RESEARCH ARTICLE

Assessment of the Dosimetric Index from IMRT and Rapid arc Plan for Oropharyngeal Cancer with Simultaneous Integrated Boost (SIB) Technique in Combination with EUD-based NTCP and TCP Radiobiological Models

Sougoumarane Dashnamoorthy[1,2], Ebenezar Jeyasingh[2]*, Karthick Rajamanickam[1], Imtiaz Ahmed[3]

Abstract

   Purpose: The current research compared radiobiological and dosimetric results for simultaneous integrated boost (SIB) plans employing RapidArc and IMRT planning procedures in oropharyngeal cancer from head-and-neck cancer (HNC) patients. **Materials and Methods:** The indigenously developed Python-based software was used in this study for generation and analysis. Twelve patients with forty-eight total plans with SIB were planned using Rapid arc (2 and 3 arcs) and IMRT (7 and 9 fields) and compared with radiobiological models Lyman, Kutcher, Burman (LKB) and EUD (Equivalent Uniform Dose) along with physical index such as homogeneity index(HI), conformity index(CI) of target volumes. **Results:** These models' inputs are the dose-volume histograms (DVHs) calculated by the treatment planning system (TPS). The values obtained vary from one model to the other for the same technique and patient. The maximum dose to the brainstem and spinal cord and the mean dose to the parotids were analysed both dosimetrically and radiobiologically, such as the LKB model effective volume, equivalent uniform dose, EUD-based normal tissue complication probability, and normal tissue integral dose. The mean and max dose to target volume with conformity, homogeneity index, tumor control probability compared with treatment times, and monitor units. **Conclusion:** Rapid arc (3 arcs) resulted in significantly better OAR sparing, dose homogeneity, and conformity. The findings indicate that the rapid arc plan has improved dose distribution in the target volume compared with IMRT, but the tumor control probability obtained for the two planning methods, Rapid arc (3 arcs) and IMRT (7 fields), are similar. The treatment time and monitor units for the Rapid arc (3 arcs) were superior to other planning methods and considered to be standard in head & neck radiotherapy.

Keywords: DVH- 3DCRT- IMRT- Rapid arc- NTCP- TCP- EUD- Python

Introduction

   Multiple planned target volumes (PTVs) can now be treated in a single plan using advances in radiation therapy (RT), such as intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT), allowing organ sparing even for complex-shaped target volumes in patients with head and neck cancer (HNC) [1]. Definitive Simultaneous integrated boost (SIB), with or without concurrent chemotherapy, is effective and safe in numerous trials [2, 3]. Intensity-modulated radiotherapy (IMRT) and volumetric arc therapy (VMAT) treatment delivery are examples of three-dimensional radiotherapy plans with highly conformal dose distributions that closely conform to tumor shape, thereby giving nearby organs

at risk (OARs) the least amount of radiation exposure. Implicit evaluation with dose volume histograms is more difficult due to the development of such advanced radiation technologies, which have led to more complex and diversified dosage distributions (DVHs).

   The radiation fields permanently damage the salivary glands [4], the most common side effects of radiotherapy for head and neck cancer is Xerostomia [5]. The Xerostomia can be persistent and seriously affect taste, deglutition function, oral cavity infections, and dental cavities. This is because of saliva's changing pH and quantity. Parotid glands produce approximately 60% of saliva and submandibular glands 20% of saliva while the rest is secreted by sublingual and accessory salivary glands [6, 7].The acute effects could be reversed if the

[1]Thangam Hospital, Namakkal, India. [2]Jamal Mohamed College (Autonomous), Affiliated to Bharathidasan University, Tiruchirappalli, India. [3]Department of Radiation Oncology KLES Dr Prabhakar Kore Hospital and MRC, Belgaum, India. *For Correspondence: ebey_ebenezar@yahoo.com

prescribed doses for the parotid glands were not exceeded. The frequent use of high-dose partial irradiation in the vicinity of a treatment target causes issues with dose distribution around the OARs. Since the parotid gland overlaps with the target in head and neck cancer, problems are a substantial danger due to partial volume irradiation with high dosage. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) dosimetry recommends a mean dosage of less than 26 Gy for bilateral parotid glands and less than 20 Gy for unilateral ones to lessen xerostomia. It has proven possible to prevent radiation-induced salivary dysfunction using a variety of techniques without compromising oncologic therapy; intensity-modulated radiotherapy (IMRT) and VMAT are two radiation therapies that do not damage the salivary glands. The radiobiological models may be more accurate than univariate analyses, such as dosimetric evaluation using a dose volume histogram (DVH).

Materials and Methods

The Equivalent uniform dose(EUD) - based mathematical model [8] is simple because it is principally based on the dose volume histogram and parameter "a " value, a parameter that has no dimension and is specific for every tissue, which determines the behaviour of the EUD-based model and is scalable to be used for both TCP and NTCP calculations. The EUD is a single value that describes the biological effect of heterogeneous dose distributions of the treatment plan. Twelve patients with locally advanced HNC were randomly selected from a list of patients previously treated with simultaneously induced boost (SIB) RT at our department who underwent

definitive radiation for oropharynx cancer utilizing IMRT or VMAT procedures. The Lyman Kutcher Burman and Niemierko model EUD-based mathematical models were used to assess the organs at risk, such as the brain stem, spinal cord, and parotids. They rely on several characteristics [9], such as TD50, n, m, etc. Using custom-written Python software [10], the dose-volume histogram (DVH) assists in the creation of these models.

