Dosimetric Influence of Acuros XB Dose-to-Medium and Dose-to-Water Reporting Modes on Carcinoma Cervix Using Intensity-Modulated Radiation Therapy and Volumetric RapidArc Technique

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Abstract

Aim: We aimed to evaluate the dosimetric influence of Acuros XB (AXB) dose-to-medium (D_m) and dose-to-water (D_w) reporting mode on carcinoma cervix using intensity-modulated radiation therapy (IMRT) and RapidArc (RA) technique. **Materials and Methods:** A cohort of thirty patients cared for carcinoma cervix was retrospectively selected for the study. Plans were computed using analytical anisotropic algorithm (AAA), AXB-D_m, and AXB-D_w algorithms for dosimetric comparison. A paired *t*-test and Pitman–Morgan dispersion test were executed to appraise the difference in mean values and the inter-patient variability of the differences. **Results:** The dose–volume parameters were higher for AXB-D_w in contrast to AAA for IMRT and RA plans, excluding $D_{98\%}$, minimum dose to planning target volume (PTV) and rectum mean dose (RA). There was no systematic trend observed in dose–volume parameters for PTV and organs at risk (OARs) between AXB-D_m and AXB-D_w for IMRT and RA plans. The dose–volume parameters for target were higher for AXB-D_m in comparison to AAA in IMRT and RA plans, except $D_{98\%}$ and minimum dose to PTV. Analysis envisaged less inter-patient variability while switching from AAA to AXB-D_m in comparison to those switching from AAA to AXB-D_w. **Conclusions:** The present study reveals the important difference between AAA, AXB-D_m, and AXB-D_w computations for cervix carcinoma using IMRT and RA techniques. The inter-patient variability and systematic difference in dose–volume parameters computed using AAA, AXB-D_m, and AXB-D_w algorithms present the possible impact on the dose prescription to PTV and their relative constraints to OARs for IMRT and RA techniques. This may help in the decision-making in clinic while switching from AAA to AXB (D_m or D_w) algorithm for cervix carcinoma using IMRT and RA techniques.

Keywords: Algorithm, cervix carcinoma, intensity-modulated radiation therapy, planning, RapidArc

INTRODUCTION

In the wake of recent advancements in radiation therapy (RT), intensity-modulated radiation therapy (IMRT) and RapidArc (RA) utilize numerous small beamlets to modulate the radiation beam to be delivered to cancer patients. IMRT and RA techniques are better at promoting organs at risk (OARs) sparing while delivering the intended radiation doses to the tumor targets. To achieve the optimal therapeutic benefit of radiation, IMRT and RA techniques require a precise dose computation engine which can perform a nuanced calculation of the modulations that the radiation beam undergoes when it passes through the heterogeneous medium encountered inside the human body.

Radiation transport and their dose deposition patterns in the medium have direct influence on the dose computation

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accuracy of a dose calculation engine.[1] Accuracy of dose estimation and reporting is an inherent feature of a dose computation engine. The American Association of Physicists in Medicine Task Group-329 has detailed about how various commercially available treatment planning systems (TPSs) deal with radiation transport and their dose deposition patterns in the clinic.[2] Dose reporting (dose-to-water ["D_w"] and dose-to-medium ["D_m"]) is also a concern of utmost importance in contemporary clinic, as the International Atomic Energy Agency advocated the accuracy related to such systematic dosimetric issues should be organized within 1%–2%.[3] Tissues have different chemical composition than water, resulting in different electron and photon interaction cross-sections. This in turn leads to difference in dose reported by different dose engines. Bragg–Gray cavity principle has been utilized to derive D_w from the D_m using unrestricted water to medium mass collision stopping power averaged over the energy spectra of primary electrons at a particular point.[4] Apart from this, radiation beam size used for the treatment, incident photon energy, and density of medium has a direct impact on the radiation dose estimations. The precision of a dose calculation engine may have a huge impact on the radiation treatment outcome. With the advancements in the simulation and computation techniques, dose computation engines too have evolved with time. The dose calculation engine has been categorized into the following three categories: correction-based (type "a"), model-based (type "b"), and grid-based linear Boltzmann transport equation (LBTE) solver (type "c").

The Acuros XB (AXB) algorithm is a grid-based LBTE solver that models the particle fluence for the interaction events occurring between radiation and matter. The AXB provides the deterministic solutions to the LBTE using iterative approach and applies medium appropriate-stopping power for obtaining the dose.[5] The AXB solutions are akin to the gold standard, "Monte Carlo" solution for dose calculations in RT. The potential influence of AXB on various clinical sites has been reported in the literature, namely lung cancer,[6,7] nasopharyngeal carcinoma,[8-11] breast sarcoma,[12-14] and prostate cancer.[15,16] Rana *et al.*[15] and Koo *et al.*[16] reported that AXB deals more accurately with heterogeneity present for prostate cancer in comparison to analytical anisotropic algorithm (AAA) using RA technique.

Cervix carcinoma is a leading cause of morbidity among women, and RT forms an integral part of the treatment strategies in its management, especially in locally advanced cases. The radiation beams used for treatment of carcinoma cervix have to encounter a heterogeneous medium comprising air, bone, muscle, and soft tissues owing to its anatomical location. In this context, the present study aims to perform a comprehensive analysis of AXB and AAA computed dose distribution in patients suffering from carcinoma cervix using IMRT and RA technique and also investigate the potential impact of AXB computation on cervix carcinoma (for both dose-reporting modes, namely "D_m" and "D_w"). The analysis

was executed based on the systematic as well as inter-patient variability between AXB and AAA algorithms. The present study tried to investigate whether switching from AAA to AXB has any bearing on prescription and dose–volume reporting for planning target volume (PTV) and OARs in carcinoma cervix radiotherapy.

