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Scientific Article

Dosimetric Impact of Acuros XB Dose-to-Water and Dose-to-Medium Reporting Modes on Lung Stereotactic Body Radiation Therapy and Its Dependency on Structure Composition

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Abstract

Purpose: Our purpose was to assess the dosimetric effect of switching from the analytical anisotropic algorithm (AAA) to Acuros XB (AXB), with dose-to-medium (Dm) and dose-to-water (Dw) reporting modes, in lung stereotactic body radiation therapy patients and determine whether planning-target-volume (PTV) dose prescriptions and organ-at-risk constraints should be modified under these circumstances.

Methods and Materials: We included 54 lung stereotactic body radiation therapy patients. We delineated the PTV, the ipsilateral lung, the contralateral lung, the heart, the spinal cord, the esophagus, the trachea, proximal bronchi, the ribs, and the great vessels. We performed dose calculations with AAA and AXB, then compared clinically relevant dose-volume parameters. Paired *t* tests were used to analyze differences of means. We propose a method, based on the composition of the involved structures, for predicting differences between AXB Dw and Dm calculations.

Results: The largest difference between the algorithms was 4%. Mean dose differences between AXB Dm and AXB Dw depended on the average composition of the volumes. Compared with AXB, AAA underestimated all PTV dose-volume parameters (-0.7 Gy to -0.1 Gy) except for gradient index, which was significantly higher (4%). It also underestimated V_5 of the contralateral lung (-0.3%). Significant differences in near-maximum doses (D_2) to the ribs were observed between AXB Dm and AAA (1.7%) and between AXB Dw and AAA (-1.6%). AAA-calculated D_2 was slightly higher in the remaining organs at risk.

Conclusions: Differences between AXB and AAA are below the threshold of clinical detectability (5%) for most patients. For a small subgroup, the difference in maximum doses to the ribs between AXB Dw and AXB Dm may be clinically significant. The differences in dose volume parameters between AXB Dw and AXB Dm can be predicted with reference to structure composition.

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Introduction

Stereotactic body radiation therapy (SBRT) is the current standard of care for early-stage, nonoperable non-small cell lung cancer[1] and is considered a compelling alternative to surgery in lung oligometastasis.[2] Lung SBRT involves stereotactic localization techniques combined with the delivery of multiple small photon fields in a few high-dose fractions.[3] The planning target volume (PTV) normally includes lung tissue and a small amount of soft tissue, although peripheral tumors may also contain high-density tissues. Under these challenging dose calculation conditions, the Acuros XB (AXB) algorithm[4]—a grid-based linear Boltzmann transport equation solver implemented in the Eclipse treatment planning system (TPS)—achieves accuracy rates comparable to Monte Carlo (MC) simulation, which is considered the most accurate dose calculation method in radiotherapy[5] and superior to the convolution/superposition algorithms still used in routine clinical practice. Numerous studies have compared AXB with measurements, MC, and convolution/superposition algorithms in slab and anthropomorphic phantoms, for representative lung SBRT planning setups.[6–14] International Commission on Radiation Units and Measurements (ICRU) report 91 recommends MC or AXB for accurate dose calculation in heterogeneous tissue.[3]

AXB calculates the energy-dependent electron fluence everywhere in the calculation volume, enabling computation of both dose-to-medium (Dm) and dose-to-water (Dw) with the corresponding energy deposition cross sections.[4] It is unclear which reporting mode is optimal for clinical practice,[5,15-17] and answering this question is beyond the scope of our study. Nonetheless, as with MC, when using AXB we must choose 1 of the 2 (Dm or Dw).

Several studies have assessed the implications of using AXB for lung SBRT treatment planning.[7-9,18-30] In most cases, the effect in dose-volume parameters is below 2% except for the target coverage, which is considerably lower, and the Dw maximum dose in bony structures, which is significantly higher, in AXB-recalculated plans, as happens when MC is adopted.[31] Certain studies used an older version of AXB (v10),[7-9,21,25,26,30] which differs from more recent versions in many respects, most importantly with regard to computed tomography (CT)-to-material conversions.[32] The number of dose-volume parameters for organs at risk (OARs) is limited in all studies, particularly those examining Dw, which is a better estimate of dose to sensitive tissue in bone than Dm.[33] Moreover, none have analyzed the distribution of differences, a critical aspect that must be considered before switching to AXB in clinical practice in terms of the composition of the volumes.

The analytical anisotropic algorithm (AAA) is a fast and widely used convolution/superposition algorithm[34] that uses the same multiple-source model as AXB.[35] Because both AXB and AAA algorithms are implemented in Eclipse, comparing them is relatively straightforward. In this context, we aimed to assess the dosimetric and clinical effect of using AXB Dm and AXB Dw instead of AAA. Specifically, we examined whether switching to AXB would require modification of PTV dose prescription, OAR constraints, or dose-volume reporting in a large cohort of lung SBRT patients. Here, we report our findings on the differences between these algorithms for a wide range of dose-volume parameters and their interpatient variability.