Each patient was placed in the supine position on an all-in-one (AIO) baseplate while immobilized with a five-clamp thermoplastic cast. Eclipse treatment planning was then used to transfer simulation CT images and accompanying outlines. Total of forty eight plans are compared with 3Dimensional -Conformal Radiotherapy (3D- CRT), IMRT and Rapid arc and each patient had three PTVs, each with a distinct dose prescription. After the initial setup, orthogonal pair of kV radiographs was manually acquired each week during treatments using the Varian Onboard Imaging (OBI) apparatus (Varian Medical Systems, USA) (manual 2D-2D) for corrective couch movements.

Treatment plan
Twelve patients in four groups, each with different target volumes and prescribed dose as shown in Table 1. For each patient, four treatment plans IMRT of 7 fields (0°,51°,102°,153°,204°,255°, and 306°),9 fields (0°,40°,80 °,120°,160°,200°,240°,280°, and 320°), Rapid arc of 2 arcs and 3 arcs were generated from Varian Clinac-iX photon beam of energy 6X, equipped with the Millennium120 multileaf collimator (MLC). The gantry is configured to rotate 360° clockwise from a starting position of 181° to a final position of 179°. It is also configured to rotate

Table 1. Planning Tumor Volume (PTV) for 70, 63, 60, 56, and 54 Gy Dose Prescriptions

	Group-A		Group-B		Group-C		Group-D	
1	PTV	Volume	PTV	Volume	PTV	Volume	PTV	Volume
	70	202.6	70	76.1	70	220.3	66	116.9
	63	172.9	60	15.3	66	192.9	60	90.7
	56	204.6	54	317.7	54	95.3	50	374.1
2	70	173.9	70	301.2				
	63	117.5	59.4	207.1				
	56	362.2	54	218.6				
3	70	106.9	70	106.4				
	63	99.9	60	101				
	56	136.4	54	157				
4	70	169	70	158.8				
	63	145.4	60	156.3				
	56	174.4	54	206.5				
5	70	130.5	70	172				
	63	52.3	59.4	171.7				
	63	52.3	54	242.7				
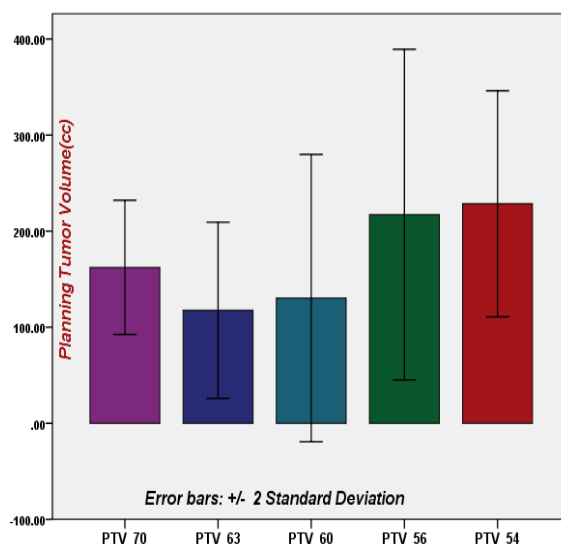
through 360° in an anticlockwise direction from a starting position of 179° to a final position of 181°. To minimize tongue and groove leakage, the collimator rotation was uniquely tuned for each patient but typically set at 30° and 330°. The target and normal tissue objective for IMRT and Rapid arc planning are similar and incorporated in optimization procedure.

Plan evaluation
Dosimetric analysis

The conformity index [11, 12] of radiation was computed after dose-volume histograms were created and the necessary parameters were used. It is defined as the ratio of the goal volume indicated as the planned target volume to the volume covered by the reference isodose, which is 95% isodose, according to ICRU (PTV).

The conformity Index (CI) = V_{ref} /TV

where V_{ref} = reference isodose volume and TV = target volume.

The homogeneity index [13, 14] is defined as the ratio between the dose measured at 95% of the PTV volume (D≥95%) and the dose measured at 5% (D≥5%) of the PTV volume.

The HI= D≥95% (within PTV)/D≥5% (within PTV)

Radiobiological analysis

The EUD [12, 9] -based model is defined as the equivalent biological dose, which when unevenly distributed, will lead to the same biological effect as the real distribution of the uneven dose distribution.

$$EUD = \left(\sum_i v_i \, D_i^a \right)^{1/a}$$

D_i is the dose received by a sub volume vi, and a is a parameter that has no dimension and is specific to every tissue. NTCP [15, 16] can be calculated with the help of a formula.

$$NTCP = 1 - \frac{1}{1+\left(\frac{TD50}{EUD}\right)^{4\gamma50}}$$

There is also a dimensionless parameter, specific for every tissue, describing the dose–response curve. TD50 is the dose given to the entire organ that would lead to a complication probability of 50%.

TCP [17] is defined as

$$TCP = 1 - \frac{1}{1+\left(\frac{TCD50}{EUD}\right)^{4\gamma50}}$$

The TCD50 is the dose producing 50% TCP. The radiobiological parameters used in this calculation are shown in Table 2.

Normal Tissue Integral Dose

Integral Dose [18-23] is the total energy absorbed by the body and is computed based on the average organ density, averaged organ dose, and volume as defined in the equation as follows:

Integral Dose= $(\bar{D})(\bar{\rho})$. V (Gy. kg)

Where $\bar{D}$ is the mean dose to the organ, is the mean organ density, and V is the organ volume. In this study, the integral dose was calculated by the following equation:

Integral Dose=Average Dose * Volume (Gy. Lit)

Statistical analysis

All dosimetrical and radiobiological parameters for organs at risk and target volume were determined using a Wilcoxon signed-rank test for related samples, and the relationship between the variables was determined using bivariate methods using SPSS statistical software version 20.0 because the data had a nonnormal distribution. Data were considered statistically significant at a p value ≤ 0.05.

