Secondary Dose Verification of Radiotherapy Treatment Plans Using Monte Carlo Simulation

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ABSTRACT

The study aims for independent secondary dose verification of radiotherapy treatment plans generated in a widely used Treatment Planning System (TPS) using a Monte Carlo (MC) simulated model of a medical linear accelerator (linac).MC simulation of a 6MV beam of a Clinac iX® linac was performed using the PRIMO MC simulation software (Version 0.3.64). An output phase-space file has been generated after simulating $5x10^8$ primary photons histories. The simulation beam parameters were validated against measured beam data obtained from the linac. MC dose verification was conducted for ten brain tumour treatment plans. The MC simulation results were validated against Anisotropic Analytical Algorithm (AAA) and either dose reporting mode of the Acuros® XB (dose-to-water (AXB-Dw) dose-to-medium (AXB-Dm) algorithm implemented in a commercial TPS. The analysis was conducted using Dose Volume Histogram (DVH) parameters and Gamma analysis. No statistically significant differences ($p^3 0.05$) were observed for the planning target volume (PTV) DVH parameters for AAA and AXB-Dm algorithms against the MC simulated model. A statistically significant difference ($p<0.05$) was observed for AXB-Dw. Gamma analysis also shows similar differences for the PTV structure for AXB-Dw. MC simulation results of Clinac® iX linac using the PRIMO code show good agreement with measured data. The study demonstrates that the PRIMO Monte Carlo model of Clinac® iX medical linac generated can be used to verify radiation therapy treatment plans developed in a treatment planning system.

Keywords: Monte Carlo simulation, PRIMO Code, Linac, Acuros® XB.

I RESEARCH PROBLEM AND MOTIVATION FOR THE WORK

Radiotherapy treatment planning has shown ongoing advancements in mathematical and computational approaches that aim toward highly accurate dose calculations. Based on dose-response data and an evaluation of dose delivery errors in a clinical setting, the International Commission on Radiation Units and Measurements (ICRU) has recommended an overall accuracy of 5% in tumour dose delivery[1]. For an overall dose delivery accuracy of 5%, a dose calculation algorithm that can predict the dose distribution with 2% accuracy is required due to uncertainties resulting from patient setup, machine calibration, and dose calculation from treatment planning systems. Currently, most algorithms are not able to handle this effectively, particularly in the case of heterogeneous patient tissues, where the effects of electron transport cannot be handled accurately with conventional, deterministic algorithms[2]. While developing treatment plan protocols and multi-institutional quality assurance audits, it is particularly important to assess the accuracy of the dose calculation provided by the algorithm applied. This is because the dose reported may affect the outcome of the study.

II BACKGROUND AND RELATED WORK

Radiotherapy is classified into teletherapy and brachytherapy. In teletherapy, radiation sources are kept at a distance (usually 80-100cm in modern machines) away from the patient's body. The devices used for teletherapy are linear accelerators (LINAC) and cobalt-60 isotope machines (telecobalt machines). Radiation therapy aims to deliver a precisely measured dose of radiation to a defined tumour volume with as minimal damage as possible to surrounding healthy tissue. High radiotherapy dosimetry and radiation treatment planning are essential to achieve this goal. The direct measurements of radiation beam characteristics in a patient body are difficult, as we cannot introduce detectors inside the human body. Mathematical modelling and computer simulations help predict doses inside the patient in such situations. Computer Simulation methods such as Monte Carlo simulations are well-established methods for solving many radiation transport problems in nuclear and particle physics[3–6]. A continual improvement can be seen in mathematical and computational techniques involved in radiotherapy treatment planning that aim at highly accurate dose calculations. MC-based calculations have been used to increase the accuracy of the simulation of radiation dose delivery since the 1980s[3]. A number of studies have concluded that MC simulation techniques are the gold standard for determining radiation absorbed doses[4][7]. For the spatial distribution of absorbed dose in heterogeneous media, MC techniques are capable of providing highly accurate results, and thus they are considered a benchmark for dose calculation accuracy[3,4,7].

MC systems are utilized as a secondary check to ensure that the verification process is completely independent of the TPS. A Monte Carlo dose calculation involves simulating each ionizing particle (generally photons and electrons) through the volume to be treated. Hence, they are considered more accurate than analytical calculation methods used in TPS. A Monte Carlo simulation results involve statistical uncertainties, which can be reduced by simulating more particle histories. The disadvantage of the long calculation time required to achieve an acceptable statistical uncertainty in dose calculation has been resolved by the development of fast MC codes such as Macro MC[8], Voxel MC[9] and dose planning method (DPM)[10].