MATERIALS AND METHODS

Patient selection, target delineation, and dose prescription

A cohort of thirty patients suffering with cervix carcinoma (stages II–IIIB) and treated using RA and IMRT techniques were selected retrospectively. The appropriate accessories were used for patient immobilization and reproducibility of the treatment setup. The computed tomography (CT) scans were executed with a Siemens SOMATOM Sensation Open CT Scanner (Siemens Medical Systems, Germany) with full bladder as per departmental protocol using slice thickness of 3.0 mm. The target volume delineation was performed on the CT images as per the Radiation Therapy Oncology Group (RTOG) guidelines.[17] The clinical target volume (CTV) included the cervix, uterus, and pelvic nodes including presacral and parametrial tissues. A margin of 5.0 mm was used isotropically to CTV to create PTV. The following OARs were also delineated: bowel, bladder, rectum, and femoral heads as per the standard RTOG definitions. The radiation treatment plans were optimized to deliver a prescription dose (PD) of 50.4 Gray (Gy) to the PTV in 28 fractions. The planning goal was to distribute 100% PD to the 95% of PTV with no more than 5% of PTV volume receiving 110% of PD. The dose to bladder and rectum was optimized in such a manner that $V_{50\,Gy}$ (volume receiving 50 Gy) should be less than 50% of OAR volume.

Planning and dose computation

Treatment plans were generated using a 6 MV photon beam with a Millennium 120 multileaf collimator (MLC) using RA and IMRT techniques in Eclipse TPS version 11 (Varian Medical Systems, Palo Alto, USA). The IMRT plans were optimized for gantry angles: 60°, 100°, 135°, 180°, 225°, 260°, and 300° without any collimator rotation, and RA plans were optimized using clockwise (CW, 179–181) and counterclockwise (CCW, 181–179) with collimator rotation of 10°–30°. The normal tissue objective was used in optimization process to spare the normal tissue. The Eclipse uses a separate optimizer, direct volume optimizer (DVO) for IMRT and progressive resolution optimizer for RA to play with the fluence map to achieve a clinically acceptable plan in adherence to the prescribed constraints. For IMRT, DVO optimizes the contour and intensity of radiation field using the simple gradient optimization approach to obtain the required dose–volume objectives. Further, the fluences were back-projected from the derivatives of the costs at each cloud point characterizing the patient volume. For RA, RPO optimizer is hinged on the postulation that complex issues like optimization of continuous variables, for example, MLC contour, MLC positions, and segment weights, pivot on the control point segmentation

of the intact arc angle and could be illuminated in steps of continuously expanding the resolution without negotiating outcome accuracy. All treatment plans were computed using AAA and AXB version 11 under identical gantry and MLC setup. A grid resolution of 0.25 cm × 0.25 cm × 0.25 cm was utilized for dose computation for all treatment plans.

Evaluation parameters

Treatment plans were estimated using the dose–volume histogram (DVH). PTV was evaluated regarding mean dose, $D_{95\%}$ (dose to the 95% volume), $D_{98\%}$, $D_{50\%}$, $D_{2\%}$, $V_{110\%}$ (volume receiving 110% of the PD), and maximum and minimum doses. The dose distribution was estimated utilizing the homogeneity index (HI), expressed as $(D_{2\%} - D_{98\%})/D_{50\%}$,[18] and conformity index (CI), expressed as (95% isodose volume/PTV volume).[19] The dose falloff around the PTV was assessed using gradient measure (GM),[20] defined as the ratio of 50% and 100% prescription isodose volumes. The integral dose to the healthy tissue, i.e., normal tissue integral dose (NTID) is defined as area under the plot of differential absolute-dose, absolute-volume. NTID is estimated as product of mean dose and volume of healthy tissue outside the PTV, considering tissue having uniform density.[20] The mean, maximum dose, and $D_{2\%}$ were estimated for OARs including $V_{50\,Gy}$ for bladder and rectum using DVH data.

Statistical analysis

A detailed analysis was performed to examine the statistical difference between dose distributions calculated using AAA and AXB (D_m and D_w) and their consistency across all the patients. The analysis was executed using a two-sample paired *t*-test (IBM SPSS version 20 [Armonk, NY: IBM Corp]) and Pitman–Morgan dispersion test (R Software version 3.4.2 [R Foundation for Statistical Computing, Austria]). $P < 0.05$ was regarded as statistically significant with confidence limit of 95%.

Pitman–Morgan test evaluates whether the ratio of variances of all dose–volume parameters was equivalent to one, looking at the comparison of AAA and AXB-D_m, AAA and AXB-D_w, and AXB-D_m and AXB-D_w. As indicated in strategy proposed by Muñoz-Montplet *et al.*,[11] two situations can be distinguished when changing from AAA to AXB (D_w or D_m) to support choice making:

(a) Inter-patient variability in dose–volume parameters is nonsignificant: The differences in the variances of respective dose–volume parameters were not statistically significant as a result of which a basic transformation factor can be used to determine dose prescriptions while switching between AXB and AAA computations

(b) Inter-patient variability in dose–volume parameters is significant: AXB cannot be a just scaled interpretation of AAA for this situation. No straightforward suggestions can be proposed.

RESULTS

The present study analyzed the 180 treatment plans of 30 patients suffering from cervix carcinoma. Table 1a and b summarizes the dosimetric parameters for IMRT, Table 2a and b summarizes the dosimetric parameters for RA plans computed utilizing AAA and AXB (D_m and D_w), respectively. Tables 3a and b encapsulate the categorization of dose–volume parameters while switching from AAA to AXB-D_m computation as per the significance of the two statistical tests.