Results

Thirty-eight treatment plans were generated from 12 patients with oropharynx head and neck cancer using 2 arcs and 3 arcs from Rapid arc, 7 fields, and 9 fields from IMRT treatment planning methods.

Target volume analysis

The mean volume of PTV70 was 159±63 cm3 (standard deviation, SD) (range=76-301), 117±46 cm3 for PTV63 (range=99-172), 130±75 cm³ for PTV60 (range=15-207), 217±86 cm³ for PTV56 (range=136-362) and 228±59 cm³ for PTV54 (range=157-31). A detailed summary of the PTV results for all three groups is shown in Tables 1 and 3.

Mean and Max dose

The mean dose of the 2 arc rapid arc for PTV70 was 7026±12.5 (standard deviation, SD), 6364±27 for PTV63, 6044±59 for PTV60, 5661±25 for PTV56 and 5389±195 for PTV54. The mean dose of the 3arc Rapid arc for PTV70 was 7024±7.9 (standard deviation, SD), 6358±11 for PTV63, 6037±47 for PTV60, 5651±22 for PTV56 and 5366±184 for PTV54. The mean dose of 7-field IMRT for PTV70 was 6916±59.1 (standard deviation, SD), 6333±62 for PTV63, 5987±79 for PTV60, 5635±65 for PTV56 and

Table 2. Parameters Used to Calculate Niemierko's EUD-based TCP and NTCP

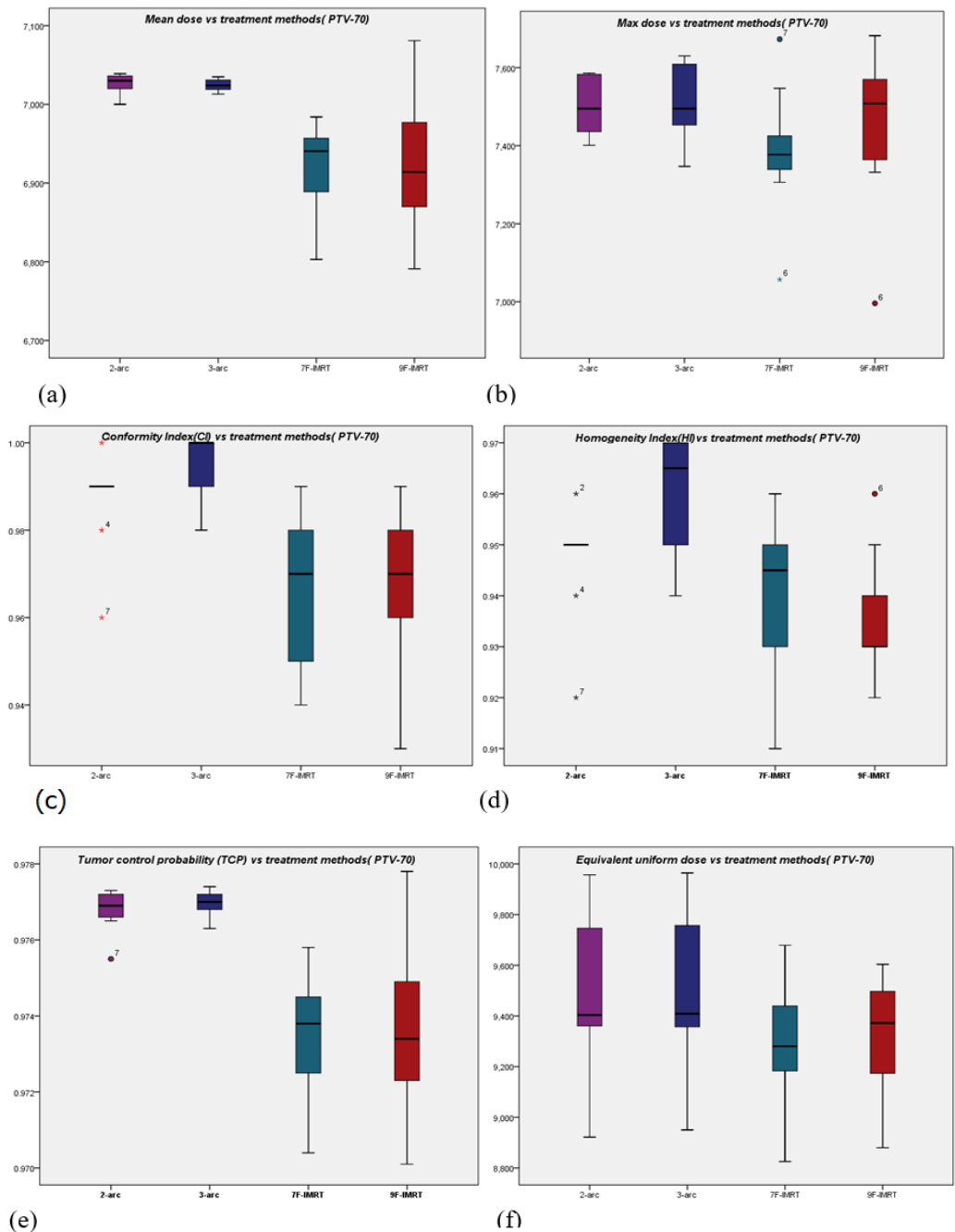| Tissue	Volume type	a value	γ50 value	TD50 (Gy)	TCD50 (Gy)	α/β (Gy)	Slope (m)
Head and Neck	Tumor	-13	2.28		51.7	10	
Brainstem	Normal	7	3	65		2.1	0.14
Spinal cord	Normal	13	4	66.5		2	0.175
Parotids	Normal	0.5	3	46		2	0.18

Figure 1. Box-Whisker Plot of PTV-70 in 2-arc, 3-arc, 7F-IMRT, and 9F-IMRT treatment methods for (a) mean dose, (b) max dose, (c) CI, (d) HI, (e) TCP and (f) EUD.