Several general-purpose Monte Carlo codes have been developed for the simulation of the radiation transport of photons and charged particles (e.g. EGSnrc[11],PENELOPE[12],MCNP[13],and Geant4[14]). A MC package, called Primo[15], can perform simulations of most medical linear accelerators. The program is based on the MC code PENELOPE. The fast MC simulation package for coupled electron and photon transport called DPM is incorporated in PRIMO. This graphical user interface combines all these features into a user-friendly environment. Primo can be used for the complete MC simulation of most linacs and estimating the dose distribution in water phantoms and computed tomography (CT). Most of the Varian medical linac (Varian Medical Systems, Palo Alto, USA) geometries are incorporated in the Primo package. In Primo, the distribution of primary electrons hitting the target is defined as a Gaussian distribution. To initiate the simulation, the user must input the primary electron beam energy values, initial energy Full Width at Half Maximum (FWHM), focal spot size FWHM, and beam divergence. The Primo code suggests a set of default values for the initial beam parameters that must be fine-tuned until the best match between simulation and physical measurement is achieved. The CT images, structure contours and treatment plan in DICOM format can be imported into PRIMO from an external TPS. The techniques used to speed up MC simulations are generally referred to as variance reduction techniques (VRTs). The VRTs incorporated in Primo helps to improve the simulation efficiency by reducing the simulation time and statistical uncertainties associated with the simulation. The information of the particles at a location in the simulation geometry is saved in a phase-space (PHSP) file. PHSP files are generally tallied at a plane perpendicular to the beam's central axis. The energy, position, direction, and user-defined parameters of the particles traversing this plane are recorded. The PHSP file or the dose distribution can be tallied in a simulation. Primo allows importing or linking the PHSP in the International Atomic Energy Agency (IAEA) format[16].

Acuros® XB (AXB) and anisotropic analytical algorithms (AAA) dose calculation algorithm implemented in the Eclipse® TPS (Varian Medical Systems, Palo Alto, USA) were used in this study. Several studies investigating the dosimetric accuracy of AXB concludes that it is a fast and accurate alternative to MC for patient dose calculations[17][18][19]. Several publications have extensively validated MC simulation for complex techniques such as Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated arc Therapy (VMAT)[18][20][7]. AXB has two dose reporting modes: dose-to-water (Dw) and dose-to-medium (Dm). The question of which dose reporting mode should be used at different anatomical sites remains controversial[21]. In this study, dose-volumetric data of AAA and either dose reporting mode of the AXB were compared against MC simulated data.

III APPROACH AND UNIQUENESS

(a) Simulation setup - The study was conducted using the PROMO simulation software version 0.3.64 (http://www.primoproject.net). It is necessary to generate MC beam models of the linear accelerator and validate beam parameters against physical measurements before using the models for simulations of treatment plans. The full MC simulation of the 6MV photon beam of the linear accelerator installed in our centre Clinac®iX (Varian Medical Systems, Palo Alto, USA) linac was performed using the PRIMO. The validation of the Clinac® iX MC model was carried out by comparing the simulated percentage depth dose (PDD) and beam profile curves against the measured data. The tuning of initial simulation parameters for the 6MV photon beam model of Clinac® iX and its validation has been described in detail in our previous publication[22].The validated MC model of Clinac®Ix has been used for all the treatment plan simulations performed in this study. In PROMO, PHSP files are tallied at three different positions. The Clinac iX PHSP file tallied at the lower end of the upper part of the linear accelerator above the jaws was used as the radiation source for the treatment plan simulations, which avoids repeating the treatment field independent part of the simulation. The patient treatment plan dependent part of the simulation was subsequently carried out and the dose was estimated in patient geometry. The particle splitting technique for variance reduction was applied in the simulation of patient geometry. The optimal value of the splitting factor must be found through an iterative process. Simulations were performed on a Dell T5600 workstation with 32 GB of RAM and 24 CPU cores operating at 2.0 GHz. the simulation efficiency ε is calculated using Equation 1. The simulation interface of PRIMO is shown in Figure 1.

$$\varepsilon = \frac{1}{\Delta^2 t} \quad \text{Eq. (1)}$$

In the above formula, Δ is the statistical uncertainty achieved in a simulation time of t seconds. PRIMO calculates the average statistical uncertainty of all voxels that accumulate more than half of the maximum amount of absorbed dose.