Methods and Materials

Patient selection, contouring and prescription

Our study included 54 patients who underwent lung SBRT in our hospital between 2012 and 2017. To ensure homogeneous treatment planning, we only included patients who had a single lesion and who had not previously undergone the procedure. Location was central in 8 cases and peripheral in the rest, according to Radiation Therapy Oncology Group (RTOG) 0813[36] and RTOG0915[37] classifications. We performed a short 4-dimensional CT scan in 10 respiratory phase bins and a conventional extended slow 3-dimensional scan with intravenous contrast using a GE Optima CT580W CT Scanner (GE Health Care, Chicago, IL). Slice thickness was 1.25 mm in all cases. The internal target volume was delineated using the maximum intensity projection by the radiation oncologist. The PTV was created by adding a 5-mm isotropic margin around the internal target volume, obtaining volumes of 9.3 cm^3 to 238.0 cm^3, with a median of 53.3 cm^3. The following OARs were contoured in accordance with RTOG protocols: ipsilateral lung, contralateral lung, heart, spinal cord, esophagus, trachea, proximal bronchi, ribs, and great vessels.[36,37]

A total dose of 60 Gy was delivered in 5 or 8 fractions, depending on tumor location and the surrounding OARs, using a Clinac iX accelerator (Varian Medical Systems, Palo Alto, CA).

Treatment planning and dose calculation

Plans were created for a 6-MV photon beam with a Millennium 120 multileaf collimator using 7 to 13 noncoplanar treatment fields in the Eclipse TPS (Varian Medical Systems). We used extended CT in all cases. The plans were then optimized for clinical acceptability, calculated using AXB Dw, and normalized so that 95% of the PTV received the prescribed dose, allowing for doses of up to 125%.

Several versions of the algorithm were used between 2012 and 2017. For our study, we recalculated the doses with version 13.0.26 of AAA and AXB (Dw and Dm) for the same number of monitor units as the original plan and with identical beam and multileaf collimator setup. Calculation grid resolution was set to 2 mm in all cases, as recommended in the literature.[3,5,7] An important aspect of our study concerns the change introduced with AXB v11 regarding the determination of tissue types from CT images.[32] The version of AXB used in our study could produce different results than those previously obtained in studies that used v10.[7-9,21,25,26,30]

Dose-volume parameters

We obtained dose-volume histogram (DVH) parameters recommended in ICRU report 91[3] and in the RTOG studies,[36,37] as well as other clinically relevant PTV and OAR dose-volume data. Mean dose (D_{mean}), near-minimum dose (D_{98}), D_{95}, median dose (D_{50}), and near-maximum dose (D_2) to the PTV were collected, where D_x is the dose covering x% of the volume. Homogeneity index (HI), conformity index (CI), and gradient index (GI), as defined in ICRU 91, were calculated as follows:

$$HI = \frac{D2 - D98}{D50} \quad (1)$$

$$CI = \frac{TV \times PIV}{TV_{PIV}^2} \quad (2)$$

$$GI = \frac{PIV_{half}}{PIV} \quad (3)$$

where TV is the target volume, PIV the prescription isodose volume, TV_{PIV} the target volume within the prescription isodose volume, and PIV_{half} the prescription isodose volume at half the prescription isodose.

These OAR dose-volume data were obtained: V_5, V_{10}, $V_{20,}$ and D_{mean} to the ipsilateral lung, where V_x is the volume receiving at least x Gy; V_5 and D_{mean} to the contralateral lung; D_2 and D_{mean} to the heart; D_2 to the spinal cord, esophagus, trachea, proximal bronchi, ribs, and great vessels.

Structure composition

We used Python to determine the PTV and OAR compositions, taking patients' CT images and radiation therapy (RT) structure digital imaging and communications standard (DICOM) files exported from the TPS as inputs and mimicking AXB media characterization for each CT voxel. The program converts the CT images into a mass density matrix by applying the same CT number-to-density calibration curve used by the TPS. It then checks the RT structures and, if manual assignment was performed for a certain volume, it assigns the corresponding material characteristics to the image voxels within the structure. The resulting density matrix is stored as an RT dose DICOM file that can be imported into the TPS, where differential DVHs were obtained with the Eclipse built-in tools for the structures considered. The final step was to export the mass density DVH for each structure and use it with the density-to-material relationship of AXB v11 to obtain its detailed composition.

Data analysis

We calculated the sample means, standard deviations (SDs), and ranges of each dose-volume parameter. Two-tailed paired *t* tests were used to analyze the difference in means between AAA and AXB Dm, AAA and AXB Dw, and AXB Dw and AXB Dm. *P* values below .05 were considered statistically significant. Mean differences and 95% confidence intervals were also obtained using SPSS version 24 (IBM-SPSS, Chicago, IL). Interpatient variability, reflected in the confidence intervals, tells us whether differences could be clinically relevant in individual patients. According to AAPM Task Group Report 105, 5% change in dose can result in 10% to 20% change in tumor control probability or up to 20% to 30% change in normal tissue complication probability if the prescribed dose falls along the steepest region of the dose-effect curves.[5] We established the threshold for clinical detectability at 5% change in dose. Mean, SD, and range of proportions of different materials in the PTV and OAR were also obtained.