Analytical anisotropic algorithm versus Acuros XB dose-to-medium

For similar PTV coverage, there were slight decrease in mean, maximum, $D_{50\%}$, $D_{2\%}$, and $V_{110\%}$ and increase in $D_{98\%}$ and minimum dose for AAA-calculated IMRT and RA plans in comparison to AXB-D_m. The inter-patient variability was also nonsignificant except PTV $D_{95\%}$ (IMRT and RA), $D_{98\%}$ (RA), $D_{50\%}$ (IMRT), and $V_{110\%}$ (IMRT and RA).

For OARs, an increase in mean dose was observed for AAA-calculated IMRT and RA plans, except mean rectum dose in IMRT. The observed differences between two algorithms were larger for $V_{50\,Gy}$ bladder (IMRT: 1.37% and RA: 1.01%), $V_{50\,Gy}$ rectum (IMRT: 6.57% and RA: 3.81%), and $D_{2\%}$ for both femoral heads (right femur [IMRT: 1.04% and RA: 1.61%] and left femur [IMRT: 1.13% and RA: 1.43%]). In addition, inter-patient variability was also nonsignificant for most of the OARs, except mean rectum dose using IMRT technique, maximum dose to the bowel, and $D_{2\%}$ for bowel and left femoral head using RA technique, respectively.

The difference between both the algorithms was mainly with respect to NTID (IMRT: 0.06% and RA: 0.43%), MUs (IMRT: 1.14% and RA: 1.00%), CI (IMRT: 0.50% and RA: 1.00%), HI (IMRT: 6.33% and RA: 7.91%), and GM (IMRT: 0.15% and RA: 0.93%), respectively.

Analytical anisotropic algorithm versus Acuros XB dose-to-water

For similar PTV coverage, the two algorithms differed with respect to $D_{2\%}$ (IMRT: 0.85% and RA: 0.83%) and maximum dose inside PTV (IMRT: 1.64% and RA: 2.76%). The variability among patients was also nonsignificant excluding $D_{50\%}$ (IMRT), $D_{95\%}$, and $D_{2\%}$ for RA and $V_{110\%}$ (IMRT and RA), respectively.

For OARs, observed differences between two algorithms were for $V_{50\,Gy}$ bladder (IMRT: 2.83% and RA: 3.70%), $V_{50\,Gy}$ rectum (IMRT: 3.84% and RA: 0.93%), and $D_{2\%}$ for both femoral heads (right femur [IMRT: 2.06% and RA: 1.79%] and left femur [IMRT: 2.63% and RA: 2.52%]), respectively. The variability among patients was also nonsignificant excluding mean dose to bladder and both femoral heads and $D_{2\%}$ to bowel for IMRT and maximum dose to bladder, bowel, and both femoral heads for RA, respectively.

The differences observed between the two algorithms were with reference to NTID (IMRT: 0.51% and RA: 1.10%), MUs (IMRT: 0.28% and RA: 0.23%), CI (IMRT: 1.43% and RA: 2.23%), HI (IMRT: 7.03% and RA: 9.31%), and GM (IMRT: 2.51% and RA: 3.22%), respectively.

Table 1a: Dose-volume parameters for planning target volume using intensity-modulated radiation therapy technique for anisotropic analytical algorithm, Acuros XB dose-to-medium, and Acuros XB dose-to-water computations along with their systematic and inter-patient variability analysis

Structure	Parameters	AAA	AXB-D_m	AXB-D_w	P					
					AAA versus D_m		AAA versus D_w		D_m versus D_w	
PTV	Mean	52.53±0.36	52.73±0.37	52.63±0.34	0.000	0.514	0.001	0.350	0.000	0.194
	D_{95}	50.40±0.01	50.40±0.01	50.40±0.01	0.575	0.039	0.528	0.884	0.246	0.063
	D_{98}	49.48±0.25	49.42±0.28	49.46±0.25	0.010	0.200	0.114	0.896	0.358	0.264
	D_{50}	52.55±0.62	52.80±0.42	52.63±0.38	0.023	0.028	0.000	0.005	0.397	0.213
	D_2	55.08±0.73	55.49±0.71	55.56±0.67	0.000	0.762	0.188	0.203	0.000	0.352
	V_{110}	1.82±2.21	3.03±3.63	2.96±2.68	0.001	0.000	0.799	0.001	0.000	0.000
	Maximum	58.70±1.46	59.04±1.24	59.69±1.60	0.029	0.128	0.013	0.463	0.000	0.107
	Minimum	42.13±2.53	41.31±2.54	41.83±2.66	0.010	0.953	0.096	0.338	0.038	0.702
NTID		311.10±56.44	311.51±57.60	309.79±57.58	0.525	0.223	0.000	0.256	0.099	0.716
MUs		1644.66±300.29	1663.20±299.63	1649.70±304.32	0.000	0.730	0.000	0.135	0.067	0.014
CI		1.027±0.028	1.032±0.029	1.042±0.031	0.029	0.630	0.000	0.124	0.000	0.268
HI		0.107±0.016	0.115±0.016	0.116±0.014	0.000	0.911	0.000	0.183	0.467	0.283
GM		4.280±0.501	4.276±0.517	4.177±0.498	0.568	0.059	0.000	0.639	0.000	0.141

AAA: Anisotropic analytical algorithm, AXB-D: Acuros XB, D_m: Dose-to-medium, D_w: Dose-to-water, PTV: Planning target volume, CI: Conformity index, HI: Homogeneity index, GM: Gradient measure, NTID: Normal tissue integral dose, MUs: Moniter units

Table 1b: Dose-volume parameters for organs at risk using intensity-modulated radiation therapy technique for anisotropic analytical algorithm, Acuros XB dose-to-medium, and Acuros XB dose-to-water computations along with their systematic and inter-patient variability analysis