Fig. 1:The Simulation interface of PRIMO

(b) Absorbed dose calculation - The absolute dose (D) in Gray (Gy) was calculated in PRIMO according to Equation 2.

$$D = \frac{D_{exp}^{ref}}{MU^{ref}} \frac{D_{MC}}{D_{MC}^{ref}} MU \quad \text{Eq.(2)}$$

Where D_{exp}^{ref} is the dose in Gy obtained from physical measurements in a water phantom under reference conditions. D_{MC}^{ref} is the dose estimated by a MC simulation (in eV/g per history) under the same 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.

(c) Clinical Plan Simulation -This retrospective dosimetric study included ten brain tumour treatment plans previously treated with Volumetric Arc Therapy (VMAT) at our centre. The CT images of the patients were acquired in a GE OptimaTM CT scanner (GE Healthcare, Waukesha, WI) at 2.5 mm slice spacing. Clinically acceptable VMAT treatment plans were generated in Eclipse® TPS (Version 15.6). AXB algorithm (Version15.6) was used for dose calculations. The plans were planned and delivered using the Clinac® iX linac. The dose prescription for the Brain tumour cases was 54 gray (Gy) in 30 fractions.

VMAT plans, CT images, and structures were exported from Eclipse® TPS in DICOM format and imported into PRIMO for MC calculations. Before each simulation, voxelized simulation geometry with the material type and mass density of every voxel in the CT image was created in PRIMO. Voxelized geometry has been created using a set of six materials (air, lung ICRP, adipose tissue, Brain (ICRP), muscle-skeletal, cartilage and compact bone) from the material assignment library in PRIMO and the CT number-to-mass density conversion curve available in PRIMO. The plans were simulated in PRIMO with the same beam settings and Monitor Units of the original TPS plan. Figure 2 shows the CT number to mass density conversion table, materials selected to generate voxelized geometry and the composite image of a CT slice after generating voxelized geometry. Figure 3 shows the MC simulated dose distribution in the axial, sagittal, and coronal planes.

(d) Plan Validation - The plan comparison was performed using the plan evaluation interface provided in PRIMO. The TPS calculated 3D-dose data in DICOM RT format was imported into PRIMO for comparison. The DVH based plan comparison was performed for PTV and OARs.

The following dosimetric parameters were extracted from DVH for plan comparison:

(i) Mean dose to the PTV (PTVmean).
(ii) Maximum dose (dose to 0.2 cm^3) to the PTV (PTVmax).
(iii) Dose received by 98% of the PTV (D98%).
(iv) Mean dose to the Brain (BRAINmean).
(v) Conformity index (CI) for PTV.
(vi) Homogeneity index (HI) for PTV.

CI determines how closely a dose conforms to its target and is determined using Equation 3 as described in the Radiation Therapy Oncology Group (RTOG) guidelines. Homogeneity index (HI) quantifies the homogeneity in dose distribution in the target volume and is determined using Equation 4 as pet the American Association of Physicists in Medicine (AAPM) Task Group 101 protocol. A lower HI value indicates more homogeneity in dose distribution.