Composition-related dose differences between Dm and Dw

To understand the differences between AXB Dw and AXB Dm and their interpatient variability, we propose a method based on the composition of the structures. Dose differences between AXB Dw and AXB Dm are due to the reporting mode of the voxel doses only. A straightforward method of converting Dm to Dw for a clinical 6 MV photon beam when using AXB v13 is to adopt the proposal of Jurado-Bruggeman et al.[38] The authors introduced a new dose quantity called "dose-to-water-like medium." The dose-to-water-like medium, Dw,m*, is defined as the dose to a voxel of water surrounded by a water-like medium (m*) with the same radiation transport characteristics as those of the original medium. Using this dose definition, the advantages of transporting in medium are kept (the same attenuation and dispersion) while the differences in particle fluence and spectrum introduced

by nonwater-like media are removed. This approach is similar to the proposal of Reynaert et al[39] to convert Dm, m to Dw,w in bone. Dw,m* distributions are derived by postprocessing Dw,m or Dm,m distributions applying a correction factor (CF) to each voxel. This CF depends on voxel's atomic composition, beam spectrum, and the original dose reporting mode. Jurado-Bruggeman et al[38] use solely dose distributions calculated within the algorithm for the considered beam to derive a set of CF. The in-depth details of the procedure and the values of the CF were previously published.[38]

Table 1 shows the CF values for AXB human tissues. In our case, the ratio of these CF can be used to switch from Dm to Dw. For a single voxel comprising 1 of the materials included in the AXB CT-to-material conversion table (mAXB), the relationship is as follows:

$$D_w = D_m \cdot \frac{CF^{6MV}_{mAXB,\ Dm}}{CF^{6MV}_{mAXB,\ Dw}} \quad (4)$$

For a volume with a uniform absorbed dose and a known composition, the contribution of each material must be considered:

$$D_{w,vol} = D_{m,vol} \cdot \sum_{mAXB} f_i \cdot \frac{CF^{6MV}_{mAXB,\ Dm}}{CF^{6MV}_{mAXB,\ Dw}} \quad (5)$$

where f_i is the fraction corresponding to material i in the composition of volume *vol*.

We predicted theoretical Dw DVH parameters ($D^T_{w,vol}$) from the clinically obtained AXB Dm corresponding values using equation 5 for the PTV and each OAR. We calculated theoretical dose differences between AXB Dm and AXB Dw as follows:

$$\Delta D^T_{\mathrm{AXBDw-AXBDm}} = \frac{D^T_{w,vol} - D_{m,vol}}{D_{m,vol}} \cdot 100 \quad (6)$$

Results

Table 2 presents the sample means, SDs, and ranges of the PTV and OAR dose-volume parameters for AAA, AXB Dm, and AXB Dw, with corresponding *P* values. Figure 1 provides a graphic depiction of the mean differences between the algorithms with 95% confidence intervals. Table 3 shows the means, SDs, and ranges of proportions of different materials in the PTVs and OARs.

AAA versus AXB Dm

Figure 1a shows that AAA significantly underestimated D_{mean}, D_{95}, D_{50}, and D_2 to the PTV compared with AXB Dm, with differences ranging from -0.31 Gy (-0.5%) for D_{95} to -0.74 Gy (-1,1%) for D_{50}. Interpatient variability is reflected in 95% confidence interval amplitude ranging from approximately ±0.2 Gy to ±0.3 Gy. AAA predicted a slightly lower CI (-0.02 ± 0.01; -1.5%) and a considerably higher GI (0.15 ± 0.08;4%).

The only significant difference in lungs was observed for V_5 of the contralateral lung, which was 0.30 ± 0.16% lower with AAA. For the ribs, the AAA-calculated D_2 was 0.91 ± 0.21 Gy (1.7%) higher. AAA produced small significant dose increases in D_2 to the remaining OARs. No other differences in this comparison reached statistical significance.

AAA versus AXB Dw

The results displayed in Figure 1b are very similar to those in Figure 1a, except in the ribs, where AAA predicted 1.6% lower D_2 (−0.87 ± 0.22 Gy).

AXB Dw versus AXB Dm

As shown in Figure 1c, no significant differences were observed in any PTV dose-volume parameters, and interpatient variability was minimal in all except D_2 (±0.31 Gy). All significant and insignificant differences in the lungs were negligible, as were their 95% confidence intervals.

A significant increase of 1.78 ± 0.30 Gy (3.4%) in D_2 to the ribs was observed. AXB Dw calculated small significant dose increases to the remaining OARs, with low interpatient variability.

In all 3 comparisons, the largest differences represented by the 95% confidence intervals shown in Figure 1 are below 4% of the mean doses reported in

Table 1 Dm and Dw CFs for AXB human tissues and a clinical 6 MV photon beam

Material	$CF^{6MV}_{mAXB,Dm}$	$CF^{6MV}_{mAXB,Dw}$	$\frac{CF^{6MV}_{mAXB,Dm}}{CF^{6MV}_{mAXB,Dw}}$
Lung	1.007	1.005	1.002
Adipose	1.004	1.024	0.980
Muscle	1.009	0.995	1.014
Cartilage	1.015	0.990	1.025
Bone	1.043	0.907	1.150

Abbreviations: AXB = Acuros XB; CF = correction factor; Dm = dose-to-medium; Dw = dose-to-water.

