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Evaluation of The Dosimetric Impact of Different Planning Algorithms in IMRT For Lung Tumors

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ABSTRACT

Purpose: Lung cancer represents a major public health concern as it is the malignancy with the highest mortality rate among all cancers. Radiotherapy is an effective treatment modality used both with curative and palliative intent in the management of lung cancer. In this study, the aim was to evaluate the effects of different treatment planning algorithms on critical organs and the target tumor by using Intensity-Modulated Radiotherapy (IMRT) techniques in patients with lung-located tumors.

Methodology: This study was accomplished in a group of 19 patients with lung localized tumors who were treated in our clinic. In the treatment planning of the patients; Elekta-Monaco with Monte Carlo (XVMC), Pencil Beam algorithm; Varian-Eclipse with Anisotropic Analytical Algorithm (AAA), Acuros XB (AXB). In these treatment planning systems, plans were done by 6MV photon energy using IMRT techniques. The prescribed dose to the PTV was 60Gy in 30 fractions. Five-field non coplanar IMRT plans were generated for each patient. The dose distribution of the planing target volume (PTV) and organs at risk (OAR) were analyzed by comparing all the plans. All differences between plans were evaluated statistically. Statistical analysis was performed using SPSS Statistics v.29.0.2.0 programme .

Findings and Conclusion: The Friedman test was used to compare independent groups, with a significance level of $p < 0.05$ considered statistically significant. If the Friedman test indicated significance, the results were evaluated using the Bonferroni-corrected Wilcoxon rank test. In the analysis of plans using the 'Step and Shoot' IMRT technique, significant differences were found among algorithms in the Dmean, D2, and D5 values for the target volume and the Dmean values for critical organs. Notably, there were marked differences in the low-dose volume regions of the total lung, contralateral lung, and ipsilateral lung.

Keywords: *Monte Carlo Algorithm, Pencil Beam Algorithm, Anisotropic Analytical Algorithm, IMRT, Lung Cancer.*

INTRODUCTION

Lung cancer is the most commonly diagnosed and the deadliest type of cancer worldwide. As of 2022, it ranked first among all cancer-related deaths, with approximately 2.48 million new cases and 1.82 million deaths reported [1]. Although it is more frequently observed in men, incidence rates among women are also increasing. China, the United States, and Japan are among the countries with the highest number of cases. In Turkey, lung cancer is the second most common cancer in men after prostate cancer [2]. Lung cancer is generally classified into two main groups: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Diagnosis is often made at advanced stages, which significantly reduces survival rates. Although treatment options have improved considerably in recent years, treatment success is largely dependent on individualized approaches. Management involves multimodal strategies including surgery, chemotherapy, radiotherapy, immunotherapy and targeted therapies. Treatment decisions for lung cancer depend on several factors, including cancer type (SCLC or NSCLC), stage, the patient's overall health and age, as well as molecular characteristics such as gene mutations. Due to the fact that lung cancer is frequently diagnosed at an advanced stage, treatment opportunities are often limited. This highlights the importance of early detection and effective therapeutic strategies. Surgery remains the primary and most effective treatment modality in early-stage lung cancer. For tumors that are inoperable due to their location, size, or the patient's overall health status, chemotherapy and radiotherapy are commonly used alternatives. Advances in technology have allowed for more precise targeting of tumor tissue, minimizing damage to healthy tissues and improving patient quality of life. The selection of the appropriate radiotherapy technique should be