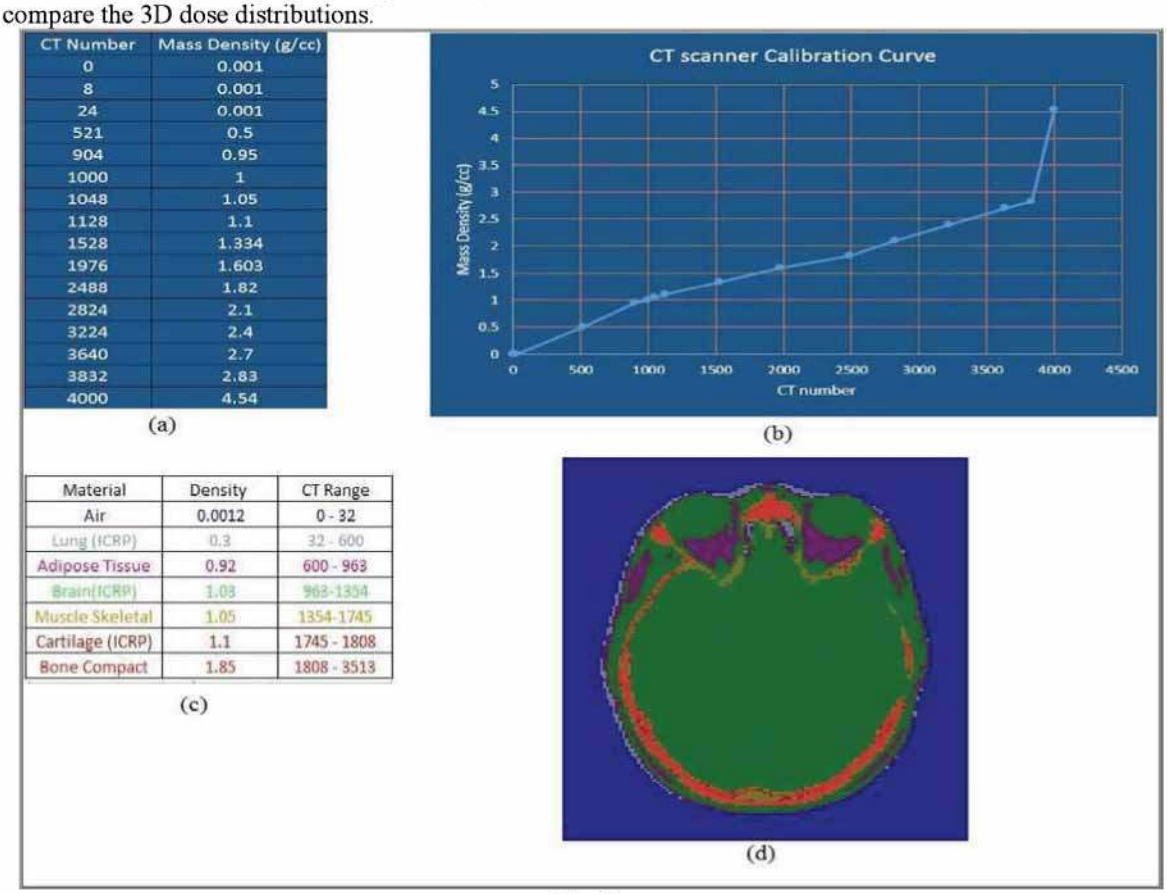
$$CI = \frac{Total\ volume\ of\ tissue\ receiving\ the\ prescribed\ dose}{Volume\ of\ PTV\ receiving\ the\ prescribed\ dose} \quad \text{Eq. (3)}$$

$$HI = \frac{D_5}{D_{95}} \quad \text{Eq. (4)}$$

D_5 = minimum dose to 5% of the target volume, D_{95} = minimum dose to the 95% of the target volume.

The gamma analysis[23] method performs a point by point evaluation of the coincidence between the calculated and measured dose distributions. The gamma analysis method with 2%, 2mm acceptance criteria (2% dose difference and 2 mm distance-to-agreement) was used to compare the 3D dose distributions.

(e) Statistical Analysis - In order to determine the feasibility of the statistical tests, data were tested for normality using the Shapiro-Wilk test. A two-tailed t-test (Wilcoxon signed-rank test) was conducted with SPSS 20.0 (IBM, Armonk, NY, USA) to compare the two plans. A p-value of < 0.05 is considered statistically significant.



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
Brain(ICRP)	1.03	963-1354
Muscle Skeletal	1.05	1354-1745
Cartilage (ICRP)	1.1	1745 - 1808
Bone Compact	1.85	1808 - 3513

(c)

(d)

Fig. 2:

a) CT number and corresponding mass density values.

b) CT number to mass density conversion curve.

c) Materials used to generate voxelized geometry and their corresponding CT number d) Blended image of a CT slice and assigned materials (Material corresponding to each colour is given in figure (c)).