Table 2 Descriptive statistics of PTV and OAR dose-volume parameters and statistical significance of central tendency over the whole sample

	AAA			AXB Dm			AXB Dw			AAA-AXB Dm	AAA-AXB Dw	AXB Dw-AXB Dm
	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Min	Max	*P* value	*P* value	*P* value
PTV												
D_{mean} (Gy)	65.8 ± 1.9	61.8	70.4	66.4 ± 1.9	62.3	70.3	66.4 ± 1.9	62.2	70.3	< .001	< .001	.954
D_{98} (Gy)	58.3 ± 1.3	56.2	61.9	58.3 ± 1.0	56.4	62.1	58.4 ± 1.0	56.7	62.1	.710	.636	.312
D_{95} (Gy)	59.8 ± 1.1	57.8	63.1	60.2 ± 0.8	58.5	63.5	60.2 ± 0.8	58.5	63.5	.030	.025	.814
D_{50} (Gy)	66.1 ± 2.0	61.9	70.8	66.9 ± 2.1	62.4	71.8	66.9 ± 2.0	62.5	71.0	< .001	< .001	.900
D_2 (Gy)	71.4 ± 3.3	64.2	78.7	71.8 ± 3.4	65.0	79.6	71.9 ± 3.7	64.3	83.4	.026	.002	.481
HI	0.20 ± 0.05	0.08	0.30	0.20 ± 0.05	0.10	0.31	0.20 ± 0.05	0.09	0.36	.600	.349	.558
CI	1.35 ± 0.11	1.20	1.74	1.36 ± 0.13	1.20	1.80	1.37 ± 0.13	1.20	1.77	.006	< .001	.129
GI	3.93 ± 0.88	2.80	7.74	3.78 ± 0.76	2.80	7.07	3.79 ± 0.78	2.78	7.15	< .001	.001	.111
Ipsilateral lung												
V_5 (%)	39.7 ± 11.5	17.1	65.6	39.6 ± 11.4	17.4	63.7	39.7 ± 11.4	17.4	63.8	.381	.579	< .001
V_{10} (%)	28.6 ± 10.3	8.9	48.3	28.6 ± 10.2	8.9	48.1	28.6 ± 10.2	8.9	48.1	.552	.585	.783
V_{20} (%)	15.5 ± 8.0	3.1	33.4	15.5 ± 7.9	3.1	33.7	15.5 ± 8.0	3.1	33.7	.897	.920	.725
D_{mean} (Gy)	9.4 ± 3.6	3.3	17.3	9.4 ± 3.6	3.3	17.3	9.4 ± 3.6	3.3	17.3	.077	.081	.946
Contralateral lung												
V_5 (%)	10.1 ± 7.1	0.0	30.8	10.4 ± 7.2	0.0	30.7	10.4 ± 7.2	0.0	30.7	.001	.001	< .001
D_{mean} (Gy)	1.7 ± 1.0	0.2	5.2	1.7 ± 1.0	0.2	5.2	1.7 ± 1.0	0.2	5.2	.307	.412	.001
Heart												
D_2 (Gy)	7.4 ± 6.7	0.1	25.4	7.4 ± 6.7	0.1	25.3	7.4 ± 6.8	0.1	25.6	< .001	.979	< .001
D_{mean} (Gy)	1.9 ± 2.4	0.0	11.5	1.9 ± 2.4	0.1	11.3	1.9 ± 2.4	0.1	11.5	.129	.327	< .001
Spinal cord												
D_2 (Gy)	11.5 ± 6.9	0.5	25.4	11.2 ± 6.7	0.5	24.6	11.3 ± 6.8	0.5	25.0	< .001	< .001	< .001
Esophagus												
D_2 (Gy)	13.3 ± 7.6	0.2	29.4	13.1 ± 7.5	0.2	29.2	13.2 ± 7.6	0.2	29.5	< .001	.033	< .001
Trachea and proximal bronchi												
D_2 (Gy)	13.8 ± 10.8	0.2	50.4	13.7 ± 10.6	0.3	50.3	13.6 ± 10.6	0.3	50.1	.001	< .001	.135
Ribs												
D_2 (Gy)	53.2 ± 17.3	19.8	75.3	52.3 ± 16.9	19.3	73.3	54.0 ± 17.6	20.1	78.2	< .001	< .001	< .001
Great vessels												
D_2 (Gy)	19.5 ± 13.1	0.2	59.7	19.2 ± 12.9	0.3	58.8	19.5 ± 13.1	0.3	59.9	< .001	.022	< .001

Abbreviations: AAA = analytical anisotropic algorithm; AXB = Acuros XB; CI = conformity index; Dm = dose-to-medium; Dw = dose-to-water; GI = gradient index; HI = homogeneity index; OAR = organs at risk; PTV = planning target volume; SD = standard deviation.

Table 2, that is, below the 5% threshold of clinical detectability.

Composition-related dose differences between Dm and Dw

Table 4 shows the theoretical dose differences when switching from AXB Dm to AXB Dw for a clinical 6-MV photon beam, using the compositions reported in Table 3 and the CFs in Table 1, and assuming a uniform absorbed dose in the volumes. The clinically obtained D_x differences in Figure 1c are all within 0.3% of the theoretical dose differences in Table 4, except for D_2 to the trachea and proximal bronchi (1.2%).

Discussion

The main findings of our study are as follows:

1. Observed dose differences between AAA, AXB Dm, and AXB Dw were unlikely to be clinically detectable in most of our patients.
2. Mean dose differences between AXB Dm and AXB Dw depended on the average composition of the structures.
3. Compared with AXB, AAA underestimated PTV dose-volume parameters — except GI, which was significantly higher — and V_5 of the contralateral lung.
4. There were significant differences in maximum doses to the ribs between AAA and AXB, and the sign of these differences depended on whether the dose was reported in medium or water.
5. AAA calculated small significant dose increases in D_2 to the rest of the OARs compared with AXB Dm, and even smaller increases compared with AXB Dw.