made by a multidisciplinary team, taking into account the tumor type, stage, location, and patient condition. The quality of radiotherapy in lung cancer is directly related to the technique used. Intensity-modulated radiation therapy (IMRT) has become widely used in the treatment of both advanced-stage NSCLC and SCLC due to its superior target dose conformity and lower radiation exposure to the lungs and heart compared to three-dimensional conformal radiotherapy (3D-CRT) [3,5]. In the RTOG 0617 trial, patients with advanced-stage NSCLC who received IMRT experienced lower rates of pulmonary toxicity [6]. Although increasing the total radiation dose generally enhances local control in various tumor types, it is often limited by early and late side effects in normal tissues. Therefore, dose escalation for tumor control must be carefully balanced within the tolerance limits of surrounding healthy tissues. Tissue damage after radiotherapy depends on several factors, including the total radiation dose, the size of the irradiated volume, daily fraction dose and number, concurrent chemotherapy, patient age and performance status (KPS), underlying chronic conditions, tissue oxygenation, and regenerative capacity [7]. Treatment planning systems (TPS) utilize various algorithms to calculate dose distributions in radiotherapy planning, and the accuracy of these calculations varies depending on the characteristics of the algorithm used. The International Commission on Radiation Units and Measurements (ICRU) has recommended a general dose accuracy of within ±5% for radiotherapy treatments [8]. Accurate dose calculation in heterogeneous media is challenging due to physical complexities and may vary significantly depending on the algorithm employed. This issue becomes particularly evident in the planning of lung tumors, where tissue heterogeneity plays a major role [9]. Knöös and colleagues initially classified dose calculation algorithms into two main groups: "correction-based" and "model-based" algorithms [10]. Model-based algorithms provide more accurate dose calculations in regions with low density and heterogeneous structures compared to correction-based algorithms. This is primarily because correction-based algorithms neglect the lateral transport of secondary electrons. In contrast, model-based algorithms combine the total energy released per unit mass through a convolution method, offering more reliable and precise dose predictions, especially in low-density heterogeneous media. Nevertheless, challenges remain in achieving accurate dose calculations in heterogeneous regions [11,12]. Recent technological advances have led to the development of "principle-based" algorithms. These algorithms have three significant advantages over correction-based and model-based algorithms: 1) they model the transport of secondary electrons more accurately, 2) they can calculate dose accumulation in biological tissues and materials with high atomic number (Z), and 3) the dose is reported as the medium dose [13].Commercially available algorithms such as Acuros XB (AXB) and Monte Carlo X-ray voxel-based Monte Carlo (XVMC) belong to the principle-based category. When compared with correction-based algorithms like Pencil Beam (PB) and model-based algorithms such as the Anisotropic Analytical Algorithm (AAA) and Convolution Superposition (CS), AXB and XVMC algorithms demonstrate superior dosimetric performance, especially in heterogeneous tissues [14]. The aim of this study was to evaluate the effects of different dose calculation algorithms on dose distribution to the target tumor volume and surrounding critical organs in treatment plans created using Intensity-Modulated Radiation Therapy (IMRT) techniques for patients with lung-located tumors.

MATERIAL AND METHODS

Patient Characteristics

This study included a total of 19 patients with non-small cell lung cancer (NSCLC) who received radiotherapy at the Department of Radiation Oncology, SBÜ Gülhane Training and Research Hospital, between January 2021 and December 2022. Patients were staged as T2–T4, N0–N1, and M0, and were inoperable or had not undergone resection. The median age of the patients was 62 years (range: 51–77 years). Among the 19 patients, 10 (52.6%) were diagnosed with adenocarcinoma, and 9 (47.4%) with squamous cell carcinoma. The median volume of the treated tumors was 300 cc (range: 153–762 cc). Regarding the location of the target volumes, 47.4% were localized in the left upper lobe (LUL), 31.5% in the right middle lobe (RML), and 21.1% in the right upper lobe (RUL).

Defining Target Volume, Critical Structure and Treatment Techniques and Planning

All patients' images were acquired using a Toshiba Aquilion computed tomography (CT) scanner equipped with the Active Breathing Control (ABC) system during moderate deep inspiration breath-hold (mDIBH). The scans were performed at 120 kVp and 100 mA, with a slice thickness of 3 mm. Patients were immobilized in the supine position with arms raised using a T-bar device. The CT images were transferred to the contouring software. In accordance with ICRU83 recommendations, the internal target volume (ITV) was delineated, and a 5 mm isotropic margin was added to the ITV to generate the planning target volume (PTV), following clinical

protocol. No margin was added to the organs at risk (OARs) [8]. The treatment plans for all patients included in the study were replanned using 6 MV X-rays by the same medical physicist, utilizing treatment planning systems (TPS) from two different commercial companies (Elekta and Varian) as specified in Table 2. Patient plans were prescribed with a total treatment dose of 60 Gy delivered in 30 fractions of 200 cGy per day [15]. All plans were designed to ensure that 100% of the prescribed dose, defined with 6 MV photon energy, would cover 95% of the PTV volume. Five non-coplanar fields were used for the plans [16,10]. Patient-specific quality assurance (PQA) was performed to verify the dosimetric accuracy of all treatment plans [17,18].