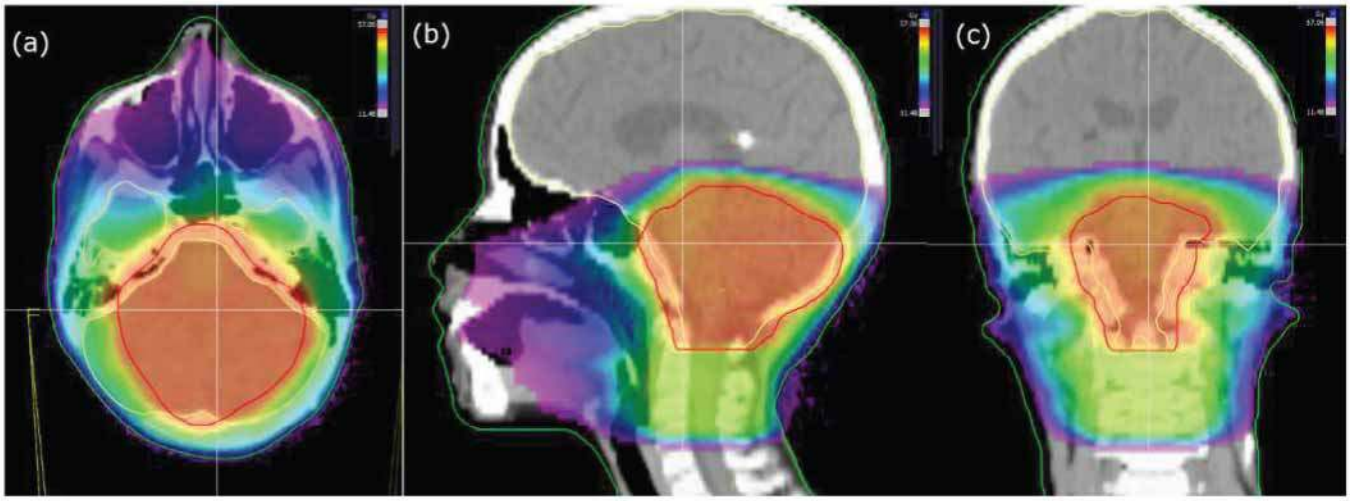


Fig. 3: The PRIMO simulated dose distribution for a Brain plan in the axial (fig-a), sagittal (fig-b) and coronal (fig-c) planes.

IV RESULTS AND CONTRIBUTIONS

A simulation was run for 5×10^8 histories. The simulation time will vary depending on the beam size, the number of beams, and the control points. For all cases, the average statistical uncertainty of the dose distributions obtained was ≤ 1.5%. The simulation time required to obtain the above uncertainty varies between 3.5 and 4.5 hours.

The results of the comparison between MC and Eclipse® TPS were presented in the form of mean±standard deviation (SD). A comparison of DVH of the PTV between TPS algorithms and MC simulation is shown in the Figure 4. The dosimetric differences in DVH parameters for PTV and Brain are tabulated. The comparison between MC simulation and AXB dose-to-medium (AXB-Dm) reporting mode is given in Table 1 and dose-to-water (AXB-Dw) reporting mode is given in Table 2. The comparison between MC simulation and AAA is given in Table 3.

Table 1
Comparison of DVH parameters between PRIMO simulation and TPS (AXB-Dm).

DVH parameter	TPS (AXB-Dm) Mean±SD	MC (PRIMO) Mean±SD	Difference (%) Mean±SD	p-Value
PTV_{mean} (Gy)	55.01 ± 0.56	54.92 ± 0.70	-0.17 ± 0.60	0.28
PTV_{max} (Gy)	57.09 ± 0.87	57.37 ± 0.91	0.48 ± 0.33	0.01
PTV D_{98} (Gy)	50.83 ± 1.72	50.36 ± 2.04	-0.95 ± 1.28	0.09
PTV D_{95} (Gy)	53.07 ± 2.08	52.55 ± 2.39	-1.03 ± 1.27	0.07
PTV D_{50} (Gy)	55.30 ± 0.95	55.09 ± 0.89	-0.38 ± 0.73	0.10
$Brain_{mean}$ (Gy)	19.72 ± 2.30	19.89 ± 2.26	0.84 ± 2.23	0.14
CI	0.88 ± 0.08	0.87 ± 0.10	-1.94 ± 5.18	0.36
HI	1.06 ± 0.06	1.06 ± 0.08	0.66 ± 2.06	0.25

DVH – dose-volume histogram, Gy- gray, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system, MC- Monte Carlo.

Table 2
Comparison of DVH parameters between PRIMO simulation and TPS (AXB-Dw).