To our knowledge, ours is the largest study to date comparing AXB (Dm and Dw) and AAA in lung patients undergoing SBRT. Previous studies have included up to 37 patients[9,19,23,28] or present results for Dm mode only,[7,8,18,24,26,27] and most report only PTV or lung-related dose-volume parameters.[7,8,18,20-25,27-29]

As most results are very similar for AXB Dm and AXB Dw, we will refer simply to AXB in the remainder of the discussion, specifying the reporting mode only where necessary.

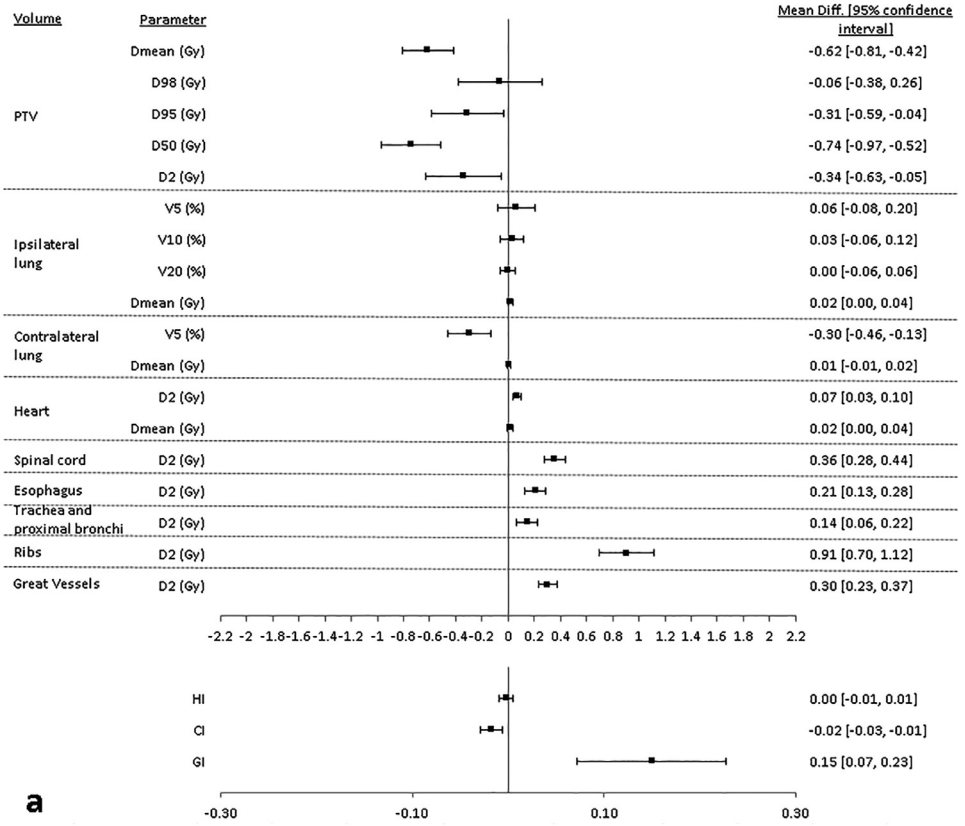
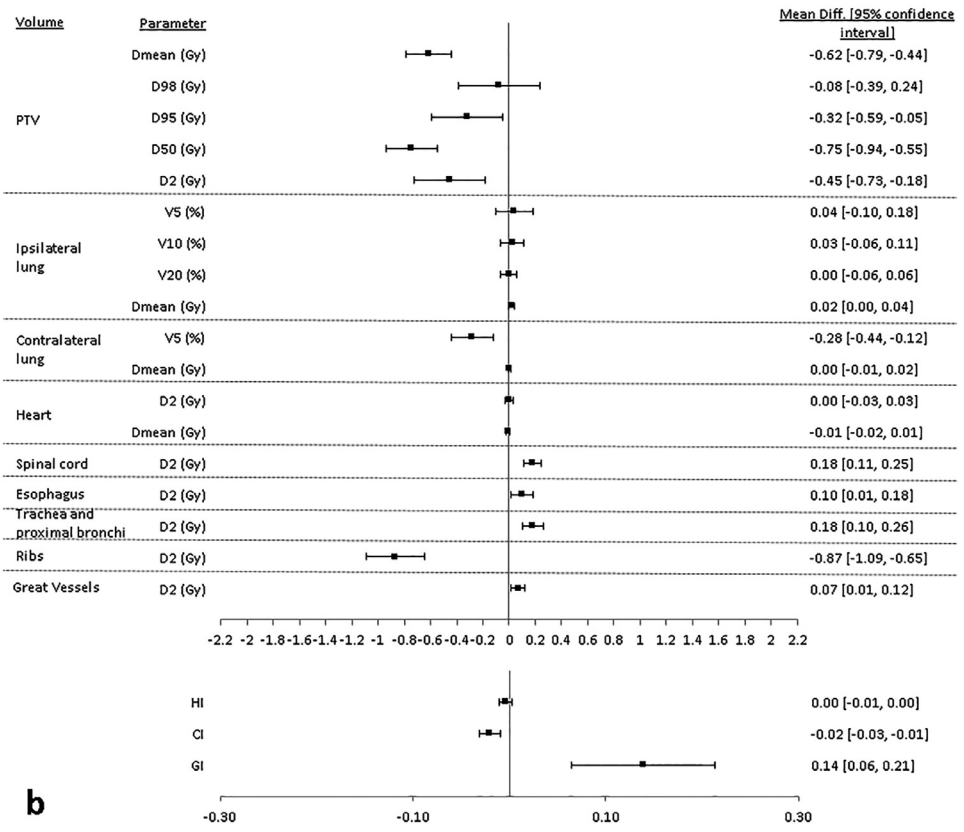


Fig. 1 Mean differences and 95% confidence intervals of planning-target-volume (PTV) and organ-at-risk dose-volume parameters for (a) analytical anisotropic algorithm (AAA) versus Acuros XB (AXB) dose-to-medium (Dm), (b) AAA versus AXB dose-to-water (Dw), and (c) AXB Dw versus AXB Dm.