Data Evaluation

In this study, dose constraints for critical organs were established based on the dose protocols routinely applied in our clinic, and the parameters used for evaluation are presented in Table3. Optimization of all treatment plans was performed based on the constraints listed in Table 3.

For each patient's plan, the maximum dose (Dmax), minimum dose (Dmin), mean dose (Dmean, also referred to as MLD), and the doses received by 95%, 98%, 2%, and 5% of the volume, denoted as D95, D98, D2, and D5 respectively, were evaluated for the PTV. For the contralateral and ipsilateral lungs, the mean dose (Dmean) and the volume percentages receiving 5 Gy, 10 Gy, and 20 Gy (V5, V10, and V20, respectively) were analyzed. For the total lung, volume percentages receiving 5 Gy, 10 Gy, 20 Gy, and 30 Gy (V5, V10, V20, V30), the mean dose (Dmean) of bilateral lungs, and dose values corresponding to 1000 cc and 1500 cc volumes were also evaluated. Additionally, the gross tumor volume (GTV) was analyzed. For the esophagus, the maximum dose (Dmax), mean dose (Dmean), and the volume percentage receiving 60 Gy (V60) were assessed; for the heart, the mean dose (Dmean) was evaluated; and for the spinal cord and ribs, the volume percentages receiving 5 Gy, 10 Gy, 30 Gy, and 60 Gy (V5, V10, V30, V60), as well as the maximum dose (Dmax), were analyzed.

Table 1. Patient characteristic

Patient No	Gender	Age	Target Volume (cc)	Target Localisation	Histology
1	Male	65	265	RML	AdenoCA
2	Male	60	200	RUL	SCC
3	Female	54	153	LUL	AdenoCA
4	Male	56	300	RML	SCC
5	Male	67	337	RUL	AdenoCA
6	Male	72	557	RUL	SCC
7	Male	63	169	RUL	AdenoCA
8	Male	77	303	LUL	SCC
9	Male	54	164	LUL	SCC
10	Male	66	256	RML	AdenoCA
11	Male	62	208	LUL	SCC
12	Male	57	209	LUL	AdenoCA
13	Male	51	482	RML	SCC
14	Male	68	240	LUL	AdenoCA
15	Male	55	401	LUL	AdenoCA
16	Male	69	762	RML	SCC
17	Male	55	373	LUL	SCC
18	Male	56	682	LUL	AdenoCA
19	Male	69	379	RML	AdenoCA

Data Analyses

In this study, the aim was to compare treatment plans generated using different algorithms in terms of dosimetric parameters. For this purpose, a total of 76 treatment plans were created and evaluated using four different algorithms across two different Treatment Planning Systems (TPS) with the Intensity-Modulated Radiation Therapy (IMRT) technique. The analysis of the treatment plans was conducted using the Computational Environment for Radiological Research (CERR) software, which operates within the MATLAB programming environment. CERR integrates plan data obtained from different TPSs with DICOM images, anatomical structures, and dose distributions, providing a comprehensive platform for treatment plan analysis. Furthermore, it enables

the consolidation of all Dose-Volume Histograms (DVHs) into a single DVH structure, allowing for systematic extraction of numerical data and facilitating comparative analyses between plans.

Table 2. TPS systems of different commercial companies and the algorithms used.