DVH parameter	TPS (AXB-Dw) Mean±SD	MC (PRIMO) Mean±SD	Difference (%) Mean±SD	p-Value
PTV_{mean} (Gy)	56.22 ± 0.57	54.92 ± 0.70	-2.37 ± 0.54	0.01
PTV_{max} (Gy)	59.97 ± 1.28	57.37 ± 0.91	-4.55 ± 2.35	0.01
PTV D_{98} (Gy)	52.88 ± 2.43	50.36 ± 2.04	-5.01 ± 2.87	0.01
PTV D_{95} (Gy)	54.50 ± 1.44	52.55 ± 2.39	-3.85 ± 3.59	0.02
PTV D_{50} (Gy)	56.58 ± 0.65	55.09 ± 0.89	-2.71 ± 1.49	0.01
Brain $_{mean}$ (Gy)	20.01 ± 2.37	19.89 ± 2.26	-0.59 ± 2.81	0.34
CI	1.03 ± 0.09	0.87 ± 0.10	-19.20 ± 5.13	0.01
HI	1.07 ± 0.05	1.06 ± 0.08	-1.18 ± 6.38	0.89

DVH – dose-volume histogram, Gy- gray, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system, MC- Monte Carlo.

Table 3
Comparison of DVH parameters between PRIMO simulation and TPS (AAA).

DVH parameter	TPS (AAA) Mean±SD	MC (PRIMO) Mean±SD	Difference (%) Mean±SD	p-Value
PTV_{mean} (Gy)	54.97 ± 0.52	54.92 ± 0.70	-0.08 ± 0.53	0.58
PTV_{max} (Gy)	56.84 ± 0.78	57.37 ± 0.91	0.91 ± 1.24	0.05
PTV D_{98} (Gy)	51.19 ± 2.78	50.36 ± 2.04	-1.60 ± 2.43	0.06
PTV D_{95} (Gy)	53.24 ± 1.40	52.55 ± 2.39	-1.43 ± 3.58	0.11
PTV D_{50} (Gy)	55.53 ± 0.55	55.09 ± 0.89	-0.82 ± 1.37	0.05
Brain $_{mean}$ (Gy)	20.07 ± 2.35	19.89 ± 2.26	-0.92 ± 3.65	0.45
CI	0.90 ± 0.08	0.87 ± 0.10	-2.77 ± 4.07	0.07
HI	1.05 ± 0.05	1.06 ± 0.08	0.65 ± 5.93	0.28

DVH – dose-volume histogram, Gy- gray, PTV – planning target volume, SD- standard deviation, TPS- treatment planning system, MC- Monte Carlo.

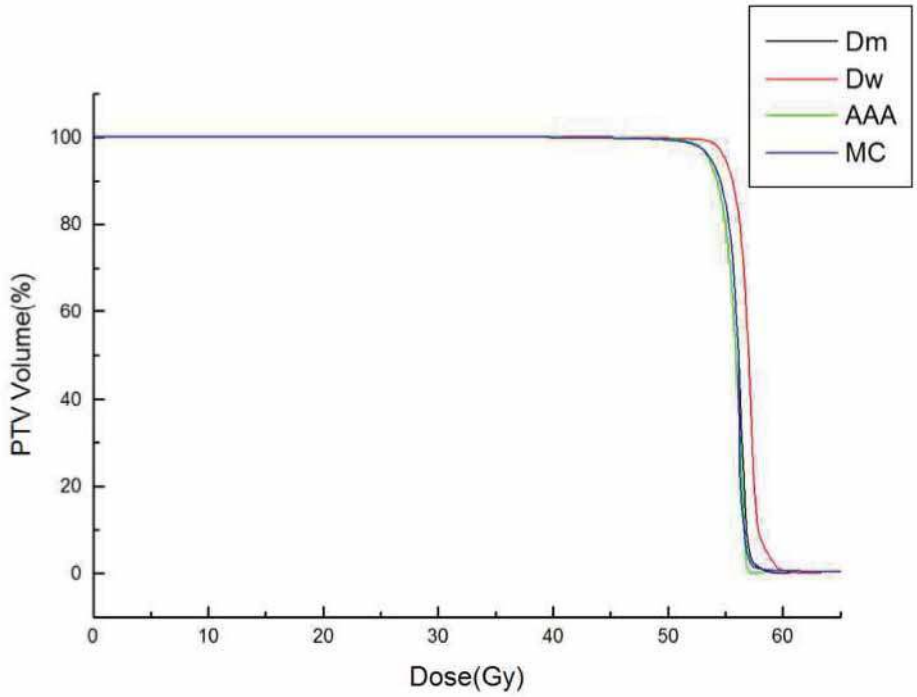


Fig. 4: Dose volume histogram comparisons of PTV doses between TPS algorithms and Monte Carlo.

