Assessment of the Impact of Different Algorithms on the Radiotherapy Planning Quality for Breast Cancer Using the UK FAST Trial

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Abstract:

Aim: Dose calculation algorithms play a pivotal role in assessing normal tissue toxicity and treatment outcomes during radiotherapy planning. Therefore, this study aimed to evaluate the Acuros External Beam (AXB) algorithm and Anisotropic Analytical Algorithm (AAA) for radiotherapy planning of left-sided breast cancer treatment with the UK FAST trial.

Methods: A total of 100 treatment plans were retrospectively calculated with AAA and AXB algorithm for 50 patients with left-sided breast cancer at an early stage who received treatment with the UK FAST trial. The field angle, geometry, energy, beam segments, and prescription point were kept the same to avoid any bias when comparing algorithms.

Results: The planning target volume (PTV) coverage parameters for AXB plans were higher than those for AAA plans, with a statistically significant difference in V90%, V105% and V107% between both calculation algorithms ($p < 0.05$). When comparing AXB with AAA calculated plans for the heart dosimetric parameters, the heart V25% for the AXB increased significantly, while the heart V5% was lower. The ipsilateral lung V30% and V15% of the AXB plans were significantly greater than those of the AAA plans. In contrast, the ipsilateral lung V5% decreased significantly. The AXB plans had a significantly increased average of 3% of the contralateral breast volume.

Conclusion: It is important to use the efficient AXB algorithm to better estimate normal tissue toxicity and treatment outcomes in the treatment of breast cancer using the UK FAST trial.

Keywords: Acuros External Beam; Anisotropic Analytical Algorithm; UK FAST trial; Breast radiotherapy planning; Deep inspiration breath-hold

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Introduction:

Breast cancer is the most common malignancy and the second most prevalent cause of death from cancer after liver cancer, with an estimated 11% mortality rate [1]. Several cancer centers recommended reducing hospital visits without compromising the oncological outcome to protect cancer patients and healthcare providers from possible exposure to the COVID-19 pandemic [2]. Therefore, hypofractionated regimens must be considered for low-relapse patients who require daily visits for three to five weeks due to comorbidities [3,4]. Hence, during the COVID-19 pandemic, the randomized UK FAST trial may be considered one of the superior regimens for breast cancer treatment. This is because, after 10 years of follow-up, the late effects on normal tissue seem to be biologically comparable between 28 Gy in five fractions once a week and 50 Gy in 25 fractions [3].

However, the randomized UK FAST trial needs more accurate dose calculations to make patients benefit from effective local control and fewer hospital visits if these treatments are given correctly. According to the International Commission on Radiation Units and the American Association of Physicists in Medicine recommendations, the radiation dose given to a patient with cancer should be accurate to within 5% of the delivered radiation dose. A 5% difference in radiation dose may reduce tumor control probability and change the expected normal tissue complication probability by about 15% and 25%, respectively. Therefore, for more

safety, the uncertainty in the delivered dose should be about 2% [5,6].

Dose calculation is still challenging in radiotherapy planning for patients with breast cancer due to tissue inhomogeneities with a complex composition, such as soft tissue, bone, and lung with a very low density [7,8]. The Varian Eclipse software currently provides the Acuros External Beam (AXB) algorithm and the Anisotropic Analytical Algorithm (AAA) for dose calculation. The AXB algorithm was established to resolve several AAA shortcomings in heterogeneous regions, particularly in the transfer from soft tissue to air. Some of these shortcomings include overestimating or underestimating the dose on the far side of high- or low-density materials and overestimating the dose in the lung [9–14].

AAA uses a Monte Carlo-generated kernel that is adjusted based on changes in local density, whereas the AXB algorithm uses a numerical solution of the Linear Boltzmann Transport Equation (LBTE) to calculate the dose to the medium, rather than the dose to water [15,16]. Additionally, the AXB algorithm considers the fundamental structure of heterogeneous tissues, increasing the accuracy in predicting the accurate dose distribution inside the patient and improving the ability to explain toxicity and clinical treatment outcomes [17,18].