TPS	Algoritma
Elekta-Monaco 5.1	Monte Carlo (XVMC) Pencil Beam (PB)
Varian-Eclipse 15.6)	AnisotropicAnalitycalAlgorithm(AAA) Acuros XB (AXB)

The statistical analysis of the data was performed using SPSS Statistics version 29.0.2.0. Descriptive statistics (mean, standard deviation, and median) were reported for both categorical and continuous variables. To determine whether there were statistically significant differences between the algorithms, the Friedman test was first applied, with the level of significance set at $p < 0.05$. In cases where the Friedman test indicated significant differences, pairwise comparisons between algorithms were conducted using the Bonferroni-corrected Wilcoxon signed-rank test, with $p < 0.008$ considered statistically significant.

Table 3. Normal Tissue Dose-Volume Constraints.

Total Lungs		**Esophagus**	
D_{mean}	MLD ≤20 Gy	D_{mean}	Mean ≤34
V_{20}	≤37%	V_{60}	<5cc
V_5	≤60%	**Heart**	
Lung minus GTV (1500cc)	≤14 Gy	D_{mean}	≤26 Gy
Lung minus GTV (1000cc)	≤15 Gy	V_{60}	< 15 cc
Spinal cord		**Contralateral-İpsilateral Lung**	
D_{max}	Max≤50Gy	D_{mean}	MLD ≤20 Gy

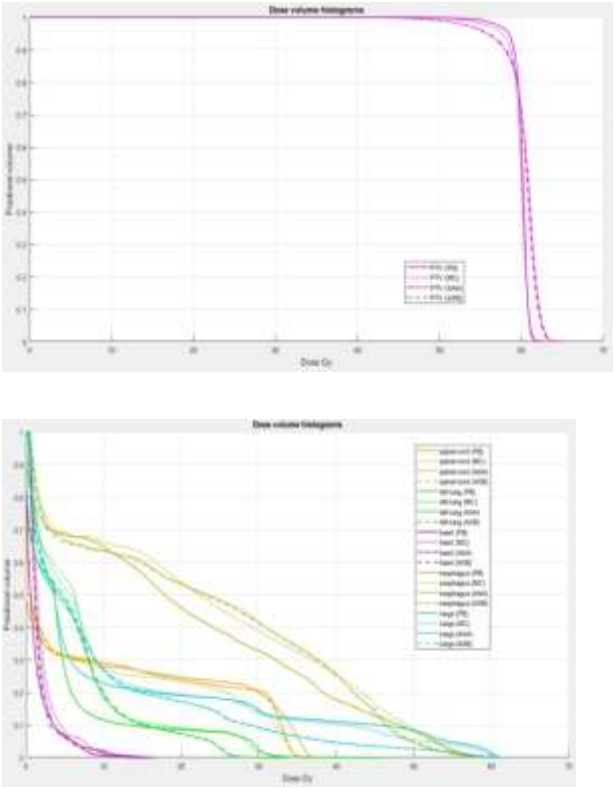

Figure 1: DVH comparison for a patient

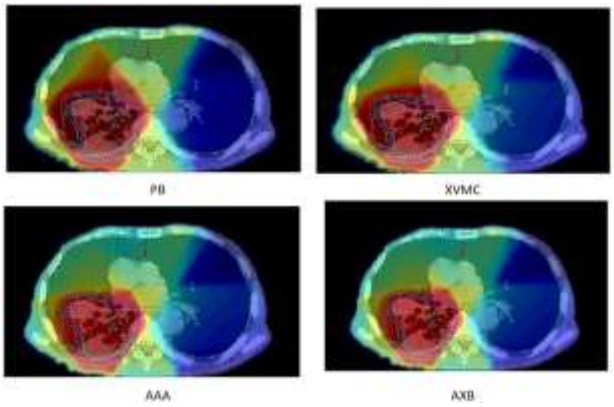

Figure 2: Dose distributions of different algorithms on the same CT slice.

RESULTS

In this study, the dose calculation accuracy of currently used algorithms was compared for a patient group with lung cancer. Data were evaluated for four different algorithms employed in two different treatment planning systems. Although IMRT does not significantly improve overall survival, it offers important advantages such as reducing toxicity, providing more precise dose distribution to the target volume, and enhancing patient comfort. Due to these features, IMRT is widely preferred in modern radiotherapy practices. As stated in the American Association of Physicists in Medicine (AAPM) Report No. 85, the level of dose differences can be clinically significant, and each center may develop its own protocols accordingly [19].

