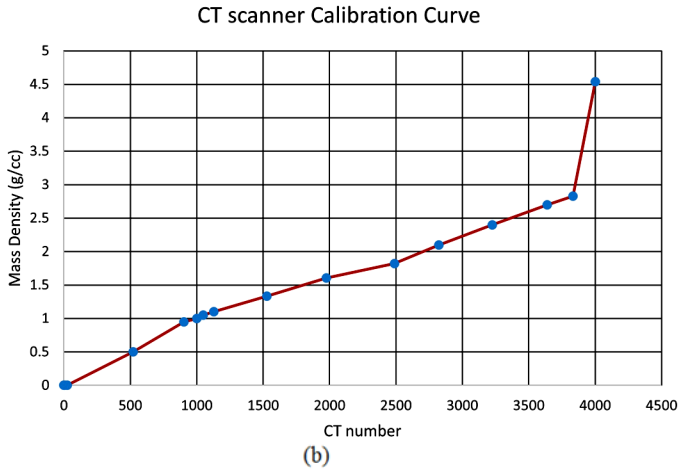
$$\% \text{ Difference} = \frac{(\text{TPS dose} - \text{MOBIUS dose}) \times 100\%}{\text{TPS dose}} \quad (3)$$

TPS dose = TPS calculated dose

PRIMO dose = PRIMO MC calculated dose

CT Number	Mass Density (g/cc)
0	0.001
8	0.001
24	0.001
521	0.5
904	0.95
1000	1
1048	1.05
1128	1.1
1528	1.334
1976	1.603
2488	1.82
2824	2.1
3224	2.4
3640	2.7
3832	2.83
4000	4.54

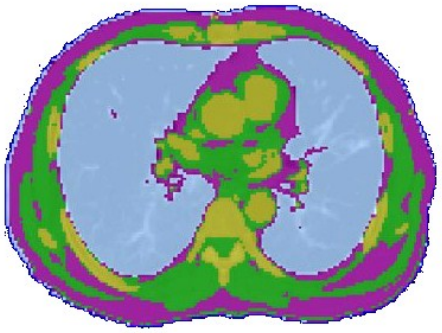
(a)



(b)

Material	Density	CT Range
Air	0.0012	0 - 32
Lung (ICRP)	0.3	32 - 600
Adipose Tissue	0.92	600 - 963
Muscle Skeletal	1.05	963 - 1088
Cartilage (ICRP)	1.1	1088 - 1808
Bone Compact	1.85	1808 - 3513

(c)



(d)

Figure 1. a) CT number and corresponding mass density value table. **b)** CT number to mass density conversion curve. **c)** List of assigned materials and their corresponding CT number interval. **d)** Blended image of a CT slice and assigned materials (Material corresponding to each colour is given in figure **(c)**).

DVH based plan comparison

In this study, the following dosimetric parameters were extracted from DVH for plan comparison:

Mean dose to the PTV (PTV_{mean}), lungs ($LUNGS_{mean}$), and heart ($HEART_{mean}$).

Maximum dose (dose to 0.03 cm^3) to the PTV (PTV_{max}) and spinal cord ($SPINE_{max}$).

The dose received by 95% of the PTV ($PTV\ D_{95}$).

The proportion of total lung volume receiving doses of 20 Gy ($LUNGS\ V_{20}$) and 5 Gy ($LUNGS\ V_5$).

The Radiation Therapy Oncology Group (RTOG) conformity index (CI_{RTOG}) [29] and Paddick's gradient index ($GI_{Paddick}$) [30] were also recorded for comparison.

The CI_{RTOG} was calculated using equation 4.

$$CI_{RTOG} = \frac{\textit{Total volume of tissue receiving the prescribed dose}}{\textit{Volume of PTV receiving the prescribed dose}} \quad (4)$$

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The $GI_{Paddick}$ was calculated using equation 5.

$$GI_{Paddick} = \frac{Volume\ of\ tissue\ receiving\ 50\%\ isodose}{Volume\ of\ PTV} \quad (5)$$

A CI_{RTOG} value closer to 1 indicates enhanced target conformity, and a small $GI_{Paddick}$ value represents a steeper dose fall-off outside the PTV.

