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Research Article

Evaluation of Dosimetric and Radiobiological Parameters for Different TPS Dose Calculation Algorithms and Plans for Lung Cancer Radiotherapy

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Abstract:

Lung cancer presents a major public health concern in our country and around the globe. Radiotherapy is one of the main treatment modalities for lung cancer management for several years. This study aims to evaluate differences in the dosimetric and radiobiological parameters and in the dose distributions of Planning Target Volume (PTV) and organs at risk (OAR) in patients with lung tumors using different Treatment Planning System (TPS) algorithms and Volumetric Modulated Arc Therapy (VMAT) technique. This study was accomplished in a group of 19 patients with lung 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) algorithms and Tomo-plan Treatment Planning System with Convolution Superposition algorithm (C/S) of Tomotherapy device were used. In these treatment planning systems, plans were done by 6 MV photon energy using Volumetric Arc Therapy (VMAT) techniques. The prescribed dose to the PTV was 60 Gy in 30 fractions. Statistical analysis was performed using SPSS Statistics v.29.0.2.0 programme. Statistically, significant differences were found in D_{mean} , D_{max} , D_2 and D_{98} values for PTV between the algorithms, while small differences were found in D_{max} values of the contralateral lung, total lung and esophagus in critical organs. It is concluded that the difference between algorithms for PTV increases especially as the volume of the target tumor decreases. TPS with C/S algorithm gave closer results with XVMC. Algorithms were found to have an impact on radiobiological parameters.

1. Introduction

Lung cancer, which is one of the main causes for cancer-related deaths today, is the second most common type of cancer after prostate cancer in men and breast cancer in women [1]. Surgical methods, chemotherapy and radiotherapy can be used alone or together in some patients in the treatment of lung cancer. The treatments to be applied are determined according to the phases of non-small cell lung cancer (NSCLC). Particularly in the early stages of NSCLC, surgery is the most effective treatment method. However, for tumors that are not suitable to surgery due to tumor location, tumor size, or the general condition of the patient, chemotherapy and radiotherapy may be the treatment option. Accordingly, today more than 50% of lung cancer

patients have radiotherapy treatment at some point in their lives.

The quality of lung cancer Radiotherapy (RT) Treatment is directly related to the treatment technique used. Intensity Modulated Radiation Therapy (IMRT) and Volumetric Arc Therapy (VMAT) techniques provide better target dose conformity and organ at risk (OAR) protection than three-dimensional conformal radiotherapy (3DCRT), thus IMRT is increasingly used for non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) management. IMRT is widely used in the treatment of cancer (NSCLC) [2,3,4]. In radiotherapy treatment planning, 3D dose distribution is calculated with the algorithms of treatment planning systems (TPS) offered

commercially by manufacturers, and the accuracy in dose calculation depends on the dose calculation algorithm used by TPS. The International Commission on Radiation Units and Measurements (ICRU83) has recommended an overall dose accuracy of $\pm 5\%$ for radiotherapy treatments [5]. Considering the uncertainties arising from patient setup and dose calculations, the device should have a dose calculation algorithm capable of calculating dose distribution with an accuracy of $\pm 3\%$.

Since dose distribution becomes complex in heterogeneous environments, dose calculation results vary depending on the algorithms. Accurate calculation of dose distribution is a complex task, especially for tumors located in the lung [6].

Knös et al. initially described two types of algorithms: "correction" and "model-based" [7]. "Model" based algorithms perform more accurate dose calculations in low-density heterogeneous regions compare to "Correction" based algorithms because "Correction" based algorithms do not account for the lateral transport of secondary electrons. In contrast, "Model"-based algorithms provide more accurate results in low-density heterogeneous regions by convolving the total energy released per unit mass. However, there are still challenges in dose calculation accuracy in heterogeneous regions [8,9]. With recent technological advancements, "principle" type algorithms have emerged. This type of algorithms has three main advantages over "Correction" and "Model" based algorithms: 1) modeling of secondary electron transport is more advanced, 2) dose accumulation can be calculated in biological tissues and in the presence of high Z materials and 3) dose is reported as dose to medium [10] Commercially available Acuros XB (AXB) and Monte Carlo X-ray voxel Monte Carlo (XVMC) can be categorized as a "Principle" type algorithm. Compared to "Correction"-based algorithms such as Pencil Beam (PB) and "Model"-based algorithms such as Anisotropic Analytical Algorithm (AAA), Convolution Superposition (CS), the dosimetric performances of AXB and XVMC "principle"-based algorithms are more accurate in heterogeneous regions [11].

This study aims to evaluate differences in the dosimetric and radiobiological parameters and in the dose distributions of Planning Target Volume (PTV) and organs at risk (OAR) in patients with lung tumors using different Treatment Planning System (TPS) algorithms and Volumetric Modulated Arc Therapy (VMAT) technique.

2. Material and Methods

2.1. Patient Characteristics

This study includes 19 cancer patients who received radiotherapy for inoperable and unresectable T2-T4 N0-N1 M0 NSCLC between January 2021 and December 2022 in the Radiation Oncology Department of Gülhane Training and Research Hospital at University of Health Sciences. The median age of the patients was 62 (51-77) and 10 of the 19 patients were diagnosed with squamous cell carcinoma (SCC) (52.6%) and 9 with Adeno CA (47.4%). The median volume of treated tumors was determined to be 300cc (153cc-762cc). 47.4% of the target volume is located in the Left Upper Lobe (LUL), 31.5% in the Right Middle Lobe (RML), and 21.1% in the Right Upper Lobe (RUL). Patient characteristics are shown in Table 1.