5318±209 for PTV54. The mean dose of 9-field IMRT was 6924±80 (standard deviation, SD) for PTV70, 6358±30 for PTV63, 6055±97 for PTV60, 5717±120 for PTV56 and 5450±242 for PTV54.

The maximum dose of the 2 arc rapid arc for PTV70 was 7055±69.8 (standard deviation, SD), 7062±110 for PTV63, 6948±163 for PTV60, 6612±311 for PTV56 and 6553±524 for PTV54. The maximum dose of the 3arc Rapid arc for PTV70 was 7503±96.5 (standard deviation, SD), 6968±142 for PTV63, 6833±141 for PTV60, 6447±374 for PTV56 and 6561±624 for PTV54.

The maximum dose of 7-field IMRT for PTV70 was 7387±159.8 (standard deviation, SD), 7154±150 for PTV63, 7044±304 for PTV60, 6654±359 for PTV56 and 6666±642 for PTV54. The maximum dose of 9-field IMRT

for PTV70 was 7462±197.6 (standard deviation, SD), 7171±92 for PTV63, 7033±335 for PTV60, 6623±443 for PTV56 and 6789±640 for PTV54. A detailed summary of the maximum dose for the PTVs for all three groups is shown in Table 3 and Figure 1(a) and (b) to Figure 5(a) and (b). The p values found are less than < 0.01 for all categories.

Conformity and Homogeneity
The conformity index of the 2 arc rapid arc for PTV70 was 0.99±.01 (standard deviation, SD), 0.97±0.01 for PTV63, 0.97±0.01 for PTV60, 0.96±.0.02 for PTV56 and 0.97±0.01 for PTV54. The conformity index of the 3arc Rapid arc for PTV70 was 0.99±.01 (standard deviation, SD), 0.97±0.03 for PTV63, 0.98±0.01 for

Table 3. Mean, Standard Deviation, and p value of Radiobiological and Dosimetric Parameters for the Planning Tumor Volume for 2 arc, 3 arc, 7 F IMRT, and 9 F IMRT Planning Methods

	Radiobiological Parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
PTV 70									
1	Volume	159.7±63	<0.01						
2	Mean dose	7026±12.5	<0.01	7024±7.9	<0.01	6916±59.1	<0.01	6924±80	<0.01
3	Max dose	7055±69.8	<0.01	7503±96.5	<0.01	7387±159.8	<0.01	7462±197.6	<0.01
4	Conformity Index(CI)	0.99±0.01	<0.01	0.99±0.01	<0.01	0.97±0.02	<0.01	0.97±0.02	<0.01
5	Homogeneity Index(HI)	0.95±0.01	<0.01	0.96±0.01	<0.01	0.94±0.02	<0.01	0.94±0.01	<0.01
6	TCP	0.98±0	<0.01	0.98±0	<0.01	0.97±0	<0.01	0.97±0	<0.01
7	EUD	9476±293	<0.01	9483±291	<0.01	9304±242	<0.01	9321±228	<0.01
PTV 63	Radiobiological Parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
1	Volume	117.6±46	<0.01						
2	Mean dose	6364±27	<0.01	6358±11	<0.01	6333±62	<0.01	6358±30	<0.01
3	Max dose	7062±110	<0.01	6968±142	<0.01	7154±150	<0.01	7171±92	<0.01
4	Conformity Index(CI)	0.97±0.01	<0.01	0.97±0.03	<0.01	0.96±0.03	<0.01	0.97±0.01	<0.01
5	Homogeneity Index(HI)	0.92±0.02	<0.01	0.93±0.03	<0.01	0.91±0.02	<0.01	0.91±0.01	<0.01
6	TCP	0.96±0.02	<0.01	0.95±0±0.01	<0.01	0.95±0.04	<0.01	0.95±0.02	<0.01
7	EUD	8756±313	<0.01	8759±319	<0.01	8681±288	<0.01	8745±300	<0.01
PTV 60	Radiobiological Parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
1	Volume	130.3±75	<0.01						
2	Mean dose	6044±59	<0.01	6037±47	<0.01	5987±79	<0.01	6055±97	<0.01
3	Max dose	6948±163	<0.01	6833±141	<0.01	7044±304	<0.01	7033±335	<0.01
4	Conformity Index(CI)	0.97±0.01	<0.01	0.98±0.01	<0.01	0.96±0.01	<0.01	0.98±0.02	<0.01
5	Homogeneity Index(HI)	0.91±0.02	<0.01	0.92±0.02	<0.01	0.91±0.02	<0.01	0.92±0.02	<0.01
6	TCP	0.09±0.03	<0.01	0.91±0.04	<0.01	0.89±0.04	<0.01	0.9±0.03	<0.01
7	EUD	8272±947	<0.01	8231±985	<0.01	8113±870	<0.01	8161±842	<0.01
PTV 56	Radiobiological Parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
1	Volume	217.2±86	<0.01						
2	Mean dose	5661±25	<0.01	5651±22	<0.01	5635±65	<0.01	5717±120	<0.01
3	Max dose	6612±311	<0.01	6447±374	<0.01	6654±359	<0.01	6623±443	<0.01
4	Conformity Index(CI)	0.96±0.02	<0.01	0.94±0.02	<0.01	0.96±0.02	<0.01	0.99±0.01	<0.01
5	Homogeneity Index(HI)	0.91±0.01	<0.01	0.89±0.01	<0.01	0.9±0.02	<0.01	0.92±0.01	<0.01
6	TCP	0.7±0.39	<0.01	0.7±0.39	<0.01	0.68±0.38	<0.01	0.71±0.40	<0.01
7	EUD	5931±3298	<0.01	5912±3276	<0.01	5798±3224	<0.01	5997±3336	<0.01
PTV54	Radiobiological Parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
1	Volume	228.5±59	<0.01						
2	Mean dose	5389±195	<0.01	5366±184	<0.01	5318±209	<0.01	5450±242	<0.01
3	Max dose	6553±524	<0.01	6561±624	<0.01	6666±642	<0.01	6789±640	<0.01
4	Conformity Index(CI)	0.97±0.01	<0.01	0.96±0.01	<0.01	0.97±0.01	<0.01	0.98±0.02	<0.01
5	Homogeneity Index(HI)	0.91±0.01	<0.01	0.91±0.01	<0.01	0.92±0.02	<0.01	0.92±0.03	<0.01
6	TCP	0.835±0.07	<0.01	0.834±0.07	<0.01	0.818±0.07	<0.01	0.848±0.07	<0.01
7	EUD	7125±450	<0.01	7116±439	<0.01	7018±501	<0.01	7230±537	<0.01