The data were presented as mean±standard deviation (SD). Normality tests were carried out on the data to determine the appropriateness of the statistical tests for analyses. A two-tailed t-test (Wilcoxon signed-rank test) was performed using SPSS 20.0 (IBM, Armonk, NY, USA) to determine the difference between the plans. The difference was considered statistically significant for P-value < 0.05.

RESULTS

Simulations were run for 5×10^8 histories. The simulation time for each case depends on the beam's size, the number of beams, and control points. The average statistical uncertainty of the dose distributions obtained was < 1.5 % for all cases. The simulation time taken to obtain the above uncertainty varies between 3.5 and 4.5 hours.

ArcCHECK™ measurements were carried out for each VMAT plan. 2D gamma analysis (2%,2mm) showed a good agreement between the measured and TPS calculated planar doses with an average gamma pass rate of 98.36±0.44%. The comparison of absolute dose measurement at the isocenter showed an average difference of 1.67±0.43% between TPS values and measurements.

The comparison of TPS (Acuros® XB algorithm) and PRIMO MC calculated dose distributions are shown in table 1. Also, the dosimetric differences in DVH parameters for PTV and OARs are tabulated. The data are presented as mean±SD. The p-value is also shown. No statistically significant differences were observed in the PTV coverage parameters PTVmean, PTV D_{95}, CI, and GI. However, a significant difference (P<0.05) difference was observed for the PTVmax dose. A mean difference of -2.4%±1.95% was observed in the case of PTVmax dose, while no differences were observed in OARs for LUNGS V_{20}, LUNGS V_5, LUNGS mean dose and SPINE max dose. The PRIMO simulated dose distribution for an SBRT plan is shown in figure 2.

The comparison of the TPS plan against the plan reconstructed from dynalog files using PRIMO is shown in table 2. The results did not detect any significant differences in PTV coverage parameters PTVmean, PTV D_{95}, CI, GI and OARs, LUNGS V_{20}, LUNGS V_5, LUNGS mean dose and SPINE max dose. Conversely, the difference was significant for the PTVmax dose (P=0.009), similar to PRIMO's independent dose check results (table 1). A mean difference of -2.8% ±2.47% was observed in the case of the PTVmax dose.

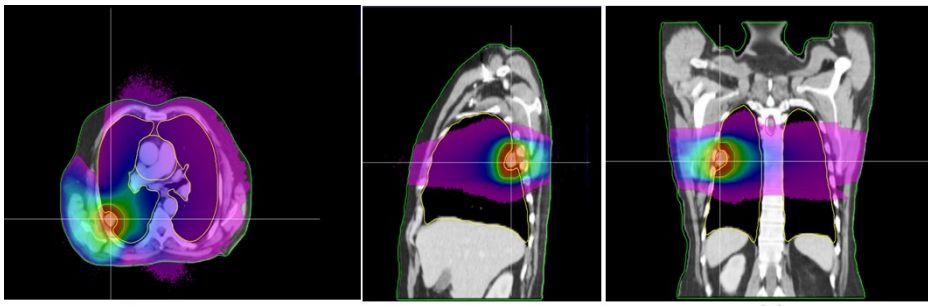

Figure 2. The PRIMO simulated dose distribution for an SBRT plan in the axial **(a)**, sagittal **(b)** and coronal **(c)** isocenter planes.

Table 1. Comparison of DVH parameters from PRIMO simulation and TPS. DVH – dose-volume histogram, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system. MC- Monte Carlo.