Table 1. Patient characteristics

Patient No	Gender	Age	Target Volume (cc)	Target Localisation	Histology
1	Male	65	265	RML	Adeno CA
2	Male	60	200	RUL	SCC
3	Female	54	153	LUL	Adeno CA
4	Male	56	300	RML	SCC
5	Male	67	337	RUL	Adeno CA
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	Adeno CA
11	Male	62	208	LUL	SCC
12	Male	57	209	LUL	Adeno CA
13	Male	51	482	RML	SCC
14	Male	68	240	LUL	Adeno CA
15	Male	55	401	LUL	Adeno CA
16	Male	69	762	RML	SCC
17	Male	55	373	LUL	SCC
18	Male	56	682	LUL	SCC
19	Male	69	379	RML	Adeno CA

2.2. Defining Target Volumes and Critical Structure

Images of all patients were acquired on the Toshiba Aquilion Computed Tomography (CT) device at 120 kVp 100 mA, at supine position with arms up, immobilized with a T-bar and at moderate deep inspiration breath-hold mDIBH inspiration, using the Active Breath Control (ABC) system with 3 mm slice thickness. The obtained images were transferred to the contouring workstation via the network. CT images were contoured to Include Internal Target Volume (ITV) in accordance with ICRU-83. Referring to the clinical protocols, a 5 mm margin was added to the ITV in all directions to create the Planning Target Volume (PTV), but no margin was added to the OAR. [5]

2.3. Treatment Techniques and Planning

The treatment plans of all patients included in the study were reiterated using 6 MV X-ray and TPS from 3 different commercial companies (Elekta, Varian, Accuray) given in Table 2.

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

TPS	TPT ¹	Algorithm
Elekta-Monaco 5.1	VMAT	Monte Carlo (XVMC) Pencil Beam (PB)
Varian-Eclipse 15.6)	VMAT	Anisotropic Analytical Algorithm (AAA) Acuros (AXB)
Acuray-TomoPlan	VMAT	Convolution/Superposition (C/S)

¹Treatment Planning Technique

Treatment of the patients was planned to be 30 fractions of 200 cGy per day with a total treatment dose of 60 Gy [12]. VMAT plans were generated in two partial arc shapes within the angle range of 45°-180° for right-sided lesions and 315°-180° for left-sided lesions [7,13,14]. Normalized as 100% of the defined dose covers 95% of the PTV. Patient-specific quality control (PQA) was performed for dosimetric accuracy of all planning [13-17].

2.4. Data Evaluation

In each patient's plan, maximum (D_{max}), minimum (D_{min}), mean (D_{mean}) (MLD), dose received by 95%, 98%, 2%, 5% volume for PTV are D_{95} , D_{98} , D_2 , D_5 ,

respectively; the average (D_{mean}) volume receiving 5 Gy, 10 Gy and 20 Gy for the contralateral and ipsilateral lungs are V_5 , V_{10} , V_{20} , respectively; for the total lung, the average (D_{mean}), 1000 cc and 1500 cc field dose values of bilateral lungs were evaluated, excluding the volume receiving 5 Gy, 10 Gy, 20 Gy and 30 Gy, V_5 , V_{10} , V_{20} , V_{30} and gross target volume (GTV), respectively. Maximum (D_{max}), mean (D_{mean}) and volume receiving 60 Gy for the esophagus V_{60} ; average (D_{mean}) for the heart and maximum (D_{max}) data for the volume receiving 5 Gy, 10 Gy, 30 Gy and 60 Gy were evaluated for V_5 , V_{10} , V_{30} , V_{60} , spinalcord and rib, respectively. The same dose limitations were used for all planning systems and the relevant values are given in Table 3.

Table 3. Normal Tissue Dose-Volume Constraints for Conventionally Fractionated Radiotherapy

Total Lungs		Esophagus	
D_{ort}	MLD ≤ 20 Gy	D_{ort}	Mean ≤ 34
V_{20}	$\leq 37\%$	V_{60}	$< 5cc$
V_5	$\leq 60\%$	Heart	
Lung minus GTV(1500cc)	≤ 14 Gy	D_{ort}	≤ 26 Gy
Lung minus GTV(1000cc)	≤ 15 Gy	V_{60}	< 15 cc
Spinal cord		Contralateral- Ipsilateral Lung	
D_{maks}	Max ≤ 50 Gy	D_{ort}	MLD ≤ 20 Gy

2.5. Data Analyses

The statistical analysis of this study was performed using the SPSS Statistics v.29.0.2.0 software. Descriptive statistics, including measures such as mean, standard deviation, and median, were provided for both categorical and continuous variables. To assess differences between the algorithms utilized in the VMAT technique, a Friedman test was initially conducted, and a significance level of $p < 0.05$ was considered statistically significant. Upon obtaining significant results from the Friedman test, the analysis proceeded with the Benferroni corrected Wilcoxon rank test for further evaluation. A significance level of $p < 0.005$ was considered statistically significant in this test.

A total of 95 treatment plans were generated to evaluate differences in dosimetric and radiobiological parameters, and all plans were analyzed using the Computational Environment for Radiological Research (CERR) software, which is

part of the MATLAB programming environment. CERR allows the analysis of treatment plans by combining plan information obtained from different commercial Treatment Planning Systems (TPSs) with DICOM images, anatomical structures, and dose distributions. Particularly, this study utilized CERR as a valuable tool for comparing plans by consolidating all plan Dose Volume Histograms (DVHs) into a single DVH, obtaining and assessing numerical data related to the plans.