Figure 5 shows the gamma analysis between MC and two different dose reporting modes of AXB for a patient. The orange shaded areas represent high gamma failures. Table 4 shows the gamma pass rate for comparing TPS algorithms against MC for the PTV structure. The histogram of gamma analysis results for ten patients is shown in figure 6.

Table 4
Gamma Pass rates for the PTV structure.

Patient No.	Gamma Pass rate (%)		
	AXB-Dm	AXB-Dw	AAA
1	99.84	79.90	98.29
2	99.61	94.52	96.92
3	98.89	83.74	95.15
4	98.54	87.68	97.06
5	98.82	87.78	96.34
6	98.95	62.67	97.32
7	99.51	79.07	99.82
8	99.56	94.02	98.20
9	99.93	84.16	97.96
10	99.86	84.10	97.89
Mean±SD	99.35 ± 0.5	83.76 ± 9.03	97.49 ± 1.36

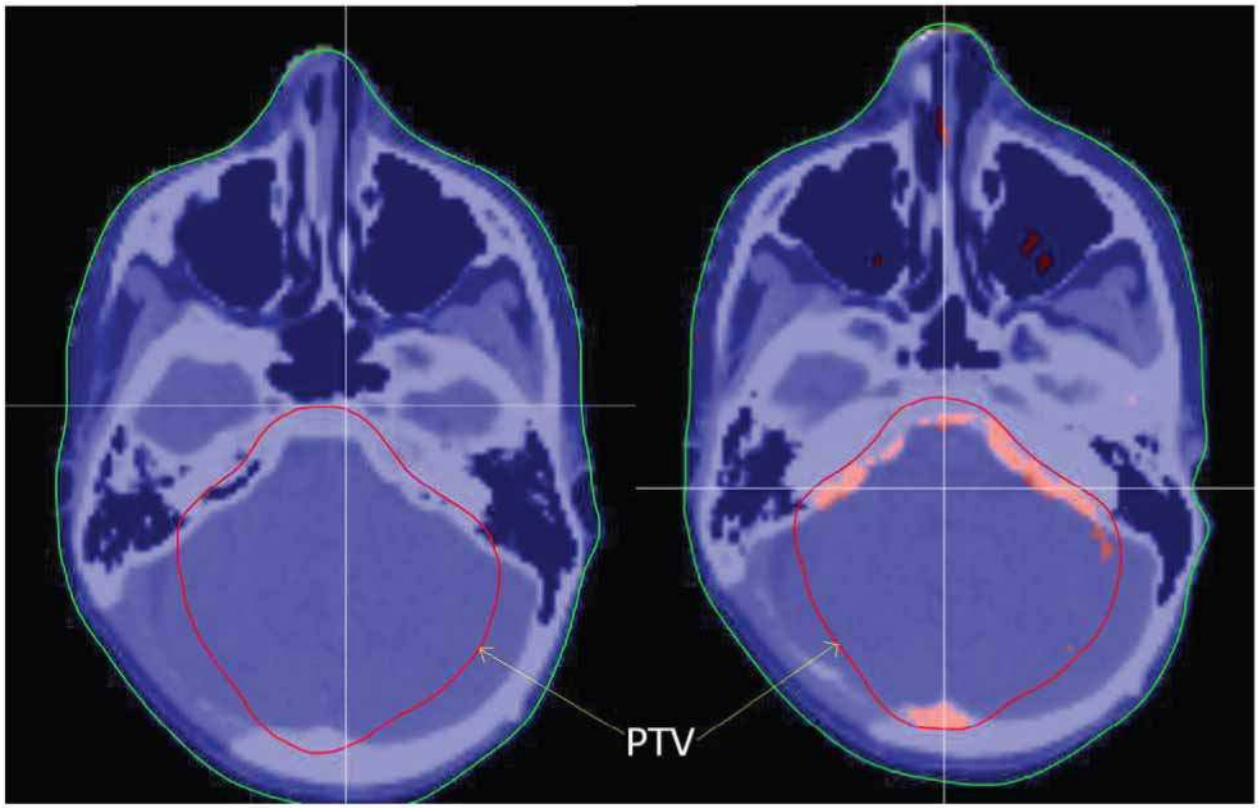


Fig. 5: Gamma analysis map for an axial slice. MC Vs AXB-Dm (Left) and MC Vs AXB-Dw (Right).