Fogliata et al. evaluated the efficacy and dosimetric benefit of using the AXB algorithm rather than AAA in the typical two tangent fields for different breast tissues (adipose versus ductal), lung densities, and lungs outside and inside the tangential fields. They reported that the two dose calculation algorithms calculated lung dose in very different ways, and significant differences in lung dose calculations were observed between the algorithms. For example, when lung density decreased and density changes were the greatest, AAA always overestimated lung dose in patients during the deep inspiration breath-hold (DIBH) technique. Hence, it was suggested that the AXB algorithm is more accurate for patient dose calculations than AAA [19].

To the best of our knowledge, no study compared the impact of dose calculations using the AXB algorithm and AAA in patients with left-sided breast cancer treated in the UK FAST trial with the high dose per fraction (28.5 Gy/5 fractions) using the DIBH technique. Therefore, this study aimed to use the AXB algorithm instead of AAA to calculate doses for planning breast radiotherapy with the UK FAST trial if a comparison of dose-volume histogram (DVH) curves represented a significant distinction in terms of how well it covers the target volume and protects organs that are at risk.

Patients and Methods:

Patient selection and computed tomography (CT) simulation

This was a retrospective study involving 50 patients with left-sided breast cancer at an early stage who underwent breast-conserving surgery. Patients received treatment with the UK FAST trial for their post-operative whole breast irradiation.

Patients were positioned and immobilized using a Q-fix supine breast board (Avondale, PA, USA), which was upraised to 15° in patients with large breasts to avoid any possible overlapping between the breast and the head of the humerus; hand support sticks to raise their arms over their heads; and two indexers for fixing the breast board in a regular couch position to maintain the reproducibility of the right-left and inferior-superior shifts.

All patients were scanned using the Real-Time Position Management System (Varian Medical System, Palo Alto, CA, USA) with the DIBH technique. A six-dot reflector marker block was positioned on the xiphoid process for every patient's upper abdomen to keep track of how they breathed during the scans. The medical physicist observed the patients' breathing cycle while the radiation therapist gave the patients instructions for DIBH. A breath-hold level would be controlled by a gating window set to 4 mm to ensure the patients could hold their breath for as long as the DIBH scan needed [20].

CT data were obtained and reconstructed every 4 mm using a CT simulator (SOMATOM Definition AS, Siemens HealthCare, Erlang, Germany). The CT scan examined a region of interest from the C3 vertebra to 5 cm below the infra-mammary fold. After that, the image data were transferred to a planning system (Eclipse version 13.6.23, Varian Medical System, Palo Alto, CA, USA) to contour the target volume and organs at risk (OARs) and calculate the treatment plan doses.

Treatment Planning

The left breast planning target volume (PTV) and risk structures (lung, heart, and contralateral breast) were delineated by the radiation oncologist using the Radiation Therapy Oncology Group breast cancer atlas [21].

The prescribed treatment plan doses were 28.5 Gy per five fractions, which would be given over 5 weeks at a frequency of 5.7 Gy per week. By applying the field-in-field technique, treatment beams were calculated using medial and lateral tangential beams with 6 MV energies for patients with slight separation and 15 MV energies for those with large separation. Furthermore, tangential fields were based on a half-beam block technique with closed jaws toward the central axis to minimize divergence into the ipsilateral lung and the heart.

Treatment plans have to meet the institutional acceptance criteria shown in Table 1 to be approved. The radiation weights were defined for the lateral and medial tangential beams to avoid hot spots. Then, based on the patient's anatomy, segments (field-in-field) were used to increase the treatment radiation dose to exposed parts that had not been fully treated by the isodose line of the dose prescription, enhancing dose homogeneity and coverage inside the PTV.

Table 1: The clinical acceptance criteria of the UK FAST trial.

Structure	Dosimetric parameter	First and second acceptance criteria
PTV	V90% (25.65 Gy)	≥90%
	V105% (29.92 Gy)	≤5%
	V107% (30.49 Gy)	≤2%
Ipsilateral lung	V30% (8.55 Gy)	≤15%–20%
	V15% (4.27 Gy)	≤30%–35%
	V5% (1.42 Gy)	≤50%–55%
Heart	V25% (7.12 Gy)	≤5%
	V5% (1.42 Gy)	≤30%–35%
Contralateral breast	V3% (0.85 Gy)	≤5%

PTV: planning target volume; VX%: the volume of the structure receiving a radiation dose equal to X%.