3. Results and Discussion

This study compared dose calculation differences among the algorithms currently in use for lung cancer patients. Data from five different algorithms belonging to three different treatment planning systems were evaluated using the VMAT technique. Table 4 presents the target coverage of the PTV and the Homogeneity Index values defined in ICRU-83 for total lung, contralateral and ipsilateral lung, spinal cord, heart, esophagus and rib critical organs. According to the statistical analysis conducted using the Wilcoxon rank test;

Target Volume, D_{95} , D_{98} , D_2 , D_5 , D_{ort} , D_{min} and D_{max} values; PB- XVMC and C/S- XVMC for D_{95} , PB- XVMC, C/S - XVMC for D_{98} ; AAA-PB, AXB-PB, C/S -XVMC, C/S -AAA C/S -AXB for D_2 , PB- XVMC, AAA-PB, AXB-XVMC, AXB-XVMC, AXB-PB, C/S -AAA, C/S -AXB, C/S -XVMC for D_5 , AXB-XVMC, AXB-PB, AXB- AAA for D_{ort} . C/S-AXB; for D_{max} , a significant difference was observed between AXB-XVMC, C/S-XVMC, C/S-AAA, C/S-AXB.

Heart, D_{ort} , V_5 , V_{10} , V_{20} , V_{30} and V_{60} data were evaluated and significant differences were observed between XVMC-PB, AXB-AAA for D_{ort} and between PB-XVMC algorithms for V_5 .

Esophagus was evaluated with D_{ort} , D_{mak} and V_{60} data and significant differences were found between D_{ort} AAA-XVMC, AAA-PB, AAA- C/S, AAA-AXB, AXB-XVMC, AXB-PB, C/S -AXB algorithms.

Contralateral lung, D_{ort} , V_5 , V_{10} , V_{20} data analysis results showed a significant difference between PB-XVMC, AAA-PB, AXB-PB, C/S-PB for D_{ort} ; PB-XVMC, AXB-AAA, C/S -PB for V_5 ; PB-XVMC, AXB-AAA, C/S-PB, C/S-AAA, C/S-AAA, C/S-AXB for V_{10} and no significant difference was observed in V_{20} .

Ipsilateral lung, D_{ort} , V_5 , V_{10} , V_{20} data analysis results PB-XVMC, AAA-XVMC, AXB-XVMC, AAA-PB, AXB-PB, C/S-AAA, C/S-AXB for D_{ort} ; PB-MC, AAA-XVMC, AXB-XVMC, C/S- XVMC, C/S-XVMC, C/S-PB, C/S-AAA, C/S-AXB for V_5 ; PB-XVMC, AAA-XVMC, AXB-XVMC, C/S-PB for

V_{10} , PB-MC, AAA-XVMC, AXB-XVMC, C/S-XVMC, C/S-PB, C/S-AAA, C/S-AXB for V_{20} significant difference was observed between the algorithms.

When the patients' DVHs were analyzed;

Since all plans were defined in such a way that the prescribed dose covered 95% of the PTV volume, it was observed that there was no difference between the algorithms in the D_{min} value, but the D_{max} values were especially high for the AAA, AXB algorithms. The difference between algorithms was found to be higher for D_{max} values for small treatment volumes. The DVH of PTV for large and small tumor volumes are shown in Figures 1,2. Regarding the critical organs, spinal cord and rib were evaluated with D_{max} values and there was no significant statistical difference between the algorithms used. On the other hand, when the DVH is analyzed, there are visual differences between the critical organs. Especially for the spinal cord, the volumetric dose difference was found to be high for large volume tumors and smaller for small volume tumors. In the comparison between algorithms, C/S was found to provide better protection for critical organs by providing volumetrically lower dose. The DVH of critical organs for large and small tumor volumes are given in Figures 3,4. When we visually examined the dose distribution in large and small volumes in the same sections, differences in volumetric dose distribution were detected (Figure 5). For large and small tumor volumes, the dose distributions of AXB and AAA were similar, whereas the dose distribution difference between PB and XVMC was high and C/S showed a distribution similar to this XVMC dose distribution. Between large and small target volumes, the dose differences in the large volume were found to be higher in the PTV, supporting the DVHs. Another important parameter for plan evaluation is the Homogeneity Index (HI), which shows how homogeneously the dose is distributed. Although there is no significant difference between XVMC (0.078 ± 0.03) and AXB (0.077 ± 0.02), HI values in the target volume are close to each other. In addition, it was observed that the low dose distribution of the C/S algorithm of the treatment device using the helical scanning technique was higher than the other algorithms.