	Parameters	AAA	AXB-D_m	AXB-D_w	P					
					AAA versus D_m		AAA versus D_w		D_m versus D_w	
Bladder	Mean	40.53±1.98	40.49±1.97	40.61±2.05	0.034	0.599	0.002	0.032	0.020	0.029
	V_{50}	34.85±5.54	35.37±5.87	35.82±5.40	0.016	0.106	0.108	0.454	0.000	0.089
	Maximum	57.03±1.39	57.14±1.27	57.32±1.30	0.216	0.176	0.105	0.400	0.007	0.764
	D_2	54.30±0.71	54.45±0.74	54.65±0.73	0.000	0.325	0.000	0.660	0.000	0.792
Rectum	Mean	42.23±3.74	42.34±3.80	42.28±3.79	0.001	0.014	0.234	0.292	0.517	0.882
	V_{50}	26.31±9.62	28.12±9.90	27.28±9.30	0.000	0.340	0.086	0.507	0.050	0.208
	Max	55.27±1.19	55.55±1.15	55.56±1.11	0.001	0.620	0.939	0.387	0.006	0.685
	D_2	53.31±0.79	53.62±0.84	53.61±0.82	0.000	0.307	0.867	0.699	0.000	0.698
Bowel	Mean	18.61±3.43	18.04±3.43	17.85±3.44	0.000	0.968	0.000	0.648	0.000	0.727
	Maximum	51.36±3.69	51.86±3.88	51.35±3.70	0.000	0.114	0.006	0.159	0.823	0.758
	D_2	40.87±4.86	41.11±4.84	40.45±4.94	0.046	0.877	0.000	0.030	0.000	0.398
Left femoral head	Mean	25.59±5.84	25.37±5.79	26.12±6.05	0.001	0.413	0.000	0.001	0.000	0.021
	Maximum	52.80±3.13	52.44±3.22	53.77±3.21	0.002	0.421	0.000	0.697	1.000	0.994
	D_2	46.18±5.31	45.70±5.49	47.44±5.58	0.004	0.224	0.000	0.083	0.000	0.738
Right femoral head	Mean	25.62±5.20	25.41±5.14	26.15±5.32	0.002	0.312	0.000	0.020	0.000	0.088
	Maximum	53.05±2.61	53.19±2.86	54.47±2.67	0.403	0.111	0.000	0.452	0.000	0.368
	D_2	47.95±4.10	47.12±4.19	48.60±4.18	0.012	0.636	0.000	0.619	0.000	0.974

AXB-D: Acuros XB, D_m: Dose-to-medium, D_w: Dose-to-water, AAA: Anisotropic analytical algorithm

Acuros XB dose-to-medium versus Acuros XB dose-to-water

For similar PTV coverage, the observed differences between the algorithms were in maximum (IMRT: 1.10% and RA: 1.11%) and minimum dose inside PTV (IMRT: 1.31% and RA: 1.39%). The inter-patient variability was nonsignificant of most of the parameters except $V_{110\%}$ using both treatment techniques.

For OARs, observed larger differences between two algorithms were for $V_{50\,Gy}$ bladder (IMRT: 1.59% and RA: 3.01%), $V_{50\,Gy}$ rectum (IMRT: 2.42% and RA: 2.37%), and $D_{2\%}$ for both femoral heads (right femur [IMRT: 3.19% and RA: 3.50%] and left femur [IMRT: 3.88% and RA: 4.05%]), respectively. The inter-patient variability was nonsignificant of most of the OARs except mean dose to bladder and left femoral head using IMRT technique, mean dose to both the femoral heads, and maximum dose to the bladder using RA technique, respectively.

The differences between both the algorithms were NTID (IMRT: 0.56% and RA: 0.66%), MUs (IMRT: 0.86% and RA: 0.77%),

Table 2a: Dose-volume parameters for planning target volume using RapidArc technique for anisotropic analytical algorithm, Acuros XB dose-to-medium, and Acuros XB dose-to-water computations along with their systematic and inter-patient variability analysis

Structure	Parameters	AAA	AXB-D_m	AXB-D_w	*P*					
					AAA versus D_m		AAA versus D_w		D_m versus D_w	
PTV	Mean	52.70±0.54	52.84±0.54	52.73±0.51	0.000	0.705	0.002	0.250	0.217	0.259
	D_{95}	50.40±0.02	50.40±0.01	50.40±0.01	0.164	0.008	0.175	0.034	1.000	0.552
	D_{98}	49.60±0.18	49.57±0.22	49.55±0.20	0.202	0.006	0.231	0.118	0.003	0.271
	D_{50}	52.83±0.59	52.97±0.59	52.87±0.56	0.000	0.966	0.000	0.232	0.156	0.325
	D_2	54.83±0.95	55.25±0.95	55.28±0.88	0.000	0.752	0.439	0.033	0.000	0.081
	V_{110}	1.86±2.85	3.20±3.87	2.99±3.33	0.000	0.000	0.321	0.008	0.000	0.006
	Max	57.16±1.47	58.17±1.36	58.81±1.61	0.000	0.314	0.003	0.406	0.000	0.188
	Min	44.01±2.22	43.13±2.26	43.69±2.14	0.029	0.918	0.122	0.591	0.037	0.727
NTID		296.36±51.39	295.21±51.84	293.29±51.84	0.000	0.105	0.000	0.007	0.000	0.118
MUs		521.37±31.64	526.67±32.45	522.58±31.93	0.000	0.007	0.000	0.471	0.006	0.197
CI		0.991±0.041	1.001±0.035	1.013±0.032	0.032	0.177	0.000	0.049	0.000	0.108
HI		0.099±0.020	0.107±0.020	0.108±0.019	0.000	0.927	0.000	0.075	0.102	0.001
GM		3.842±0.341	3.807±0.341	3.722±0.328	0.000	0.388	0.000	0.248	0.000	0.127