DVH parameter	TPS(Acuros XB) Mean±SD	MC(PRIMO) Mean±SD	P-Value
PTV_{mean} (Gy)	51.16 ± 0.85	51.31 ± 0.88	0.074
PTV_{max} (Gy)	56.05 ± 2.11	57.37 ± 2.49	0.007
PTV D_{95} (Gy)	46.74 ± 1.63	46.93 ± 1.61	0.169
LUNGS V_{20} (%)	5.93 ± 1.42	5.79 ± 1.23	0.102
LUNGS V_5 (%)	19.31 ± 3.24	20.33 ± 3.39	0.061
$LUNGS_{mean}$ (Gy)	4.38 ± 0.68	4.38 ± 0.65	0.953
$SPINE_{max}$ (Gy)	12.00 ± 3.88	11.94 ± 3.95	0.541
CI	1.08 ± 0.04	1.09 ± 0.04	0.058
GI	4.31 ± 0.38	4.3 ± 0.40	0.683

Table 2. Comparison of DVH parameters from PRIMO dynalog reconstructed plan and TPS.DVH – dose-volume histogram, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system. MC- Monte Carlo.

DVH parameter	TPS (Acuros XB) (Mean±SD)	MC(PRIMO) Mean±SD	P-Value
PTV_{mean} (Gy)	51.16 ± 0.85	51.33 ± 0.92	0.093
PTV_{max} (Gy)	56.05 ± 2.11	57.63 ± 2.89	0.009
PTV D_{95} (Gy)	46.75 ± 1.65	47.05 ± 1.98	0.139
LUNGS V_{20} (%)	5.93 ± 1.42	5.60 ± 1.34	0.083
LUNGS V_5 (%)	19.31 ± 3.24	20.63± 3.55	0.056
$LUNGS_{mean}$ (Gy)	4.38 ± 0.68	4.33± 0.67	0.484
$SPINE_{max}$ (Gy)	12.00 ± 3.88	12.17 ± 4.09	0.203
CI	1.08 ± 0.04	1.10 ± 0.04	0.101
GI	4.31 ± 0.38	4.45 ± 0.56	0.799

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The dosimetric differences resulting from TPS vs. independent dose check with PRIMO and TPS vs. independent dose check with Mobius3D are shown in table 3. Also, a difference was noted in mean dose to PTV, OARs and maximum dose to spine. Subsequently, PRIMO showed good agreement with TPS with a mean difference of less than 1% for PTV and OARs. Mobius also showed a <1% difference with TPS for PTV and OARs except for SPINE max, which showed a mean difference of 2.22% ±0.98%. The 3D gamma analysis results of comparing the TPS dose to the dose recalculated in PRIMO and Mobius are shown in table 4 for the PTV and body structures. PRIMO's average gamma pass percentage was 98.55 ±1.27 inside the PTV and 99.79 ±0.21 inside the entire body. The average gamma pass percentage in the case of Mobius was 94.46±1.03 and 98.63±0.74, respectively.

The comparison of the TPS plan against the dynalog reconstructed plans generated with PRIMO and Mobius agreed with the TPS with a mean difference of <1% for PTV and OARs except for SPINE max. For SPINE max, a mean difference of -1.11% ± 2.47% was observed for PRIMO, and a mean difference of -3.57% ± 2.56% was observed for Mobius. The 3D gamma analysis results of comparing the TPS dose to that reconstructed from dynalog files using PRIMO and Mobius are shown in table 5 for the PTV and BODY structures. The RMS values were <0.3 mm for all dynalog files. PRIMO's average gamma pass percentage was 96.6±1.92 for the PTV and 99.7±0.38 for the entire body structure. The average gamma pass percentage in the case of Mobius was 93.1±1.82 and 98.1±0.89, respectively.

Table 3. Relative difference in DVH parameters: comparison of PRIMO and MOBIUS against TPS.

VH parameter	Independent dose check		Dynalog verification	
	PRIMO (Mean±SD)	MOBIUS (Mean±SD)	PRIMO (Mean±SD)	MOBIUS (Mean±SD)
PTV_{mean}	-0.28% ± 0.38%	-0.28% ± 1.16%	-0.33% ± 0.59%	-0.41% ± 1.16%
$PTV\ D_{95}$	-0.42% ± 0.88%	0.97% ± 1.095%	-0.64% ± 1.25%	1.02% ± 2.04.%
$LUNGS_{mean}$	-0.15% ± 2.84%	-0.69% ± 0.68%	0.85% ± 3.17%	1.02% ± 2.04.%
$SPINE_{max}$	0.68% ± 2.55%	-2.22% ± 0.98%	-1.11% ± 2.47%	-2.57% ± 1.56%

DVH – dose-volume histogram, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system.