Although the quality of the radiotherapy plan and the comparison of plans is usually based on radiation dose and dose-volume parameters, the report of the therapy physics committee of the American Association of Physicists in Medicine previously suggested the use of biologically-based models for treatment planning [18]. Radiobiological modeling based on DVH data provides a better understanding of clinical outcomes such as tumor control

probability (TCP) and normal tissue complication probability(NTCP). Although modern treatment planning systems (TPS) have integrated biological models to aid in plan optimization, these models have their own different formulations. In this study,

for radiobiological analysis, the DVHs of the plans were used to calculate the equivalent uniform

Table4. Dosimetric index of target and organ at risk

	PBmean ± SD	MCmean ± SD	AAAmean± SD	AXBmean± SD	C/Smean ± SD	P*value
PTV						
D ₂ ,Gy	62,67±0,63	62,94±0,94	64,00±1,57	63,83±1,02	62,03±0,62	<,001
D ₅ ,Gy	62,23±0,75	62,49±0,53	63,33±1,32	63,43±0,8	61,71±0,57	<,001
D ₉₅ ,Gy	59,80±0,75	59,10±0,70	59,30±0,61	59,76±0,64	59,89±0,37	<,001
D ₉₈ ,Gy	59,73±1,76	58,28±0,97	58,89±0,86	59,22±0,52	59,15±0,34	<,001
D _{min} ,Gy	52,11±0,32	51,28±0,41	53,87±0,25	52,01±0,26	52,41±0,51	<,027
D _{max} Gy	65,82±1,87	65,71±1,55	67,30±2,25	67,15±1,05	63,88±1,39	<,001
D _{mean} , Gy	60,97±0,43	60,75±0,80	61,08±0,92	61,47±0,70	60,76±0,53	<,001
HI	0,055±0,02	0,078±0,03	0,085±0,03	0,077±0,02	0,048±0,01	<,001
TotalLungs						
V ₅	0,46±0,14	0,52±0,13	0,50±0,11	0,51±0,11	0,57±0,12	<,001
V ₁₀	0,31±0,09	0,33±0,10	0,32±0,09	0,32±0,09	0,40±0,12	<,001
V ₂₀	0,21±0,07	0,22±0,07	0,20±0,07	0,20±0,07	0,25±0,07	<,001
V ₃₀	0,15±0,06	0,14±0,05	0,13±0,05	0,13±0,05	0,16±0,06	<,001
D _{mean}	12,00±3,46	12,95±3,44	11,13±4,02	11,19±4,04	13,86±3,30	<,001
Lungs-GTV(1500cc/14gy)	7,32±4,67	8,67±4,72	7,90±3,94	8,12±4,12	10,88±5,15	<,001
LungsGTV(1000cc/15gy)	13,28±7,77	14,72±7,77	13,12±6,27	13,39±6,31	15,89±7,23	<,001
ContralateralLung						
V ₅	0,35±0,21	0,44±0,18	1,84±6,12	1,89±6,26	0,49±0,16	<,001
V ₁₀	0,12±0,10	0,15±0,11	0,14±0,1	0,15±0,10	0,23±0,15	<,001
V ₂₀	0,02±0,02	0,02±0,03	0,02±0,03	0,02±0,03	0,04±0,05	<,017
D _{mean}	4,35±1,89	5,30±1,86	5,30±1,68	5,36±1,72	6,28±2,19	<,001
ipsilateralLung						
V ₅	0,60±0,16	0,64±0,14	0,59±0,12	0,61±0,14	0,68±0,14	<,001
V ₁₀	0,55±0,16	0,57±0,14	0,53±0,14	0,54±0,14	0,62±0,14	<,001
V ₂₀	0,48±0,15	0,45±0,14	0,44±0,13	0,44±0,13	0,50±0,14	<,001
D _{mean}	21,74±5,69	22,71±5,81	19,32±6,54	20,18±4,98	22,64±7,41	<,001
Esophagus						
V ₆₀	0,002±0,008	0,003±0,005	0,006±0,015	0,009±0,018	0,008±0,015	<,017
D _{max}	45,45±20,93	45,59±20,34	50,11±17,58	50,60±17,75	45,98±20,92	<,001
D _{mean}	12,89±6,99	13,46±6,81	14,78±6,04	14,66±6,08	11,94±6,12	<,001
Heart						
V ₅	0,32±0,33	0,34±0,35	0,34±0,34	0,35±0,33	0,39±0,31	<,002
V ₁₀	0,21±0,24	0,23±0,26	0,25±0,3	0,25±0,27	0,23±0,22	<,325
V ₃₀	0,035±0,058	0,043±0,075	0,053±0,103	0,036±0,053	0,029±0,042	<,573
V ₆₀	0,000±0,001	0,000±0,001	0,002±0,005	0,001±0,003	0,004±0,013	<,121
D _{mean}	5,78±5,64	6,61±5,96	7,06±6,47	6,86±6,19	6,30±4,55	<,001
Spinal cord						
D _{max}	21,91±10,12	23,15±10,14	28,32±8,70	27,08±10,96	23,44±7,49	<,002
Rib						
D _{mak}	55,99±9,42	57,71±7,66	57,02±10,85	56,36±11,30	51,00±13,22	<,014