PTV60, 0.94±.02 for PTV56 and 0.96±0.01 for PTV54. The conformity index of 7-field IMRT was 0.97±.02 (standard deviation, SD) for PTV70, 0.96±0.03 for PTV63, 0.96±0.01 for PTV60, 0.96±.02 for PTV56 and 0.97±0.01 for PTV54. The conformity index of 9-field IMRT was 0.97±.02 (standard deviation, SD) for PTV70, 0.97±0.01 for PTV63, 0.98±0.02 for PTV60, 0.99±.0.01 for PTV56 and 0.98±0.02 for PTV54.

The homogeneity index of the 2 arc Rapid arc for PTV70 was 0.95±.01 (standard deviation, SD), 0.92±0.01 for PTV63, 0.91±0.01 for PTV60, 0.91±.0.01 for PTV56 and 0.91±0.01 for PTV54.The homogeneity index of

the 3arc Rapid arc for PTV70 was 0.96±.01 (standard deviation, SD), 0.93±0.03 for PTV63, 0.92±0.01 for PTV60, 0.89±.0.01 for PTV56 and 0.91±0.01 for PTV54. The homogeneity index of 7-field IMRT was 0.94±.02 (standard deviation, SD) for PTV70, 0.91±0.02 for PTV63, 0.91±0.02 for PTV60, 0.90±.0.02 for PTV56 and 0.92±0.02 for PTV54. The homogeneity index of 9 IMRT fields was 0.94±.02 (standard deviation, SD) for PTV70, 0.91±0.01 for PTV63, 0.92±0.02 for PTV60, 0.92±.0.01 for PTV56 and 0.92±0.03 for PTV54. A detailed summary of the conformity and homogeneity index for the PTVs for all three groups is shown in Table 3 and Figure 1(b)
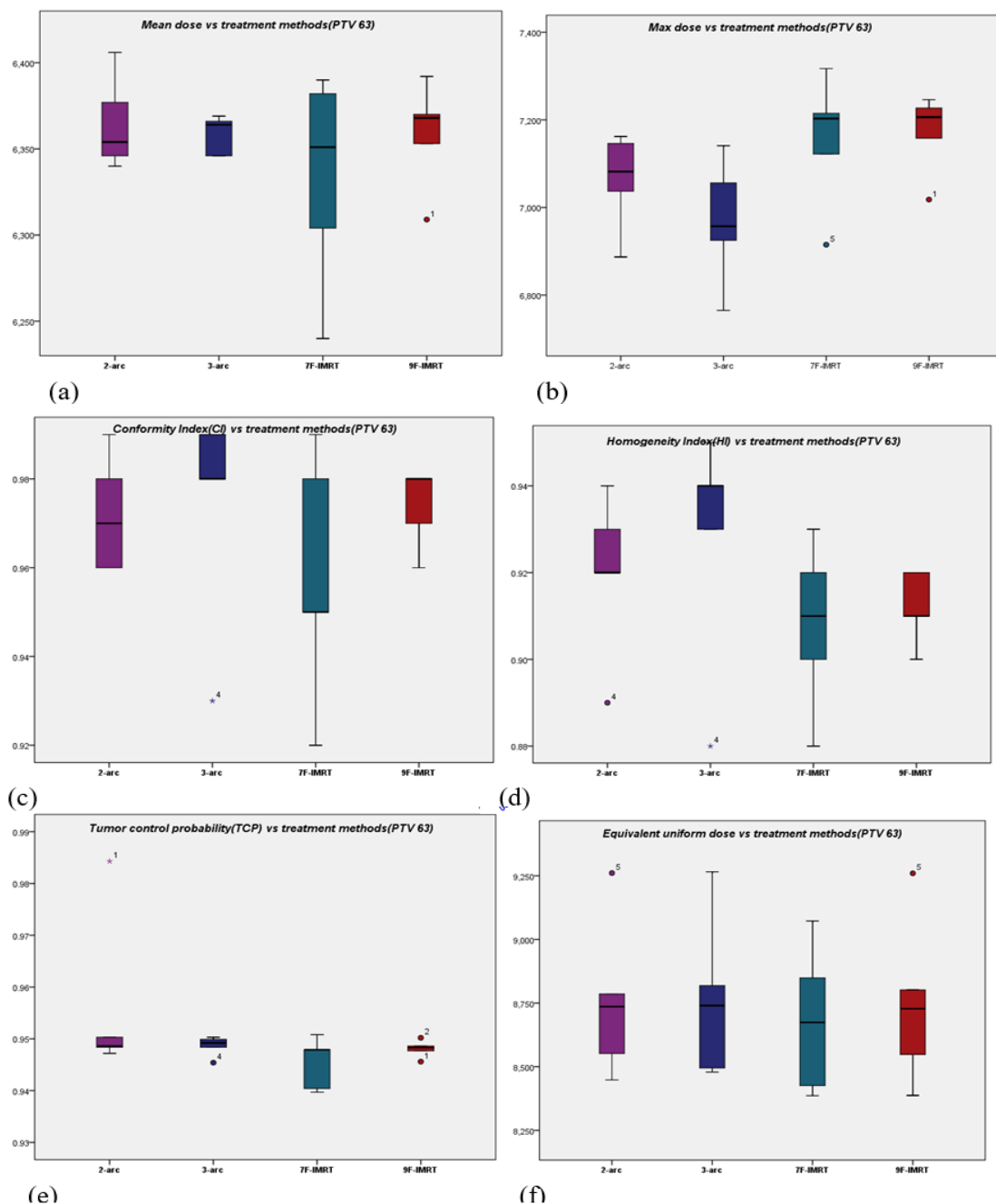
Figure 2. Box-Whisker Plot of PTV-63 in 2-arc, 3-arc, 7F-IMRT, and 9F-IMRT treatment methods for (a) mean dose, (b) max dose, (c) CI, (d) HI, (e) TCP and (f) EUD.