Table 4. Gamma pass percentage for PRIMO and Mobius against TPS (independent dose check).

Plan	PTV Gamma Pass Rate (2%,2mm)		BODY Gamma Pass Rate (2%,2mm)	
	PRIMO	Mobius	PRIMO	Mobius
SBRT1	99.4	96.1	99.9	98.5
SBRT2	99.1	93.9	99.6	98.7
SBRT3	98.6	95.8	99.8	99.4
SBRT4	96.5	94.3	99.9	99.7
SBRT5	99.6	93.1	99.9	98.3
SBRT6	99.8	94.4	99.3	99.1
SBRT7	96.8	95.1	99.8	99.1
SBRT8	99.9	95.0	99.9	98.4
SBRT9	98.1	93.8	99.7	97.2
SBRT10	97.3	93.1	99.8	97.9
Mean ±SD	98.5±1.27	94.5±1.03	99.7±0.21	98.6±0.74

Table 5. Gamma pass percentage for PRIMO and Mobius against TPS for the dynalog reconstructed plan.

Name	PTV Gamma Pass Rate (2%,2mm)		BODY Gamma Pass Rate (2%,2mm)	
	PRIMO	Mobius	PRIMO	Mobius
SBRT1	98.2	95.2	99.9	98.2
SBRT2	97.4	93.6	99.8	98.5
SBRT3	95.0	95.5	99.9	98.9
SBRT4	95.8	93.3	99.1	99.3
SBRT5	98.2	91.2	99.9	98.1
SBRT6	98.9	91.4	99.9	98.7
SBRT7	95.0	94.6	99.8	98.6
SBRT8	98.9	93.9	99.0	97.4
SBRT9	95.5	90.1	99.4	96.3
SBRT10	95.1	92.1	99.8	97.3
Mean±SD	96.8±1.7	93.1 ±1.82	99.7 ±0.38	98.1 ±0.89

PTV – planning target volume, TPS- treatment planning system.

DISCUSSION

In this study, two PSQA methods, viz. independent TPS dose check and log files based QA, were performed and compared for ten VMAT lung SBRT plans. The fast MC algorithm DPM and the variance reduction techniques available in PRIMO helped to achieve a statistical uncertainty of less than 1.5% in all cases. In independent dose verification, PRIMO showed a good agreement for the PTV and OARs DVH parameters against the Acuros®XB algorithm (TPS plans) except for the PTVmax dose. Paganini *et al.* [31] reported a similar average gamma pass rate (98.9 ± 0.6%) between PRIMO MC and Acuros dose calculation for five clinical VMAT plans. Sottiaux *et al.* [32] reported a gamma pass rate above 95% between PRIMO MC and Acuros for eleven VMAT clinical plans.

Tsuruta *et al.* [33] reported good dosimetric agreements between Acuros XB and MC for PTV coverage. There is a slight difference in mass density assignment between the AXB algorithm and the PRIMO MC model when generating the voxelized geometries from a CT data set. Ojala *et al.* [34] suggest avoiding point doses in the dose distribution analysis due to the statistical noise associated with MC simulations. The difference in the maximum dose to PTV is due to the differences in material assignments and the statistical noise associated with MC simulations [35]. Tsuruta *et al.* [33] reported a similar result showing Acuros®XB yielding lower values (within±3%) than the X-ray Voxel MC (XVMC) algorithm in terms of the maximum doses of PTV for Lung SBRT plans. A good agreement of the dose distributions was obtained between the plan imported from the TPS and the plan reconstructed from actual leaf positions, except for the PTVmax dose.