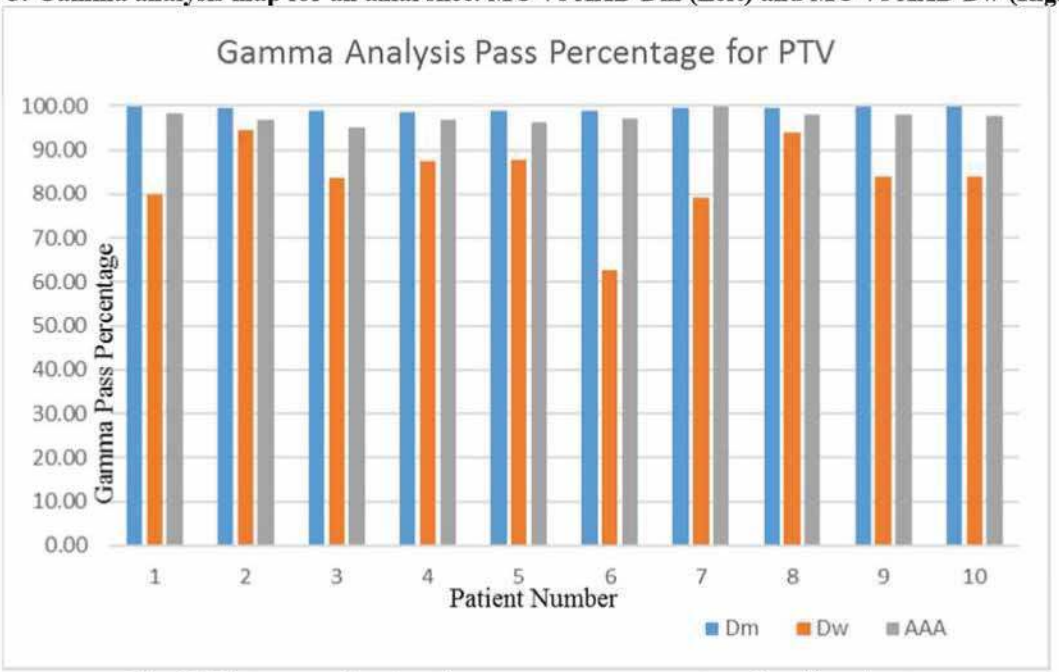


Fig. 6: Histogram showing the gamma pass percentage for 10 patients.

V DISCUSSIONS

This study evaluated the accuracy of the dose distributions obtained with the MC simulated model against TPS algorithms currently used in radiotherapy treatment planning. The comparison of MC simulation against AXB - Dm reporting mode shows no statistically significant differences ($p>0.05$) in the DVH parameters PTVmean, PTV D98, PTV D95, PTV D50, Brain mean, CI, and HI. The maximum differences between MC and AXB-Dm for the PTV and Brain were less than 2%. A significant difference was observed for the PTVmax dose ($p\leq0.05$). The comparison of MC simulation against the AAA algorithm also shows no significant difference in

DVH parameters. The maximum difference observed was less than 3%. The difference observed in maximum dose between MC and AXB-Dm is due to the slight difference in the mass density assignment between the AXB algorithm and the PRIMO MC model when the voxelized geometries are derived from CT data [24]. Ojala et al.[25] suggest avoiding point doses due to the statistical noise associated with MC simulations in the dose distribution analysis. The maximum differences between MC and AXB-Dm for the PTV and Brain were less than 2%. The gamma analysis also agrees with MC for both AXB-Dm and AAA algorithms. The minimum gamma pass rate was 98.5% for AXB-Dm and 95% for AAA.

The comparison of MC simulations against AXB-Dw in Table 2 shows a statistically significant deviation in DVH parameters for PTV and Brain structures. The DVH curve in Figure 4 shows a 2 -3% overestimation of dose to PTV structure in the case of AXB-Dw compared to other algorithms. The gamma analysis results in Figure 5 shows a significant dose difference in high-density bone regions for AXB-Dw. Similar overestimation of dose by AXB-Dw has also been reported in other publications[26,27].

Overall, no clinically significant dose differences were observed between our MC simulated model and commercial treatment planning algorithms AXB-Dw and AAA. The differences between AXB-Dw and MC have a little clinical impact on tissue-like media. The differences may become clinically significant if bony structures are involved in the planning volume.

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