and (c) to Figure 5(b) and (c). The p values found are less than < 0.01 for all categories.

Tumor control probability and equivalent uniform dose

The tumor control probability of the 2 arc rapid arc for PTV70 was 0.98±.0 (standard deviation, SD), 0.96±0.0 for PTV63, 0.90±0.01 for PTV60, 0.70±.39 for PTV56 and 0.83±0.07 for PTV54.

The tumor control probability of the 3arc Rapid arc for PTV70 was 0.98±.0 (standard deviation, SD), 0.95±0.01 for PTV63, 0.91±0.04 for PTV60, 0.70±.39 for PTV56 and 0.83±0.07 for PTV54. The tumor control probability of 7-field IMRT for PTV70 was 0.97±.0 (standard deviation, SD), 0.95±0.04 for PTV63, 0.89±0.04

for PTV60, 0.68±.38 for PTV56 and 0.81±0.07 for PTV54. The tumor control probability of 9-field IMRT was 0.97±.0 (standard deviation, SD) for PTV70, 0.95±0.02 for PTV63, 0.90±0.03 for PTV60, 0.71±.40 for PTV56 and 0.84±0.07 for PTV54.

The equivalent uniform dose of the 2 arc Rapid arc was 9476±293 (standard deviation, SD) for PTV70, 8756±313 for PTV63, 8272±947 for PTV60, 5931±3298 for PTV56 and 7125±450 for PTV54. The equivalent uniform dose of the 3 arc Rapid arc was 9483±291 (standard deviation, SD) for PTV70, 8759±319 for PTV63, 8231±985 for PTV60, 5912±3276 for PTV56 and 7116±439 for PTV54. The equivalent uniform dose of 7-field IMRT was 9304±242 (standard deviation, SD) for PTV70, 8681±288 for

Table 4. Mean and Standard Deviation of Radiobiological and Dosimetric Parameters for the Organ at Risk (OARs) from 2 arc, 3 arc, 7 F IMRT, and 9 F IMRT Planning Methods