A Varian TrueBeam linear accelerator with a kilovoltage imaging system and a millennium multileaf collimator (MLC) was used to treat patients. MLC comprises 80 leaves on the inside that have a resolution of 0.5 cm at the isocenter and 40 leaves on the outside that have a resolution of 1 cm.

Dose Calculation

The treatment plans were generated retrospectively from the AAA plans using the AXB algorithm's dose-to-medium option for dose reporting. The field angle, geometry, energy, beam segments, and prescription point were kept the same. Both algorithms used a 0.25 cm grid for calculations to reduce errors as much as possible. Heterogeneity corrections were turned on for all calculations.

AAA

AAA superimposes photon and electron convolution doses for each beamlet to get the final dose distribution. Kernels that describe the dose distribution of secondary particles at the point of interaction and energy transport are created using Monte Carlo particle transport codes. AAA predicts tissue heterogeneity in all three dimensions of the treated area using the Monte Carlo kernels. This is performed via radiological scaling of the dose deposition functions and electron density-based scaling of the photon scattering kernels in four different directions so that they are the same length and density as water in normal directions [22].

AXB

The AXB algorithm solves the LBTE, which determines radiation particle macroscopic behavior, to calculate the absorbed dose. Unlike convolution and superposition algorithms, which handle heterogeneities by applying dose kernels calculated in water to the irradiated volume of a patient, the AXB algorithm must know the chemical composition and density of specific material for each voxel of the patient image through which particles flow to predict how radiation interacts with matter and calculate dose correctly. Therefore, the AXB library has 16 non-biological materials and five biological materials (muscle, lung, adipose tissue, cartilage, and bone) [15].

Dosimetric evaluation

DVHs were calculated for all structures, including PTVs and OARs, with each algorithm (AXB and AAA). The PTV dose distributions calculated using the AXB algorithm and AAA were evaluated by determining V90%, V105%, and V107% parameters, which are the volumes of the PTV that were at least 90%, 105%, and 107% of the dose, respectively. The OARs were evaluated in terms of the volumes of the ipsilateral lung getting 5%, 15%, and 30%, the volumes of the heart getting 5% and 25%, and the volumes of the contralateral breast getting 3% of the prescribed treatment dose.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20.0 (IBM Corp, Armonk, NY, USA). The calculation results were expressed as the mean value and standard deviation. The results were compared using a two-sample paired t-test. A p-value of less than 0.05 was considered statistically significant with a 95% confidence interval.

Results:

A total of 100 treatment plans were analyzed for 50 patients with breast cancer on the left side in the UK FAST trial. This study aimed to compare the given dose using a forward-planning field-in-field approach calculated with the AXB algorithm with that calculated with AAA. DVH curves showed how the dose calculations were different for the PTV and OARs when the AXB algorithm and AAA were used in a patient, which better reflects the evaluated patient plans (Figures 1 and 2). Figure 3 shows the AXB-AAA differences in DVH parameters for PTV coverage and OARs across all patients.

The PTV coverage and the OAR dosimetric parameters were assessed to evaluate the dosimetric impact of both the AXB and AAA dose calculation algorithms (Table 2).

The dosimetric parameters of OARs were statistically different when comparing the distributions from the two calculation algorithms. The heart V25% for the AXB calculated plans increased significantly compared with that for the AAA calculated plans. However, the AXB calculated plans had a lower heart V5% than the AAA calculated plans. The ipsilateral lung dosimetric values of the AXB calculated plans, including V30% and V15%, were significantly greater than those of the AAA calculated plans. In contrast, when comparing AXB calculated plans with AAA calculated plans, the ipsilateral lung V5% decreased significantly. The AXB plans had a significantly

increased average of 3% of the contralateral breast volume compared with the AAA plans. However, it was found that the PTV coverage parameters for AXB plans were higher than those for AAA plans, with a statistically significant difference in V90%, V105% and V107% between both calculation algorithms.