*Friedman test p<0.05

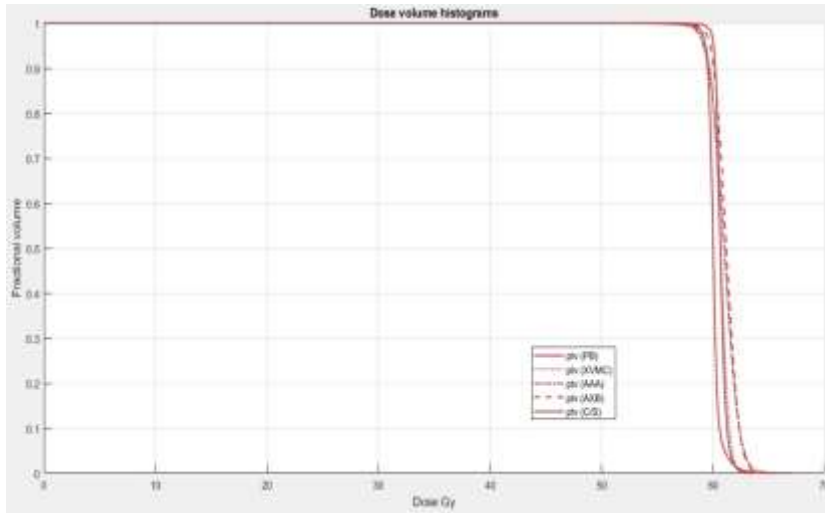


Figure 1. DVH of PTV for large tumor volume (762cc)

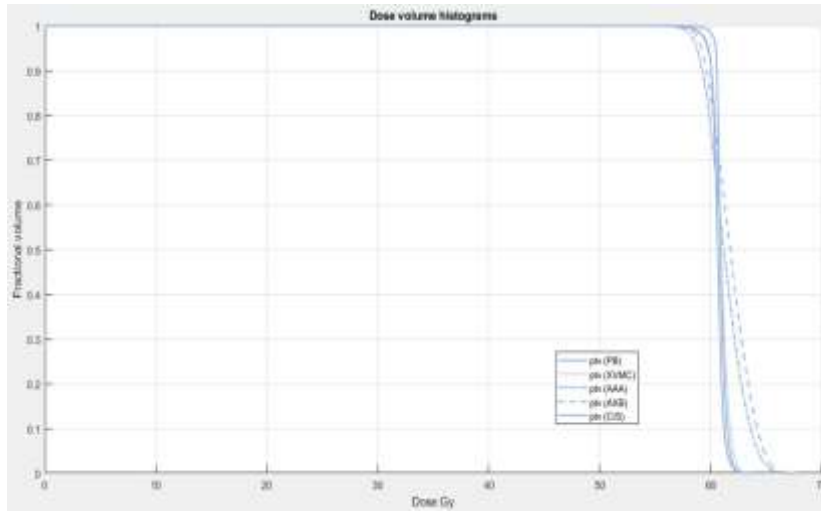


Figure 2. DVH of PTV for small tumor volume (169cc)

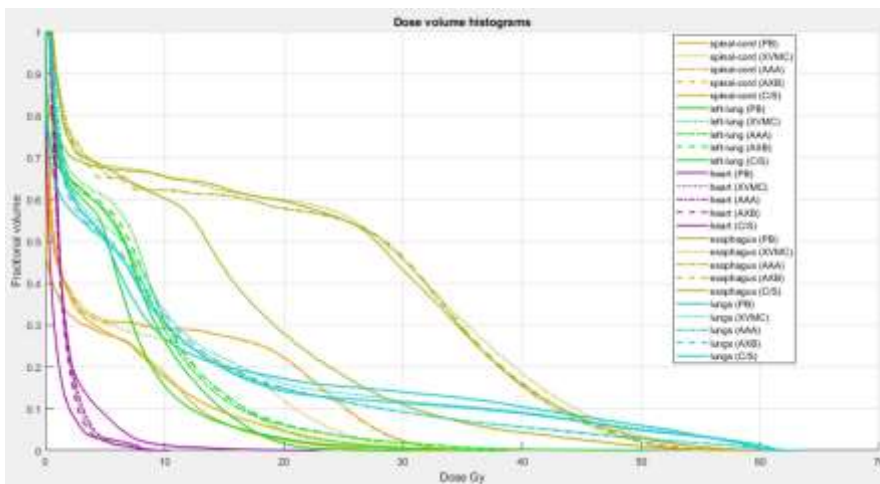


Figure 3. DVH of critical organs for large tumor volume (762cc)

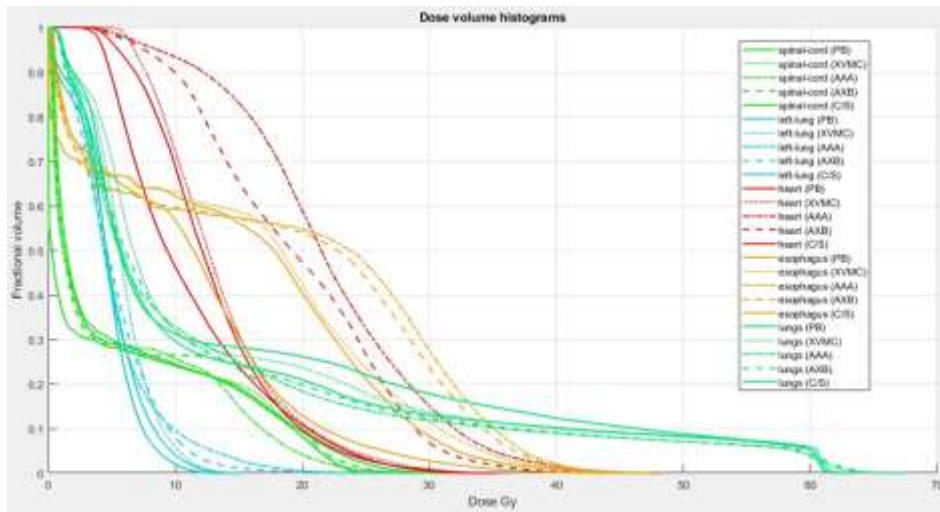
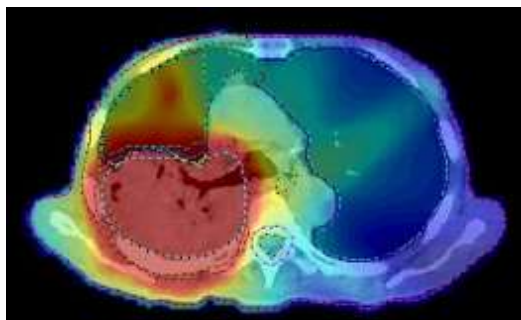
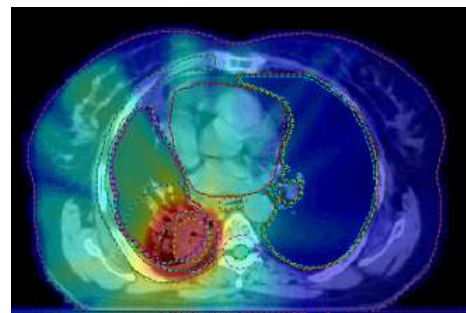