Organ at risk(OAR)	2-Arc	p value	3- Arc	p value	7F- IMRT	p value	9F- IMRT	p value
Brain stem								
Volume	30.88±5.4	<0.01						
Max Dose	3208±1163	<0.01	2805±932	<0.01	3585±1114	<0.01	3568±1182	<0.01
NTCP	0.059±0.05	<0.01	0.043±0.03	<0.01	0.077±0.015	<0.01	0.068±0.04	<0.01
Effective Volume	0	<0.01	0	<0.01	0	<0.01	0	<0.01
EUD	5545±122	<0.01	5534±139	<0.01	5474±158	<0.01	5499±218	<0.01
NTID	3.3±1.9	0.001	3±1.5	<0.01	3.28±1.3	<0.01	2.98±1.4	<0.01
Spinal cord								
Volume	28.68±7.7	<0.01						
Max Dose	3306±696	<0.01	3112±451	<0.01	4074±529	<0.01	4357±531	<0.01
NTCP	0.045±0.05	<0.01	0.033±0.02	<0.01	0.054±0.03	<0.01	0.074±0.02	<0.01
Effective Volume	0	<0.01	0	<0.01	0	<0.01	0	<0.01
EUD	6092±134	<0.01	6080±153	<0.01	6015±174	<0.01	6042±240	<0.01
NTID	5.7±2.4	0.001	5.2±2.6	0.001	6.6±3.4	0.001	7.2±3.5	0.001
Parotid_Rt								
Volume	19.9±5.3	<0.01						
Max Dose	3329±755	<0.01	3228±733	<0.01	3231±494	<0.01	3205±550	<0.01
NTCP	0.96±0.07	<0.01	0.96±0.07	<0.01	0.97±0.03	<0.01	0.97±0.04	<0.01
Effective Volume	1.79±0.53	<0.01	1.76±0.51	<0.01	1.8±0.45	<0.01	1.83±0.43	<0.01
EUD	3310±73	<0.01	3304±83	<0.01	3185±342	<0.01	3283±130	<0.01
NTID	24.3±9.5	0.001	19.8±7.1	<0.01	23.48±8.7	<0.01	19.15±8	<0.01
Parotid_Lt								
Volume	19.1±4.7	<0.01						
Max Dose	3299±754	<0.01	3225±781	<0.01	3350±904	<0.01	3229±618	<0.01
NTCP	0.77±0.16	<0.01	0.76±0.20	<0.01	0.77±0.15	<0.01	0.77±0.14	<0.01
Effective Volume	0.91±0.43	<0.01	0.91±0.43	<0.01	0.97±0.56	<0.01	0.9±0.36	<0.01
EUD	4049±89	<0.01	4039±102	<0.01	3998±116	<0.01	4016±160	<0.01
NTID	20.7±7.9	0.001	20.6±8	0.001	21.9±6.1	0.001	17.5±6	0.001

PTV63, 8113±870 for PTV60, 5798±3224 for PTV56 and 7018±501 for PTV54. The equivalent uniform dose of 9-field IMRT was 9321±228 (standard deviation, SD) for PTV70, 8745±300 for PTV63, 8161±842 for PTV60, 5997±3336 for PTV56 and 7230±537 for PTV54. A detailed summary of the tumor control probability and equivalent uniform dose for all PTVs for all three groups is shown in Table 3 and Figure 1(e) and (f) to Figure 5(e) and (f). The p values found are less than < 0.01 for all categories.

OAR analysis
Brainstem
The brainstem volume was 30.88±5.4 cm3, and the maximum doses of Rapid arc from 2 arcs and 3 arcs and IMRT from 7 fields and 9 fields were 3208 ±1163, 2805±932, 3585±1114 and 3568±1182, respectively. The NTCP values were 0.059±0.05, 0.043±0.03, 0.077±0.015 and 0.068±0.04, respectively. The EUDs are 5545±122, 5534±139, 5474±158 and 5499±218, respectively. The normal tissue integral doses were 3.3±1.9, 3±1.5, 3.28±1.3 and 2.98±1.4, respectively. The LKB's model effective volume remains 0 in all treatment planning methods. The

p values and detailed summary of the results are shown in Table 4 and plotted in Supplementary Figure 7.

Spinal cord
The spinal cord volume was 28.68±7.7 cm3, and the maximum doses of Rapid arc from 2 arcs and 3 arcs and IMRT from 7 fields and 9 fields were 3306±696, 3112±451, 4074±529 and 4357±531, respectively. The NTCP values were 0.045±0.05, 0.033±0.02, 0.054±0.03 and 0.074±0.02, respectively. The EUDs were 6092±134, 6080±153, 6015±174 and 6042±240, respectively. The normal tissue integral doses were 5.7±2.4, 5.2±2.6, 6.6±3.4 and 7.2±3.5. The LKB model effective volume remains 0 in all planning methods. The p values and detailed summary of the results are shown in Table 4 and plotted in Supplementary Figure 8.