The treatment plans were evaluated based on the data obtained from Dose–Volume Histograms (DVHs), as well as cross-sectional and three-dimensional isodose distributions. Differences in target coverage, dose homogeneity, and conformity were qualitatively and quantitatively assessed. Notable variations in isodose distributios were observed between the algorithms, particularly in high-dose regions and at the target peripheries. DVH comparison and the typical isodose distribution were given in Figures1 and 2 for a patient. The PTV was 762cc. The lesions were located in the right middle lobe of the right lung. Table 4. includes the coverage rates of the PTV along with the Homogeneity Index (HI) values calculated according to the ICRU-83 criteria. Additionally, detailed dose distribution data for critical organs such as the total lung, contralateral and ipsilateral lungs, spinal cord, heart, esophagus, and ribs are also presented in Table 5.

According to this analysis; Target Volume parameters including D95, D98, D2, D5, Dmean, Dmin, and Dmax were evaluated. Since all plans were defined in a way that the defined dose would cover 95% of the PTV volume, it was observed that there was no difference between the algorithms in Dmin and Dmax values. Statistical pairwise analyses were performed among the dose calculation algorithms to evaluate differences in target volume parameters, specifically D2, D5, D95, D98, and Dmean ($p<0,008$). Significant differences were observed for D95 between PB-MC and AAA-PB, and AAA-AXB; for D98 between PB-MC and AAA-AXB; for D2 between MC-AXB and PB-AXB; for D5 between AXB-MC and AXB-PB.

Spinal cord and rib cage were evaluated by Dmax, and no significant differences were found between the algorithms. Heart, Dmean, V5, V10, V20, V30, and V60 parameters were assessed, and no significant differences were found for V10 , V30 , V60. The pairwise statistical analysis performed for V5 and Dmean revealed statistically significant differences between MC and PB algorithms ($p<0,001$). Esophagus was evaluated by Dmean, Dmax, and V60 parameters, with significant differences detected for Dmean between PB-MC, AAA-PB, and AXB-PB algorithms($p<0,003$). Pairwise statistical analyses performed among different dose calculation algorithms revealed significant differences in both ipsilateral and contralateral lung dose parameters. Contralateral lung analysis for Dmean, V5, V10, and V20 showed significant differences for Dmean and V10 between PB-MC, AAA-PB, and AXB-PB; for V5 between PB-MC, AXB-AAA, and AXB-PB; however, no significant difference was found for V20. Ipsilateral lung analysis of Dmean, V5, V10, and V20 revealed significant differences among all algorithms in IMRT technique ($p<0,001$).

In this study, when comparing target volume values, it was found that the Pencil Beam (PB) algorithm overestimates PTV coverage and underestimates doses to critical organs due to its neglect of certain physical parameters. The PB algorithm tends to underestimate the dose in heterogeneous tissue regions such as the contralateral and ipsilateral lungs, and therefore may not accurately reflect the true risk of radiation-related complications, including pneumonitis. The Anisotropic Analytical Algorithm (AAA) and Acuros XB (AXB) algorithms demonstrated similar dose values and distributions for both the PTV and critical organs. Among the algorithms evaluated, these two showed higher maximum dose values within the tumor volume. It was concluded that replacing the PB and AAA algorithms with the Monte Carlo (MC) algorithm could be more advantageous. Furthermore, both MC and AXB algorithms exhibited good accuracy in heterogeneity correction and are recommended for use in tumor volumes adjacent to heterogeneous structures.

Table 4. PTV coverage data for treatment plans generated using different algorithm.