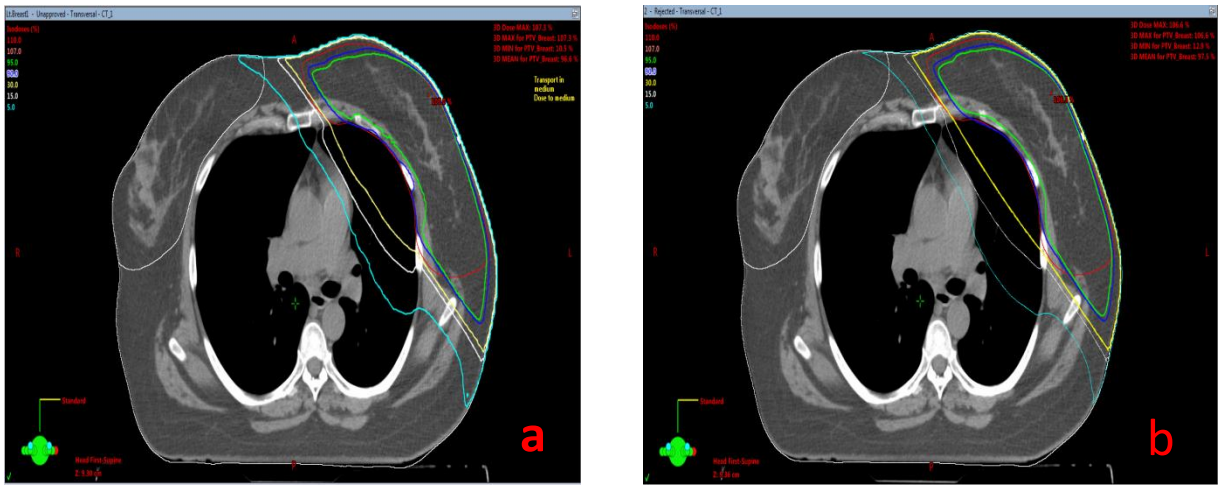

Fig. 1: Isodose distributions on axial plans were calculated using (a) AXB algorithm and (b) AAA, respectively.