AXB-D: Acuros XB, D_m: Dose-to-medium, D_w: Dose-to-water, AAA: Anisotropic analytical algorithm, PTV: Planning target volume, CI: Conformity index, HI: Homogeneity index, GM: Gradient measure, NTID: Normal tissue integral dose, MUs: Moniter Units

Table 2b: Dose-volume parameters for organs at risk using RapidArc technique for anisotropic analytical algorithm, Acuros XB dose-to-medium, and Acuros XB dose-to-water computations along with their systematic and inter-patient variability analysis

Structure	Parameters	AAA	AXB-D_m	AXB-D_w	*P*					
					AAA versus D_m		AAA versus D_w		D_m versus D_w	
Bladder	Mean	41.67±1.76	41.57±1.77	41.69±1.77	0.000	0.884	0.001	0.780	0.409	0.864
	V_{50}	33.85±4.76	34.17±4.63	35.15±4.60	0.012	0.292	0.002	0.632	0.001	0.899
	Maximum	55.92±1.30	56.12±1.32	56.49±1.91	0.035	0.774	0.102	0.004	0.021	0.003
	D_2	53.98±0.88	51.95±9.92	54.20±0.86	0.340	0.712	0.291	0.568	0.000	0.422
Rectum	Mean	43.08±2.89	43.06±2.90	42.99±2.90	0.372	0.714	0.132	0.913	0.039	0.916
	V_{50}	26.27±8.33	27.34±8.59	26.59±8.27	0.005	0.462	0.141	0.886	0.439	0.527
	Maximum	54.92±1.09	55.19±1.19	54.94±1.19	0.003	0.224	0.222	0.572	0.909	0.997
	D_2	52.92±0.711	53.15±0.73	53.11±0.65	0.000	0.673	0.534	0.180	0.000	0.166
Bowel	Mean	18.17±2.87	18.09±2.87	17.88±2.85	0.000	0.740	0.000	0.192	0.000	0.135
	Maximum	51.59±3.28	52.08±3.56	51.42±3.61	0.000	0.012	0.000	0.023	0.244	0.717
	D_2	41.29±4.02	41.42±4.08	40.82±4.06	0.000	0.008	0.000	0.128	0.000	0.559
Left femur	Mean	21.32±3.79	21.00±3.85	21.59±3.69	0.000	0.520	0.000	0.126	0.000	0.021
	Maximum	50.43±3.75	50.21±3.76	51.85±4.22	0.019	0.238	0.000	0.026	0.000	0.262
	D_2	45.36±3.97	44.88±3.96	46.46±4.23	0.000	0.019	0.000	0.087	0.000	0.267
Right femur	Mean	21.37±3.88	20.99±3.91	21.61±3.77	0.000	0.356	0.000	0.686	0.015	0.000
	Maximum	51.14±3.93	50.89±3.91	52.64±4.41	0.012	0.628	0.000	0.035	0.000	0.208
	D_2	46.17±4.06	45.49±4.08	47.00±4.49	0.007	0.684	0.000	0.315	0.019	0.050

AXB-D: Acuros XB, D_m: Dose-to-medium, D_w: Dose-to-water, AAA: Anisotropic analytical algorithm

CI (IMRT: 0.93% and RA: 1.27%), HI (IMRT: 0.85% and RA: 1.68%), and GM (IMRT: 2.29% and RA: 2.22%), respectively.

Figures 1 and 2 show the variations in mean value and the density plots (similarity of variance using Pitman–Morgan test) for (a) PTV $D_{50\%}$, (b) left femur $D_{2\%}$, and (c) right femur $D_{2\%}$ for IMRT and RA plans computed using AAA, AXB-D_m, and AXB-D_w for individual patients, respectively. The density plot is the smoothed version of histogram (independent of the number of bins used) and illustrates the distribution of a numeric variable employing the kernel density estimates to depict the probability density function. Figure 3 illustrates the outline of mean difference and CI % for the various parameters of PTV and OARs between (a) AAA-AXB-D_m, (b) AAA-AXB-D_w, and (c) AXB-D_m-AXB-D_w using IMRT and RA.

Discussions

The present study details no significant difference in target coverage for IMRT and RA treatment plans computed

Table 3a: Arrangement of the dose-volume parameters while switching from anisotropic analytical algorithm to Acuros XB dose-to-medium computation as per the significance of the statistical test

D_m		Dose-volume parameters' systematic differences			
		IMRT		RA	
		Nonsignificant	Significant	Nonsignificant	Significant
Dose-volume parameters inter-patient variability	Nonsignificant	NTID, GM	PTV: Mean, $D_{98\%}$, $D_{2\%}$ Maximum, minimum, MUs, CI, HI Bladder: Mean, V_{50Gy}, $D_{2\%}$ Rectum: V_{50Gy}, maximum, $D_{2\%}$ Bowel: Mean, maximum, $D_{2\%}$	Bladder: $D_{2\%}$ Rectum: Mean	PTV: Mean, $D_{50\%}$, $D_{2\%}$, Maximum, minimum, NTID, CI, HI, GM Bladder: Mean, V_{50Gy}, Maximum Rectum: V_{50Gy}, maximum, $D_{2\%}$ Bowel: Mean
	Significant		PTV: D_{50Gy}, $V_{110\%}$ Rectum: Mean	PTV: $D_{95\%}$, $D_{98\%}$	PTV: $V_{110\%}$, MU Bowel: Maximum, $D_{2\%}$ Left femur: $D_{2\%}$

IMRT: Intensity-modulated radiation therapy, RA: RapidArc, GM: Gradient measure, PTV: Planning target volume, CI: Conformity index, HI: Homogeneity index, D_m: Dose-to-medium, NTID: Normal tissue integral dose, MUs: Moniter units

Table 3b: Arrangement of the dose-volume parameters while switching from anisotropic analytical algorithm to Acuros XB dose-to-water computation as per the significance of the statistical test