	***PB*mean ± SD**	***MC*mean ± SD**	***AAA*mean± SD**	***AXB*mean± SD**	***P***
PTV					
D_2 ,Gy	62,27±0,57	62,30±0,51	63,33±1,95	63,48±1,21	**<,001**
D_5,Gy	61,79±0,48	61,90±0,39	62,94±1,74	63,10±1,16	**<,001**
D_{95},Gy	59,61±0,74	58,97±0,81	58,75±0,92	59,58±0,53	**<,001**
D_{98},Gy	58,99±1,17	58,18±1,24	58,21±1,09	58,76±0,71	**,002**
$D_{min,}$Gy	51,09±4,98	50,57±6,03	54,06±2,92	51,43±1,90	,018
$D_{max,}$Gy	64,93±1,87	64,86±1,40	65,42±2,28	65,65±1,38	,035
$D_{mean,}$Gy	60,71±0,29	60,52±0,33	60,74±1,51	61,44±0,77	**<,001**
HI	0,068±0,025	0,075±0,024	0,085±0,034	0,079±0,027	,02
CI	0,751±0,046	0,737±0,027	0,779±0,066	0,763±0,031	,02

Table 5. OAR Sparing Data for treatment plans generated using different algorithms.

	***PB*mean ± SD**	***MC*mean ± SD**	***AAA*mean± SD**	***AXB*mean± SD**	***P***
TotalLungs					
V_5	45,37±9,94	51,24±10,43	50,56±11,28	50,80±11,33	**<,001**
V_{10}	30,53±8,92	32,99±9,60	32,42±9,5	33,58±11,04	**<,001**
V_{20}	23,95±7,35	24,45±7,43	22,50±6,32	22,59±6,36	,005
V_{30}	17,45 ±5,86	18,41±6,67	13,06±4,07	13,63±4,16	**<,001**
$D_{mean,}$ Gy	12,87±3,5	13,78±3,57	12,19±2,88	12,31±2,93	**<,001**
Lungs-$GTV_{(1500cc/14gy)}$	7,98±5,68	8,51±4,86	8,20±4,74	8,47±4,98	,006
Lungs-$GTV_{(1000cc/14gy)}$	15,62±9,82	16,48±9,51	14,94±7,54	15,08±7,51	,013
ContralateralLung					
V_5	31,96±12,65	39,22±13,47	41,34±11,17	41,84±11,37	**<,001**
V_{10}	9,93±8,19	13±10,15	16,18±10,89	17,42±12,15	**<,001**
V_{20}	4,23±426	4,13±4,39	5,05±3,90	5±3,83	,194
$D_{mean,}$Gy	4,38±1,81	5,31±2,0	5,54±1,88	5,63±1,93	**<,001**
İpsilateralLung					
V_5	62,33±14,44	66,71±14,05	62,81±14,55	63,11±14,20	**<,001**
V_{10}	56,77±14,32	58,27±14,14	54,25±14,03	55,06±13,90	**<,001**
V_{20}	49,26±14,22	50,45±13,83	45,64±12,79	45,83±12,85	**<,001**
$D_{mean,}$Gy	23,65±0,63	24,55±0,620	20,79±0,487	21,02±0,5	**<,001**
Esophagus					
V_{60}	0,459±0,841	0,259±0,632	1,29±2,32	1,20±2,21	0,06
$D_{max,}$Gy	50,37±16,01	51,64±12,93	54,64±10,37	55,32±10,63	**<,001**
$D_{mean,}$Gy	13,79±6,48	14,35±6,62	16,24±6,26	16,17±6,35	**<,001**
Heart					
V_5	31,53±28,17	33,12±29,08	31,88±28,28	29,86±28,73	**0,006**
V_{10}	21,25±22,48	23,35±24,05	20,76±22,37	23,66±23,92	,027
V_{30}	4,08±8,5	4,00±5,98	5,21±9,6	3,42±4,53	,853
V_{60}	0,16±0,49	0,041±0,15	0,15±0,32	0,19±0,35	,082
$D_{mean,}$Gy	6,23±5,67	7,07±5,67	6,89±5,51	6,85±5,54	**<,001**
Spinal cord					
$D_{max,}$Gy	32,10±6,40	32,20±6,74	35,04±8,47	33,50±4,60	,373
RIB					
$D_{max,}$Gy	59,73±5,97	61,05±5,28	58,68±9,36	58,49±9,96	,185