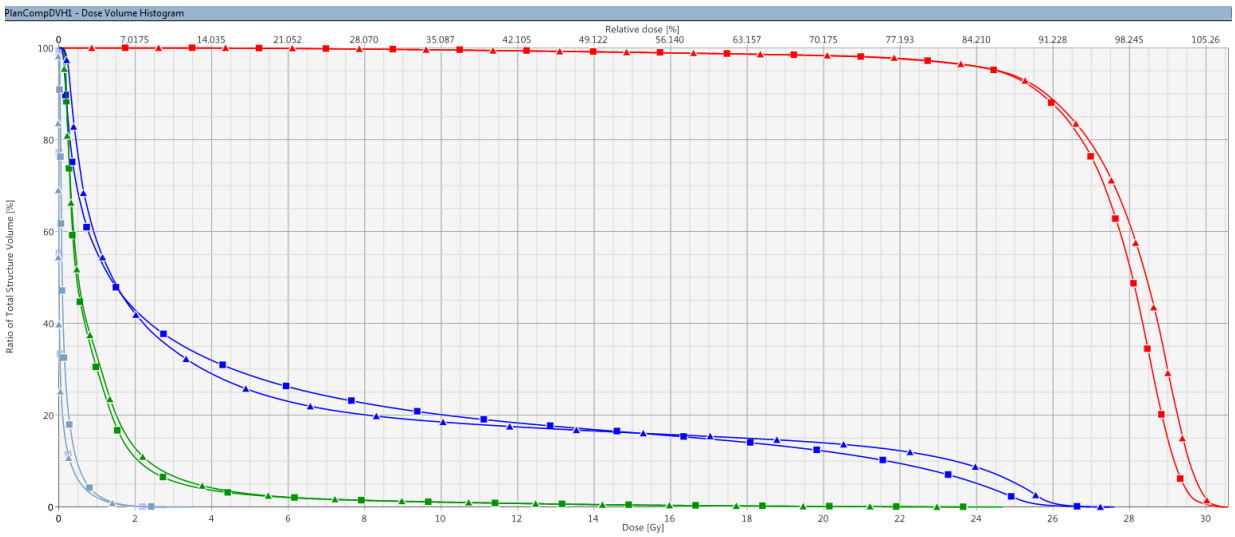

Fig. 2: Comparison between the two DVHs for PTV (Red line), Lung (Blue line), Heart (Green line) and Contralateral breast (Gray line) using AXB (Square) algorithm and AAA(Triangle) algorithm.

Table 2: Paired sample T-test results of the dosimetric comparison of the PTV coverage and OARs parameters.

Structure	Dosimetric parameter	Mean ± SD		*p*-value
		AXB (%)	AAA (%)	
PTV	V90%	95.3 ± 3.2	94.5 ± 2.7	0.04
	V105%	3.7 ± 1.9	3.1 ± 1.2	0.03
	V107%	0.3 ± 0.3	0.01 ± 0.04	<0.0001
Ipsilateral lung	V30%	18.1 ± 3.3	16.7 ± 2.9	<0.0001
	V15%	26 ± 4.8	24.4 ± 3.8	<0.0001
	V5%	45.3 ± 5.1	50.3 ± 4.5	<0.0001
Heart	V25%	2.2 ± 1.8	2.1 ± 1.7	<0.0001
	V5%	17.9 ± 6.6	19.7 ± 5.9	<0.0001
Contralateral breast	V3%	3.1 ± 2.3	1.3 ± 1.5	<0.0001

PTV: planning target volume; SD: standard deviation.

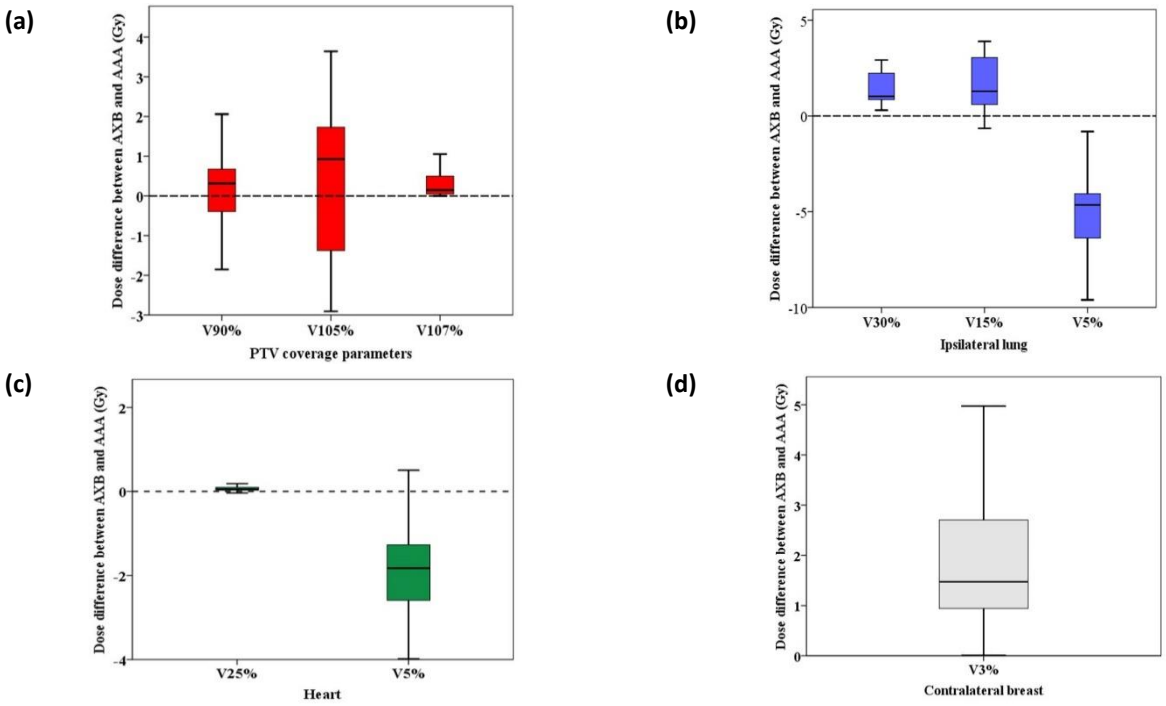

Fig. 3: Differences in DVH parameters between AXB algorithm and AAA (a) PTV, (b) ipsilateral lung, (c) heart, and (d) contralateral breast. Whiskers indicate the range of the data. Boxes indicate the 25–75 percentiles.