D_w		Dose-volume parameters systematic differences			
		IMRT		RA	
		Nonsignificant	Significant	Nonsignificant	Significant
Dose-volume parameters inter-patient variability	Nonsignificant	PTV: $D_{95\%}$, $D_{98\%}$, $D_{2\%}$, minimum Bladder: V_{50Gy}, maximum Rectum: Mean, V_{50Gy}, Maximum, $D_{2\%}$	PTV: Mean, maximum, NTID, MU, CI, HI, GM Bladder: $D_{2\%}$ Bowel: Mean, Maximum left femur: Maximum, $D_{2\%}$ Right femur: Maximum, $D_{2\%}$	PTV: $D_{98\%}$, minimum Bladder: $D_{2\%}$ Rectum: Mean, V_{50Gy}, maximum, $D_{2\%}$	PTV: Mean, D_{50Gy}, maximum MU, HI, GM Bladder: Mean, V_{50Gy}
	Significant		PTV: D_{50Gy} Bladder: Mean Bowel: $D_{2\%}$ Left femur: Mean Right femur: Mean	PTV: $D_{95\%}$, $D_{2\%}$ Bladder: Maximum	PTV: $V_{110\%}$, NTID, CI Bowel: Maximum Left femur: Maximum Right femur: Maximum

IMRT: Intensity-modulated radiation therapy, RA: RapidArc, GM: Gradient measure, PTV: Planning target volume, CI: Conformity index, HI: Homogeneity index, D_w: Dose-to-water, NTID: Normal tissue integral dose, MUs: Moniter units

using AAA, AXB-Dm and AXB-Dw algorithm. This can be attributed to the fact that treatment plans were normalized to 95% isodose line for dosimetric evaluation compared to other dosimetric parameters (i.e., D_{98}, D_{max}, D_{min}, etc.). The main findings of the study were as follows: (1) all dose–volume parameters were higher for AXB-D$_w$ in comparison to AAA for IMRT and RA plans, except $D_{98\%}$, minimum dose to PTV, and rectum mean dose (RA). (2) There was no systematic trend found in dose–volume parameters for the target and OARs between AXB-D$_m$ and AXB-D$_w$ for IMRT and RA plans. (3) The dose–volume parameters for target were higher for AXB-D$_m$ in comparison to AAA in IMRT and RA plans, except PTV $D_{98\%}$ and minimum dose to PTV. Bladder and rectum were also pursuing the drift except bladder mean dose, bladder $D_{2\%}$ (RA), and mean dose to rectum (RA). On the contrary, dose–volume parameters for femoral heads were higher for AAA in comparison to AXB-D$_m$ in IMRT and RA plans, except maximum dose to the left femoral head in IMRT.

In all cases, the largest systematic difference was found in $V_{50\,Gy}$ of rectum and $D_{2\%}$ of femoral heads using IMRT and RA techniques, respectively. AAA predicts significantly lower CI, HI, and MUs in contrast to AXB-D$_m$ and AXB-D$_w$ for IMRT and RA plans. On the contrary, AAA predicts higher NTID and GM in contrast to AXB-D$_m$ and AXB-D$_w$ for IMRT and RA plans.