*p<0,05

DISCUSSION

The evaluation of the clinical effectiveness of treatment plans and the determination of dose calculation accuracy are made possible through comparative analyses between different treatment planning systems. Such comparisons not only reveal the computational capabilities of algorithms but also provide valuable insights into which systems deliver more reliable results in clinical practice. In this study, dose calculations of algorithms used in different TPS were compared to assess their agreement and discrepancies. Fundamentally, these differences arise from how the physical interactions between radiation and matter are modeled, leading to calculation variations between algorithms. Additionally, factors such as tumor location and size, as well as beam orientation, can influence these differences, causing variability in the observed discrepancies.

Bosse et al. compared dose values obtained using 6-10 MV photon energies for 18 lung cancer patients across the Pinnacle, Monaco, and Eclipse treatment planning systems, concluding that differences in dose calculations may exist between planning systems [7]. Similarly, our study identified variations in dose calculations. In the intensity-modulated radiotherapy technique, the AAA and AXB algorithms showed agreement with the PB algorithm in high-dose regions such as the ipsilateral lung, whereas they diverged in low-dose regions like the contralateral lung.

Christopher M. Bragg and colleagues aimed to evaluate the dosimetric accuracy and clinical validation of the Anisotropic Analytical Algorithm (AAA) used in the Eclipse TPS within IMRT techniques. The AAA algorithm provides more accurate and reliable dose calculations compared to the Pencil Beam Convolution (PBC) algorithm, especially in regions with low-density tissues such as the lung. Our study yielded similar results in multiple assessments [20].

In the evaluation of treatment plans, another important parameter is HI and CI, which indicate how uniformly and homogeneously the dose is distributed within the target volume. HI is a robust indicator reflecting the balance of dose distribution within the target volume; however, the factors influencing this index remain unclear in the literature. Some studies have reported various relationships between treatment parameters (such as target volume size or anatomical location) and plan quality indicators like HI and CI. For example, Knöös et al. reported in their Radiation Conformity Index (RCI) analyses that better dose conformity was achieved in pelvic tumor cases compared to lung and advanced-stage breast cancer cases [21].

In our study, although there were significant differences in HI and CI values among algorithms, no significant difference was observed between XVMC and AXB, with HI values in the target volume being close to each other. Recent studies suggest that achieving an ideal HI value is not always necessary in every case. In certain clinical scenarios, heterogeneity may be desirable, as delivering higher doses to areas with increased malignant cell density or resistant cell populations within tumors containing heterogeneous cell populations can be beneficial. Such heterogeneous dose escalation to the central tumor region may improve local control but can also increase the risk of complications [22,23]. Therefore, calculating these risks during planning can contribute to improving treatment quality.

The study findings indicate that the choice of dose calculation algorithm can lead to significant differences not only in target volume dosimetry but also in the doses delivered to critical organs. This underscores the importance of careful algorithm selection in treatment planning, especially when sensitive structures are involved. In clinical practice, the use of advanced algorithms with higher heterogeneity sensitivity and improved calculation accuracy, such as Acuros XB (AXB) and Monte Carlo (MC), is recommended to enhance planning reliability and patient safety.

CONCLUSION

These findings demonstrate that different algorithms can cause significant variations in dose calculation accuracy, especially in heterogeneous regions such as lung parenchyma, thereby impacting the quality of treatment plans. Moreover, dose differences between algorithms are influenced not only by calculation methods but also by clinical parameters including tumor anatomical location, volume, and beam orientation. Consequently, understanding the differences inherent to algorithm-based dose calculations is critical for interpreting plan quality and optimizing treatment decisions. Therefore, it is recommended that each clinic evaluate algorithms according to their specific conditions and patient profiles, and develop institution-specific protocols if necessary.

Conflict of Interest

There are no conflicts of interest and no acknowledgements.

ETHICS STATEMENT

Ethical approval for this retrospective study was obtained from the Health Sciences University Gülhane Scientific Research Ethics Committee (February 25, 2021; Decision No: 2021-03). The study was conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to its retrospective design.

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