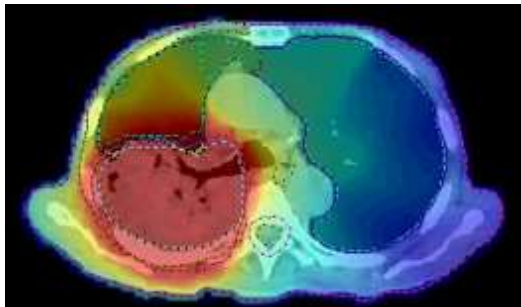
Figure 4. DVH of critical organs for small tumor volume (169cc)



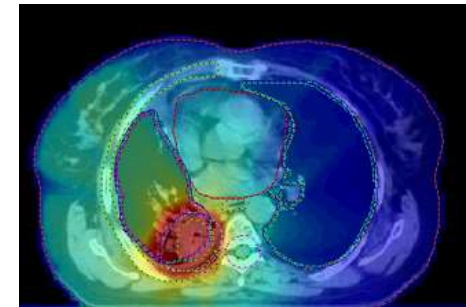
PB



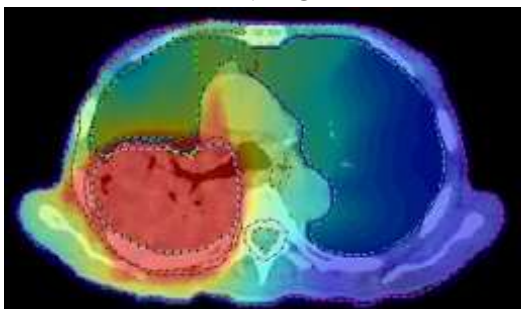
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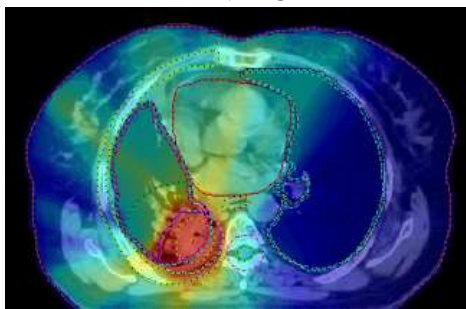
XVMC



XVMC



AAA



AAA

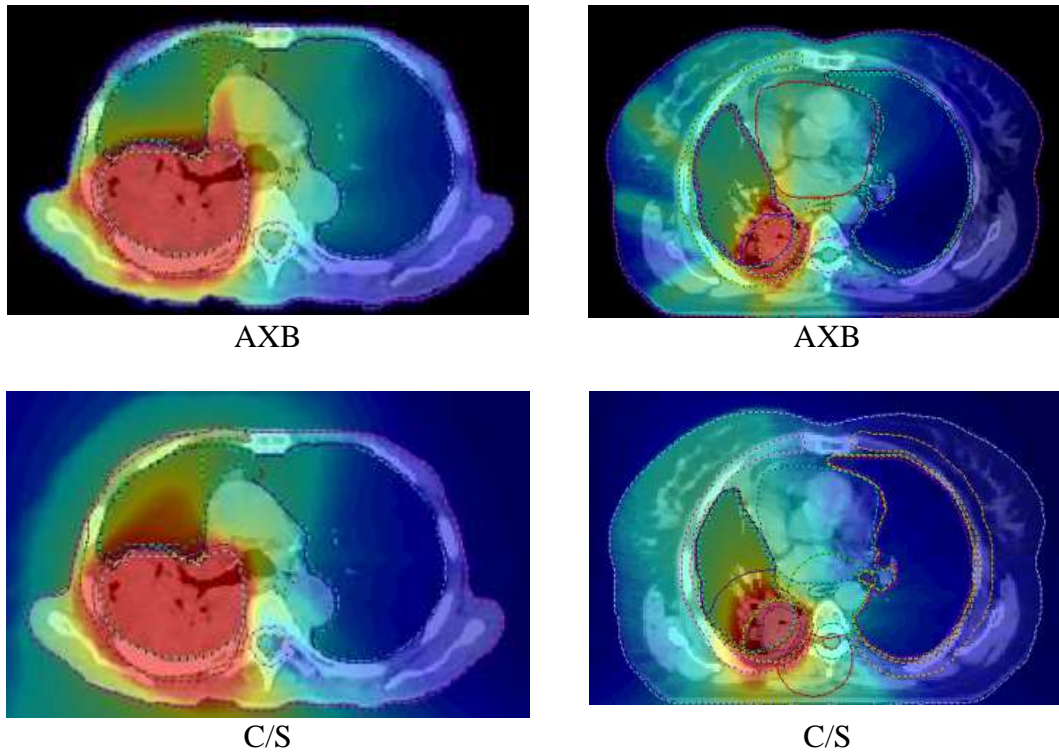


Figure 5. Dose distribution images of two different volumes in the same CT Slices.