The present study reveals that AAA predicts lower maximum and higher minimum doses to PTV compared to AXB-D$_m$ and AXB-D$_w$. Rana *et al*.[15] studied the dosimetric impact of AXB-D$_m$ on prostate cancer using RA and concluded no significant contrast between AAA and AXB-D$_m$. In that study, AAA estimates higher minimum and maximum doses to the target. In another study, Koo *et al*.[16] reported lower maximum and higher minimum doses to target for AAA in comparison to those calculated using AXB-D$_m$ for prostate RA technique using endorectal balloon. Kumar *et al*.[21] also detailed the use of AXB on cervix carcinoma using RA technique compared to AAA.
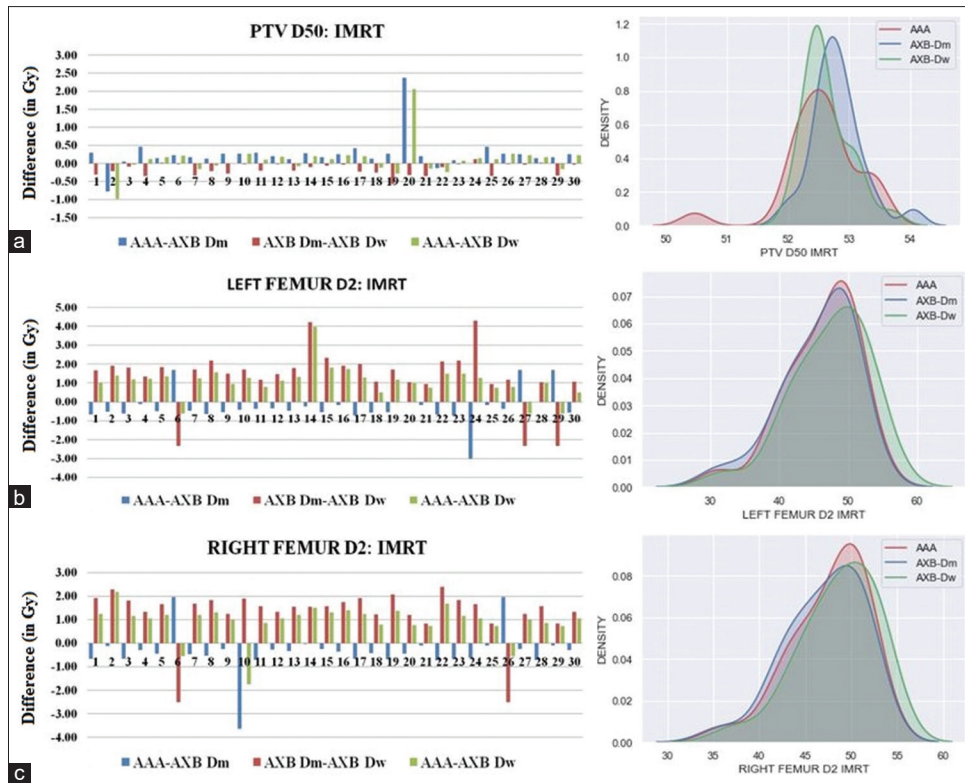
Figure 1: Illustration of variation and respective density plots for (a) planning target volume $D_{50\%}$, (b) left femur $D_{2\%}$, and (c) right femur $D_{2\%}$ using intensity-modulated radiation therapy
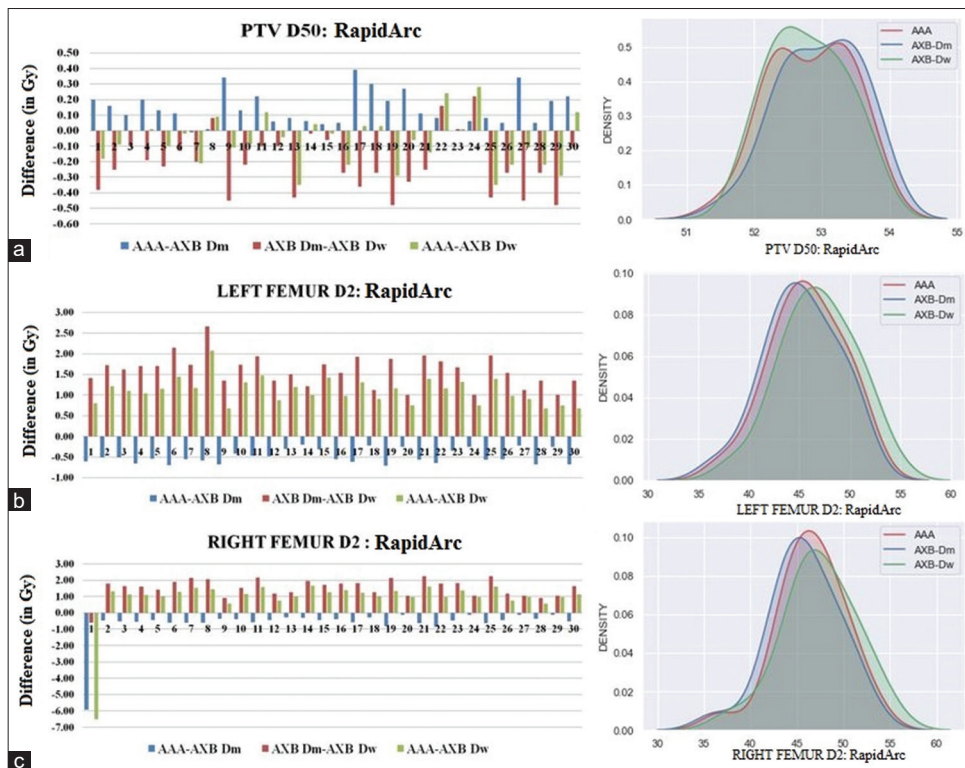

Figure 2: Illustration of variation and respective density plots for (a) planning target volume $D_{50\%}$, (b) left femur $D_{2\%}$, and (c) right femur $D_{2\%}$ using RapidArc

The average difference between AAA, AXB-D_m, and AXB-D_w was <1.0% for mean dose to PTV and OARs, except mean dose to the femoral heads with a maximum difference of 4.05% (RA, AXB-D_m versus AXB-D_w). This higher difference
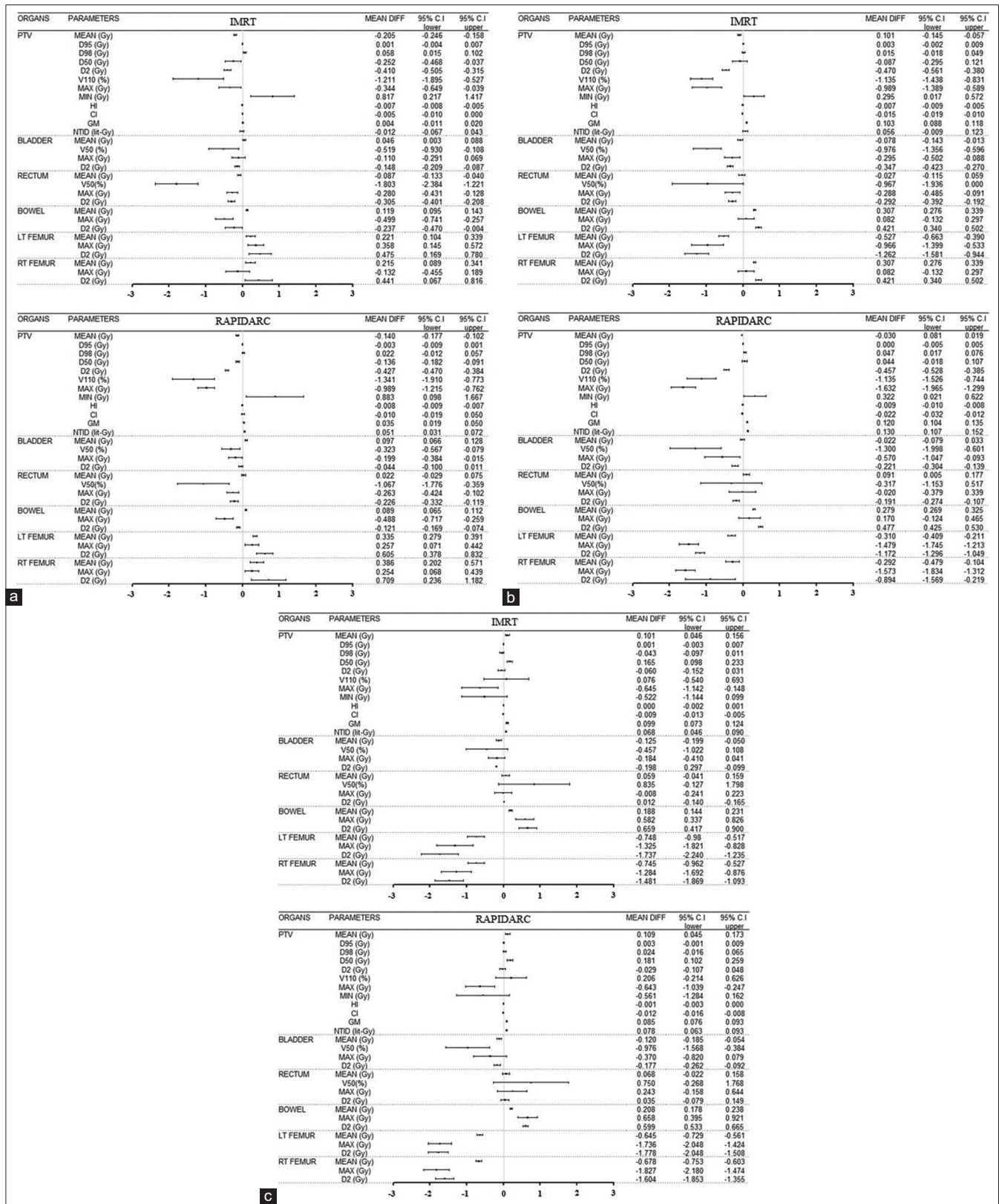
Figure 3: The outline of mean difference and conformity index % for the various parameters of planning target volume and organs at risk between (a) analytical anisotropic algorithm–Acuros XB–dose-to-medium, (b) analytical anisotropic algorithm–Acuros XB–dose-to-water, and (c) Acuros XB–dose-to-medium–Acuros XB–dose-to-water using intensity-modulated radiation therapy and RapidArc