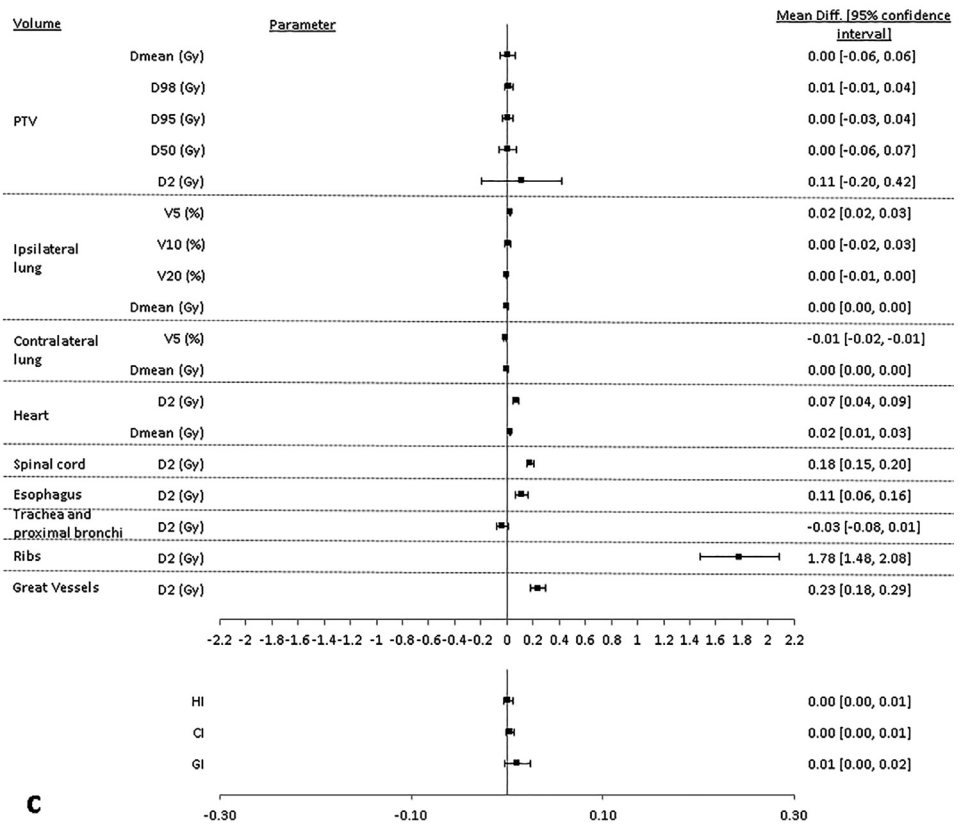


Fig. 1 **Continued.**

Table 3 Descriptive statistics of proportions of different materials in PTV and OARs

	Air (%)			Lung (%)			Adipose (%)			Muscle (%)			Cartilage (%)			Bone (%)		
	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Min	Max
PTV	0.0 ± 0.0	0.0	0.2	66.7 ± 22.4	10.9	99.2	18.3 ± 10.1	0.8	40.9	12.0 ± 11.9	0.0	45.1	2.6 ± 3.6	0.0	16.4	0.5 ± 1.1	0.0	7.0
Ipsilateral lung	0.1 ± 0.2	0.0	0.7	94.4 ± 2.9	83.3	97.3	5.5 ± 2.9	2.7	16.7	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0	0.0	0.0
Contralateral lung	0.1 ± 0.2	0.0	1.3	94.7 ± 2.6	85.4	98.5	5.2 ± 2.6	1.3	14.6	0.0 ± 0.0	0.0	0.1	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0	0.0	0.0
Heart	0.0 ± 0.0	0.0	0.0	0.1 ± 0.2	0.0	1.3	8.2 ± 5.9	0.9	20.7	84.0 ± 6.0	70.3	94.8	7.7 ± 3.3	3.1	20.9	0.0 ± 0.2	0.0	0.9
Spinal cord	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0	0.0	0.0	0.7 ± 0.7	0.0	3.7	86.1 ± 7.3	64.7	98.8	13.1 ± 7.1	1.1	34.2	0.1 ± 0.1	0.0	0.4
Esophagus	0.0 ± 0.0	0.0	0.0	2.9 ± 4.3	0.0	24.9	22.1 ± 9.9	5.8	51.1	71.6 ± 13.4	32.5	92.2	3.1 ± 3.4	0.5	23.5	0.3 ± 2.3	0.0	16.7
Trachea and proximal bronchi	1.2 ± 7.1	0.0	51.1	70.8 ± 11.6	42.0	89.3	25.0 ± 8.9	0.0	48.8	2.7 ± 4.0	0.0	15.3	0.3 ± 0.6	0.0	2.8	0.0 ± 0.1	0.0	0.4
Ribs	0.0 ± 0.0	0.0	0.0	0.3 ± 0.6	0.0	2.6	5.5 ± 3.5	0.0	12.6	19.7 ± 10.3	0.2	49.4	64.7 ± 8.8	42.1	83.5	9.8 ± 6.4	0.8	25.5
Great vessels	0.0 ± 0.0	0.0	0.0	0.1 ± 0.2	0.0	0.8	8.2 ± 4.3	1.3	22.5	84.6 ± 4.9	67.1	93.4	6.9 ± 2.5	2.8	12.4	0.2 ± 0.3	0.0	1.7

Abbreviations: OAR = organs at risk; PTV = planning target volume; SD = standard deviation.