Table 5. Radiobiological parameter data for Target Volume and Critical organs

Structures		PB	XVMC	AAA	AXB	C/S
PTV	EUD	61,061±0,306	60,902 ±0,355	61,135±0,758	61,518±0,557	60,713±0,477
	TCP	0,999±0,0001	0,999±0,0015	0,999±0,0009	0,999±0,0011	0,999±0,0001
Spinal cord	EUD	2,1826±1,0852	3,1161±1,2788	3,4487±1,4114	3,5191±1,3735	3,0661±1,0103
	NTCP	0,1320±0,2099	0,1433±0,2122	0,1242±0,1988	0,1511±0,2198	0,1414±0,2000
Heart	EUD	2,1826±1,0852	5,8553±5,4471	6,1671±6,0681	6,0417±5,7942	5,6880±4,2731
	NTCP	0,1387±0,1177	0,1891±0,1772	0,1405±0,1291	0,1370±0,1169	0,1205±0,0799
Esophuagus	EUD	9,6506±5,5131	10,7604±5,6113	11,6094±5,0200	11,4968±4,9930	9,5985±4,8385
	NTCP	0,2011±0,1146	0,2251±0,1263	0,2411±0,1175	0,2382±0,1160	0,1952±0,1046
Rib	EUD	15,60703316	16,51447895	14,72868947	14,58647947	16,62348947
	NTCP	0,3488±0,2247	0,3695±0,2168	0,3217±0,2020	0,3180±0,1999	0,3936±0,2325
Cont.lung	EUD	3,4789±1,6165	4,6228±1,6823	4,5487±1,4605	4,6399±1,5038	5,4629±1,9650
	NTCP	0,0803±0,0195	0,0950±0,0228	0,0938±0,0196	0,0949±0,0200	0,1076±0,0291
T.Lung	EUD	8,7314±3,1691	10,1075±3,2122	9,1672±2,8274	9,2804±2,8362	11,0774±3,2507
	NTCP	0,1970±0,0681	0,1683±0,0730	0,1756±0,0608	0,1779±0,0606	0,2187±0,0789

dose (EUD) and normal tissue complication probability (NTCP) with the Lyman-Kutcher-Burman (LKB) model in the CERR program. Table 5. shows the biological evaluation results obtained for different structures. EUDs (Gy) and NTCPs (%) were calculated for PB, XVMC, AAA, AXB and

C/S, respectively. The critical structures analyzed were heart, spinal cord, esophagus, contralateral lung and total lung. p value <0.001 was found significant. In the comparison between the algorithms with the Wilcoxon rank test, the p-value <0.001 was found to be significant between PB and

the other algorithms. This confirms that PB does not take into account radiation scattered around the calculation point, i.e. lateral transport of energy with varying densities, secondary electron formation and heterogeneity correction.

The dose calculations of the algorithms used in different TPSs were compared and their agreement and differences were evaluated. Basically, the differences are related to the modeling of the physical interaction between radiation and matter, which leads to differences in calculation between algorithms, and may also be influenced by many other factors such as tumor location, tumor size and the beam orientation used.

In this study, when the target volume values were compared, it was found that the PB algorithm overestimated the PTV winding and underestimated the critical organ doses because it did not take into account certain physical parameters. For the AAA and AXB algorithms, both PTV and critical organ doses and dose distributions were similar. Among the algorithms we evaluated, the maximum dose values within the tumor volume were higher in these two algorithms. The C/S algorithm provided similar dose wrapping to MC, but the cumulative dose distribution was higher due to the helical scanning feature. Hasenbalg (2007) et al. made a similar comparison to our study using the PB algorithm [17]. They also found that AAA and Collapsed Cone Convolution Superposition (CCCS) algorithms performed well compared to the Monte Carlo version of XVMC, while PD tended to overestimate dose coverage, especially in regions of high heterogeneity. Similar to our study, the DVHs obtained from Hasenbalg's study show that AAA overestimates PTV coverage while C/S is more evenly matched with XVMC.

Bosse (2020) et al. compared dose calculations for Pinnacle, Monaco and Eclips treatment planning systems for 18 lung cancer patients using 6-10 MV energized photons and concluded that there may be differences in dose calculations between treatment planning systems. Although relatively small, these differences became apparent when compared using DVH [6]. In our study, similar to this study, differences were found in dose calculations, especially in the D_{max} value of PTV and some of the critical organs.

Dong Wonk (2020) et al described various dose calculation algorithms used in treatment planning systems for radiation therapy from past to present. Dose calculation algorithms are generally classified into three main groups and information about them is presented. He states that in the near future, in order

to improve treatment quality, next generation dose calculation algorithms will include calculations that include biological equivalent doses or effective doses [16]. Therefore, we included the results of EUD, NTCP in this study.