in the femoral doses occurs due to its composition (Stopping power ratio of cartilage and cortical bone is 1.035 and 1.111, respectively).[22] Zifodya *et al*.[23] reported an average difference of 2% for mean dose to PTV and OARs among AAA, AXB-D$_m$,

and AXB-D_w, and a maximum difference of 4.6% between AXB-D_m and AXB-D_w in nonwater biological medium (i.e., compact bone). Fogliata *et al.*[24] also reported a comparable finding with AXB-D_w estimating 5% higher doses in the bone contrast to AXB-D_m. These differences in AXB-D_m and AXB-D_w computations occur due to the difference in stopping power ratio of water and material of different densities.

The present study reveals that higher systematic significant difference exists in volume of rectum receiving 50 Gy among AAA, AXB-D_m, and AXB-D_w. This can be attributed due to the presence of air/gas heterogeneity in rectum. In a measurement study with low-density heterogeneous medium, Kumar *et al.*[25] reported that AXB predicts fewer discrepancies (1.3%–2.2%) with ion chamber measurements than the AAA (1.6% to −3.6%) in low-density medium. Koo *et al.*[16] reported better agreement in air cavity and air tissue interface for AXB calculation than compared to those AAA calculated. Further, Koo *et al.*[16] reported that for precise rectal dose analysis in prostate cancer, AXB should be considered over AAA.

Pitman–Morgan test was performed on the dose distribution calculated via AAA, AXB-D_m, and AXB-D_w to evaluate the significant difference in variances of the computed dose distributions. Analysis estimated less inter-patient variability while switching from AAA to AXB-D_m in comparison to those switching from AAA to AXB-D_w. The results acquired in the present study could assist in decision-making in clinic when adopting AXB algorithm for carcinoma cervix using IMRT and RA techniques. For example, $V_{50\ Gy}$ rectum was higher (6.57% – IMRT and 3.81% –RA) for AXB-D_m, and in addition, inter-patient variability was nonsignificant. It was corresponded to situation (a); therefore, the increased probability of rectal toxicity may not be expected for higher values of AXB-D_m. In addition, the same situation was noticed for PTV $D_{50\%}$ while switching from AAA to AXB-D_m and from AAA to AXB-D_w using RA technique, respectively. Despite these outcomes, it is essential to accentuate that inter-patient variability was too high to even consider establishing the basic suggestions for most of the parameters, and it is corresponding to the situation (b) in both cases, i.e., while switching from AAA to AXB-D_m or AAA to AXB-D_w. In these cases, further clinical investigations are required in regard to forecast of clinical results from the dose–volume parameters determined by AXB at the point, when they contrast from the dose–volume parameters determined with AAA, which supports the contemporary clinical knowledge. A similar result has been reported by Muñoz-Montplet *et al.*,[11] for head-and-neck cancer, while evaluating the impact of AXB (D_m and D_w dose-reporting modes) on volumetric-modulated arc therapy technique. Nevertheless, it was not possible to establish a simple recommendation based on the inter-patient variability in the results due to its dosimetric nature of the study and cohort size. In these situations, further studies are still required to draw the conclusion for clinical outcomes from dose–volume parameters calculated using AXB algorithm in comparison to AAA algorithm calculated dose–volume parameters.

CONCLUSIONS

The present study reveals the important difference between AAA, AXB-D_m, and AXB-D_w computations for cervix carcinoma using IMRT and RA techniques. The inter-patient variability and systematic difference in dose–volume parameters computed using AAA, AXB-D_m, and AXB-D_w algorithms present the possible impact on the dose prescription to PTV and their relative constraints to OARs for IMRT and RA techniques. This may help in decision-making in clinic while switching from AAA to AXB (D_m or D_w) algorithm for cervix carcinoma using IMRT and RA techniques.

Conflicts of interest

There are no conflicts of interest.

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