Regarding PTV coverage parameters, our results differed from those published in the literature. Although we found a lower D_{95} and no significant difference in D_{98} when comparing AAA with AXB, it is widely reported that AAA overestimates these parameters and the minimum dose.[7,9,18-22,25-27,30] The reason for this discrepancy is that while our plans were initially optimized for AXB and then recalculated, keeping identical beam parameters for AAA, most prior studies adopted the opposite method. Because we normalized by guaranteeing PTV coverage with AXB, we could not observe the known underestimation of the lack of lateral electron scatter from the lung tissue when calculating D_{95} or D_{98} with AAA.[3] For the same reason, we found no significant differences in HI, though a worsening of homogeneity is usually observed when switching from AAA to AXB,[21,22,24] and our CI differences were smaller than in comparable studies using the reciprocal Paddick CI.[9,22,24]

PTV dose differences between AAA and AXB are the result of a complex 2-effect interaction involving the previously mentioned difference in the predicted lateral electronic disequilibrium and the difference in central axis depth dose curves. The diameter of a sphere equivalent to our median PTV is 4.7 cm, meaning the average field size involved in treatment planning was around 5 × 5 cm^2. For these field sizes and a 6-MV photon beam, differences in lateral electron scattering between AAA and AXB is a minor effect that might only affect the periphery of the PTV.[6,10,14,18,38] Concerning the depth dose curves, AAA underestimates the dose in the lung surrounding the GTV, but overestimates secondary build-up in the lung-GTV interface, leading to a higher dose in the GTV region.[6,10,13,18,38] As our PTVs contained 66.7% lung tissue on average, the first phenomenon outweighed the second, and the AXB-calculated D_{mean} and D_{50} were higher than the AAA values. Of the other studies using AXB v11 or later, some reported findings similar to ours with regard to these parameters,[18-20] others found no differences,[22,24] and 1 found an underestimation of AXB-predicted D_{mean} of approximately 1%.[27] Differences in all cases were below 1.5%. In contrast, studies based on AXB v10 found that AAA overestimated D_{mean} or D_{50} by up to 4%.[7,9,21,25,26,30] This finding, probably attributable to the different material assignment between version 10 and 11, may affect PTV dose prescription. Although results obtained with v10 appear to require re-escalating PTV dose prescription when moving from AAA to AXB, the small differences observed in v11 do not.

Another discrepancy probably attributable to differences in material assignment is the dose fall-off. While studies based on v10 observed higher or equal GI for AXB compared with AAA,[8,21,30] AXB-calculated GI was significantly lower in our study.

Regarding D_2 to the PTV, our results are compatible with those of previous studies, which report increases of

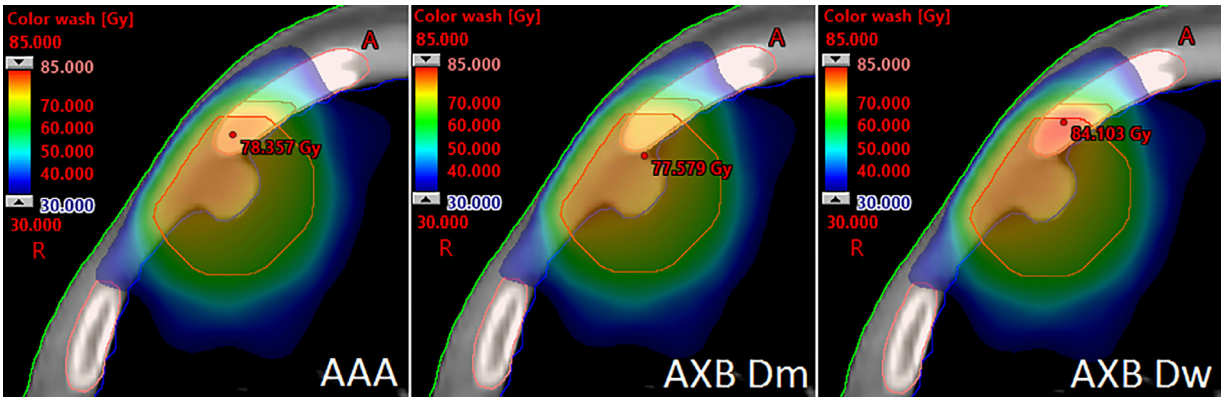


Fig. 2 Difference in dose distributions between analytical anisotropic algorithm (AAA), Acuros XB (AXB) dose-to-medium (Dm), and AXB dose-to-water (Dw) in a case where a high density rib is inside the planning target volume (PTV). Dmax is 78.4, 77.6, and 84.1 Gy for AAA, AXB Dm, and AXB Dw, respectively.