4. Conclusion

According to this study, it was concluded that there are dosimetric and radiobiological differences between the dose calculations of the algorithms used in commercial TPSs. Although these differences were relatively small, significant differences were observed when plan DVHs were compared. It was concluded that the difference between the algorithms increased especially as the volume of the target tumor decreased. The XVMC Monte Carlo simulation method, which is specially designed for the Monaco treatment planning system, can make more accurate calculations by modeling the dose in the tissue closer to reality, and the MC method is considered to be the most accurate method for calculating the dose. In our study, TPS with C/S algorithm gave closer results with XVMC. It was concluded that the AAA Algorithm and AXB gave very close results and higher dose values than they were.

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References

- [1] American cancer Society (2023) <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>
- [2] Grills IS, Yan D, Martinez AA, Vicini FA, Wong JW (2003) Potential for reduced toxicity and dose escalation in the treatment of inoperable

- non-small cell lung cancer: A comparison of intensity-modulated radiation therapy (IMRT), 3D conformal radiation, and elective nodal irradiation. *Int J Radiat Oncol Biol Phys* 57: 875-890. doi:10.1016/S0360-3016(03)00743-0
- [3] Bezjak A, Rumble RB, Rodrigues G, Hope A (2012) Intensitymodulated radiotherapy in the treatment of lung cancer. *Clin Oncol* 24: 508-520. doi.org/10.1016/j.semradonc.2014.11.002 1053-4296/
- [4] H. Murshed, H. H. Liu, Z. Liao et al.(200) , Dose and volume reduction for normal lung using intensity-modulated radiotherapy for advanced-stage non-small-cell lung cancer. *International Journal of Radiation Oncology Biology Physics*, vol. 58, no. 4, pp. 1258–1267. doi:10.1016/j.ijrobp.2003.09.08
- [5] International Commission on Radiation Units and Measurements (ICRU). Determination of absorbed dose in a patient irradiated by beams of X or gamma rays in radiotherapy procedures. ICRU Report 24. Washington (DC): ICRU, 1976: 67.
- [6] C. Bosse, G.Narayanasamy et al (2020). Dose Calculations Comparisons Between Three Modern Treatment Planning Systems. Dose Calculation Comparisons between Three Modern Treatment Planning Systems. *J Med Phys*.Jul-Sep; 45(3):143–147. doi:10.4103/jmp.JMP_111_19
- [7] Knöös T, Wieslander E, Cozzi L, Brink C, Fogliata A, Albers D, Nyström H, Lassen S. (2006) Comparison of dose calculation algorithms for treatment planning in external photon beam therapy for clinical situations. *Phys Med Biol*; 51: 5785-5807 .DOI: 10.1088/0031-9155/51/22/00
- [8] Esch AV, Tillikainen L, Pyykkonen J, Tenhunen Mikko, Helminen H, Siljamäki S, et al. (2006); Testing of the analytical anisotropic algorithm for photon dose calculation. *Med Phys* 33(11):4130–48. doi: 10.1118/1.2358333
- [9] Chow JC, Leung MK, Van Dyk J. (2009) Variations of lung density and geometry on inhomogeneity correction algorithms: a Monte Carlo dosimetric evaluation. *Med Phys*; 36(8): 3619–30. doi: 10.1118/1.3168966
- [10] Ojala J. (2014) The accuracy of the Acuros XB algorithm in external beam radiotherapy – a comprehensive review. *Int J Cancer Ther Oncol*;2(4):020417. doi:10.14319/ijcto.0204.17
- [11] Tsuruta Y, Nakata M, Nakamura M, Matsuo Y, Higashimura K, Monzen H, et al.(2014). Dosimetric comparison of Acuros XB, AAA, XVMC in stereotactic body radiotherapy. *Med Phys*;41(8):081715. doi: 10.1118/1.4890592
- [12] NCCN Guidelines Version 2.2024 Non-Small Cell Lung Cancer.
- [13] AAPM Task Group 218 Analysis of clinical patient-specific pre-treatment quality assurance with the new helical tomotherapy platform, following the AAPM TG-218 report (2021). doi:10.1186/s13014-021-01952
- [14] N. Dogan, B. J. Mijnheer et al. AAPM (2023). Task Group 307: Use of EPIDs for Patient-Specific IMRT and VMAT QA.
- [15] S.L. Gulliford, M. Partridge, M.R. Sydes, S. Webb, P.M. Evans and D.P. Dearnaley (2012). Parameters for the Lyman Kutcher Burman (LKB) model of Normal Tissue Complication Probability (NTCP) for specific rectal complications observed in clinical practise, *Radiother Oncol* 102(3) 347–351.
- [16] D. Wook Kim, K. Park , H. Kim , J. Kim (2020). History of the Photon Beam Dose Calculation Algorithm in Radiation Treatment Planning System. *Medical Physics* 31(3), <https://doi.org/10.14316/pmp.2020.31.3.54>.
- [17] Hasenbalg F, Neuenschwander H, Mini R, Born EJ (2007). Collapsed cone convolution and analytical anisotropic algorithm dose calculations compared to VMC++ Monte Carlo simulations in clinical cases. *Physics in Medicine & Biology*; 52:3679. DOI: 10.1088/0031-9155/52/13/002
- [18] M. Mazonakis E. Tzani, E. Lyraraki and John Damilakis (2022). Automatic Radiobiological Comparison of Radiation Therapy Plans: An Application to Gastric Cancer *Cancers*, 14, 6098. doi.org/10.3390/cancers1424609.