In a similar study conducted by Rodriguez *et al.* [9], the sensitivity of PRIMO dose reconstruction to the errors in the MLC leaf position was extensively evaluated for the prostate and head & neck cases. They conclude that PRIMO dose reconstructions were sensitive to dynalogs with RMS errors ≥ 0.2 mm if the

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errors are predominantly in one direction. RMS > 1.2 mm produced detectable deviations in the dose when errors occurred in both directions. The commercial verification system Mobius3D® agrees with TPS with a mean deviation of less than 1.5% for the PTV in independent dose verification and dynalog based plan verification.Mobius3D® results show a higher mean deviation up to 2.57% for OARs than PRIMO (mean deviation <1.5%). Han *et al.*[36] reported similar results in a dose check and log files-based quality assurance study. There were no significant differences in the PTV coverage, but average dosimetric differences of more than 3% were observed in the OARs. To our knowledge, no published article is available which compares Mobius3D® log-file-based plan reconstruction against full Montecarlo simulation. Gamma index evaluation results demonstrated that independent dose check and log files based QA with PRIMO agree with TPS. Results from tables 4 and 5 show that gamma indices verifications give consistent results for PRIMO. Mobius3D® shows a slightly lower gamma pass rate compared to PRIMO for both PTV and BODY structures. The differences between Mobius and Eclipse are due to differences between the customized and fine-tuned beam models used in Eclipse and PRIMO and the standard beam model used in Mobius.

A phantom study validated Mobius® against Eclipse® TPS by McDonald *et al.*[14] reached in a similar conclusion. The better agreement between TPS and PRIMO is due to Acuros®XB calculations being closer to MC than Collapsed Cone Convolution (CCC) algorithm used in Mobius in bone and lung regions. Han *et al.*[37] reported a similar improvement in dose prediction accuracy for the lung region using the Acuros XB algorithm than the CCC in an MC validation study. MC simulations can provide accurate and complete dose verification in a heterogeneous and low-density area without such limitations. PRIMO's 3D gamma verification capability helps determine the discrepancy that cannot be figured out from DVH based analysis. The limitation of log file-based verification is its inability to detect the error due to the output variation of the treatment machine. Machine log file analysis is a more sensitive tool for verifying the machine's data transfer and delivery performance than measurement-based techniques [4]. A comprehensive measurement-based QA program is required to ensure all machine parameters, including the MLC mechanical calibration, are within tolerance [38].

A study by Teke *et al.*[7] demonstrated that MC based QA using linac log files could be used to assess physical delivery accuracy and dose calculation accuracy in water-equivalent material of VMAT treatments.Sun et al. also concluded in a log-file-based QA study that independent dose calculations and a machine log analysis may be used to complement experimentally based verification methods [4]. The disadvantage of MC-based plan verification is its long calculation time. The DPM code incorporated in PRIMO and the variance reduction techniques help reduce the calculation time. PRIMO may be used as an independent PSQA tool for randomly selected plans from an efficiency perspective. PRIMO can also be used as an audit tool for the performance of the TPS dose calculation algorithm, as it can point out the errors in heterogeneity calculation or beam modelling, which helps to avoid systematic errors in treatment planning. Chen *et al.* [39] , Paganini *et al.* [31] and Fogliata, *et al.* [40] arrived in a similar conclusion from the clinical validation of PRIMO. As Rodriguez *et al.* [9] concluded in a similar study, the advantage of MC-based secondary dose verification for treatment verification is that it does not rely on the dose calculated by the TPS.As MC algorithms are highly accurate in dose calculation, their use in an independent log-based verification system helps identify TPS's dose calculation errors, and errors in TPS's beam data.

CONCLUSION

The independent dose verification, pretreatment QA checks, and log file-based QA showed clinically acceptable agreement between TPS and PRIMO for the VMAT Lung SBRT plans. Better agreement between Acuros®XB and PRIMO MC was found in the case of log-file-based plans reconstruction compared to Mobius3D®. This work has shown that the validated MC model of PRIMO can be used as an accurate secondary dose verification and quality assurance tool for lung SBRT plans.

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