Table 4 Theoretical dose differences between AXB Dw and AXB Dm ($\Delta D^{T}_{AXBDw\text{-}AXBDm}$) for a clinical 6 MV photon beam, assuming average composition of the volumes and uniform absorbed dose

Volume	$\Delta D^{T}_{AXBDw\text{-}AXBDm}$ (%)
PTV	0.1
Ipsilateral lung	0.0
Contralateral lung	0.0
Heart	1.2
Spinal cord	1.5
Esophagus	0.7
Trachea and proximal bronchi	-1.5
Ribs	3.3
Great vessels	1.2

Abbreviations: AXB = Acuros XB; Dm = dose-to-medium; Dw = dose-to-water; PTV = planning target volume.

up to 1.7% for D_2 or maximum dose when moving from AAA to AXB.[7,18,20-22,26,27,30]

The significant 0.3% increase in AXB-calculated V_5 of the contralateral lung found in our study was not observed by Huang et al,[26] who are the only other authors to report this parameter to date. Other studies observed small and insignificant increases in V_5 of total lung for AXB.[7,20,30] Most studies, like ours, show clinically negligible differences between AAA and AXB for lung-related parameters.[8,9,19,20,26,30]

There are scarce data on differences in dose-volume parameters for the remaining OARs. Only Huang et al[26] provide any data on the esophagus, trachea, proximal bronchi, great vessels, and ribs. They found slightly lower AXB-calculated maximum and mean doses to the esophagus, as we did for D_2. Although we also found small decreases in D_2 to the trachea, proximal bronchi, and great vessels with AXB, Huang et al found no significant differences in maximum doses to the bronchial tree and the aorta, though they reported a significantly lower mean dose to the aorta. In any case, all these differences are clinically negligible, and the greater significance in our calculations is probably due to our larger sample size. Regarding the heart, the studies of Huang et al[26] and Ong et al[30] are similar to ours in that they report no significant differences between AAA and AXB for maximum and mean doses.

Our findings regarding the ribs are striking, as AXB Dw and AXB Dm produced very different results. Huang et al[26] analyzed D_{mean}, V_{45}, V_{30}, and V_{20} of the chest wall, finding a significant 1.8% decrease in D_{mean} — in line with the 1.7% difference in D_2 found in our study — and small decreases in the volumetric parameters with AXB Dm versus AAA. In contrast, when comparing AXB Dw with AAA, we found a 1.6% increase in D_2. This finding has not been previously reported in lung SBRT and may be relevant in terms of constraints to the ribs, which are usually in the high-dose region (Table 2). The observed interpatient variability in differences between AAA, AXB Dm, and AXB Dw for this parameter probably reflects the varying presence of cartilage and bone in the ribs (Table 3). AAA is insensitive to this type of heterogeneity, whereas Dm decreases and Dw increases for AXB[15,16] (Table 1). It should be noted that the 2% volume of ribs receiving the highest doses is typically around 2 cm^3, meaning its composition is reasonably representative of that of the entire organ. Figure 2 shows an extreme case where a high-density rib is inside the PTV.

Finally, several authors have studied maximum or near-maximum doses to the spinal cord. Ojala et al[9] and Ong et al[30] found no significant difference when switching from AAA to AXB, Huang et al[26] found a 6.0% decrease in AXB-calculated maximum dose, and Valve et al[19] observed an increase of approximately 3% and 5% in D_2 with AXB Dm and Dw, respectively. The inconsistency between these studies is probably related to their small sample sizes. We observed a statistically significant dose decrease of 3.2% and 1.6% for AXB Dm and Dw, respectively. As the spinal cord is in the low-dose region,

these differences should not have a clinical effect in the context of lung SBRT.

Regarding the comparison between AXB Dm and AXB Dw, previous studies reported similar PTV and OAR dose-volume parameters for the 2 modes.[19,23,28] In our study, the only large significant difference was in the ribs, as discussed previously.

The excellent correlation between the results presented in Table 4 and Figure 1c validates the theoretical dose differences as a suitable method for predicting dosimetric differences between AXB Dm and AXB Dw in clinical practice. This agreement implies that, as with the ribs, the volumes involved in dose parameters are representative of the whole organ in composition. The proposed method is a valuable tool for predicting interpatient variability and comparing results when different reporting modes are used, for example when studying the predictive power of AXB Dm versus AXB Dw for osteoradionecrosis or fracture in ribs. Although the differences found in our study are below the threshold of clinical detectability for most patients, in a small subgroup with a higher proportion of bone, D_2 to the ribs differs by more than 5% between AXB Dm and AXB Dw, which could have a clinical effect. Walters et al[33] stated that Dw was a better estimate of dose to sensitive tissue in bone, but Dm is increasingly used in clinical practice. Our proposed method would allow approximate mass conversion of dose distributions in medium to doses in water using the DICOM-RT objects without recalculation. Gathering this information, along with registered toxicities in the ribs in multi-institutional studies would help to determine which reporting mode is more suitable in lung SBRT.

Conclusions

The differences between AXB Dw, AXB Dm, and AAA in lung SBRT are below the threshold of clinical detectability for most patients, though for a small subgroup, the difference in near maximum doses to the ribs between AXB Dw and AXB Dm may be clinically significant. The differences in dose volume parameters between AXB Dw and AXB Dm can be predicted with reference to structure composition. This method could help to better assess the predictive accuracy of Dw versus Dm for bone toxicity and the need to reconsider the corresponding rib dose constraints.

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