Discussion:

It is essential to take into consideration the significant differences between both algorithms (AXB algorithm and AAA) and how this change will impact the overall quality of the treatment plan in clinical practice before using a dose calculation algorithm to treat patients with breast cancer with the UK FAST trial. This study evaluated the impact of alteration of dose calculation algorithms (AXB algorithm instead of AAA) on the dosimetric parameters for planning breast cancer radiotherapy.

The results revealed significant differences between both algorithms for PTV coverage and OAR parameters. These differences were related to the used methods for dose calculations and the DIBH technique. The lung density in patients with the DIBH technique was lower than that of patients with the free-breathing technique, so it has less attenuation, and the dose is deposited farther from the scattered electrons of the interaction point than the kernel-based AAA predicts. Then, the difference in dose between the two algorithms is based on the assumptions made about how electrons

move sideways in low-density lung tissue other than water [23].

Hence, it was suggested that the AAA's assumption that electrons move laterally in low-density lung tissue does not seem to be accurate enough for a reliable dose calculation. The AXB algorithm calculates the dose distribution to a medium by modeling the interaction of radiation with different body tissues that have very different chemical compositions. Thus, our findings were consistent with those of earlier studies that reported that lung and heart volumes receiving intermediate doses show a significant increase, whereas volumes receiving high and low doses show a significant decrease when comparing the calculated volumes using the AXB algorithm with those calculated using AAA [8,24,25].

Guebert et al. reported a significant dosimetric difference between the dose calculation algorithms of AXB and AAA because the beam's path through the lung affects the calculated dose for a patient with great separation, and this is predicted since the AXB algorithm can handle interfaces and heterogeneities with more precision than AAA [26].

Additionally, the AXB plans had a significantly higher average contralateral breast volume (V3%) than the AAA plans, as reported by Panettieri et al. (2009), who evaluated the dose in the AAA buildup region, which was much lower than what Monte Carlo calculations predicted in the initial few millimeters of tissue; the lung volume increased primarily when the beam was given at a large angle, as it is in breast radiotherapy, and the DIBH scan was used [27]. These conditions made the modeling of how radiation particles scatter laterally worse for AAA, whereas the AXB algorithm is shown to be closer to the gold standard of Monte Carlo calculations in the buildup regions of air-to-tissue transitions [19,28,29].

When treating left breast cancer with radiation, the heart and lungs are also exposed to radiation, which can result in radiation-induced ischemic heart disease and lung toxicities like acute pneumonitis and sub-acute or late fibrosis. The amount of lung and heart tissue irradiated, the total dose, and the fractionation are all factors that affect toxicity [30,31]. Because of this, the high dose per fraction in the UK FAST trial is likely to trigger more complications in normal tissues. Therefore, dose calculations would be improved with the use of more complex algorithms and the ability to take into account the correct elemental makeup of the different tissues in the human body. This makes it possible to know more about how the actual dose is distributed inside the patient, which could help in the future to better predict the clinical outcomes in certain situations. This shows the importance of using the AXB algorithm when employing an ultra-hypofractionation protocol to treat patients with breast cancer.

Conclusion:

In the UK FAST trial, patients with left-sided breast cancer were treated. The study results revealed that the AXB algorithm and AAA for low lung density associated with the DIBH technique have significantly different PTV and OAR dose-volume parameters. Therefore, this study showed that it is important to use the efficient AXB algorithm to better estimate normal tissue toxicity and treatment outcomes in clinical practice when trying to make the real and calculated treatment radiation doses match up better.

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