Right Parotid
The volume of the right parotid was 19.9±5.3 cm3, and the mean doses of Rapid arc from 2 arcs and 3 arcs and IMRT from 7 fields and 9 fields were 3329±755, 3228±733, 3350±904 and 3205±550, respectively. The NTCP was 0.96±0.07, 0.96±0.07, 0.97±0.03 and
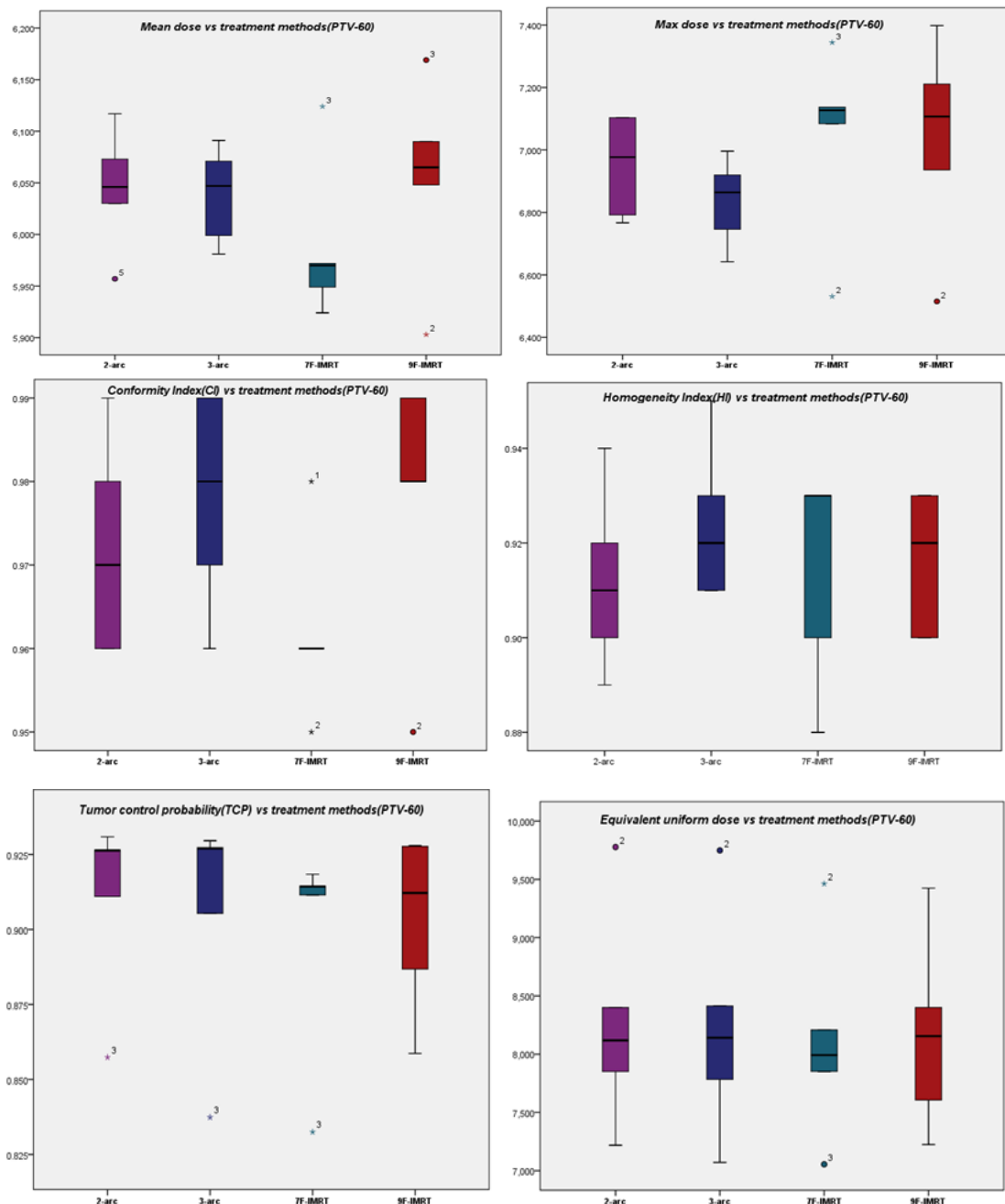
Figure 3. Box-whisker plot of PTV-60 in 2-arc, 3-arc, 7F-IMRT and 9F-IMRT treatment methods for (a) Mean dose (b) Max dose (c) CI and (d) HI (e) TCP and (f) EUD

0.97±0.04, respectively. The EUDs are 3310±73, 3304±83, 3185±342 and 3283±130, respectively. The NTIDs were 24.3±9.5, 19.8±7.1, 23.48±8.7 and 19.15±8. The LKB model effective volumes were 1.79±0.53, 1.76±0.51, 1.8±0.45 and 1.83±0.43 cm³, respectively. The effective volume is compared against NTCP and plotted on a line graph, as shown in Supplementary Figure 6 (a). The p values and detailed summary of the results are shown in Table 4 and plotted in Supplementary Figure 9.

Left Parotid

The volume of the left parotid was 19.1±4.7 cm3, and the mean doses of the Rapid arc from 2 arcs and 3 arcs and IMRT from 7 fields and 9 fields were 3299±754, 3225±781, 3350±904 and 3229±618, respectively. The NTCP was 0.77±0.16, 0.76±0.20, 0.77±0.15 and

0.77±0.14, respectively. The EUDs are 4049±89, 4039±102, 3998±116 and 4016±160, respectively. The normal tissue integral doses were 20.7±7.9, 20.6±8, 21.9±6.1 and 17.5±6, respectively. The LKB model effective volumes were 0.91±0.43, 0.91±0.43, 0.97±0.56 and 0.9±0.36 cm3, respectively. In Supplementary Figure 6 (b), the effective volume is compared to NTCP and plotted as a line graph. The p values and detailed summary of the results are shown in Table 4 and plotted in Supplementary Figure 10.

The effective volume of the LKB model is linearly related to the normal tissue complication probabilities of both the right and left parotids as shown in Supplementary Figure 6. for each of the four planning techniques. As soon as the effective volume threshold is reached, the

Table 5. p value between 2 arc and 3 arc, 2 arc and 7 F IMRT, 2 arc and 9 F IMRT, 3 arc and 7 F IMRT, 3 arc and 9 F IMRT, 7 F IMRT and 9 F IMRT for all radiobiological and dosimetric parameters of the brainstem, spinal cord, right parotid and left parotid. P values ≤ 0.05 were considered statistically significant.

Radiological and Dosimetric parameter	Comparison of Techniques	Brain stem p value	spinal cord p value	Parotid right p value	Parotid left p value
Mean/Max dose(cGy)	2 arcs- 3 arcs	0.003	0.182	0.05	0.117
	2 arcs- 7F IMRT	0.028	0.008	0.388	0.666
	2 arcs- 9F IMRT	0.028	0.003	0.209	0.556
	3 arcs-7F IMRT	0.003	0.002	0.937	0.875
	3 arcs-9F IMRT	0.004	0.002	0.583	0.388
	7F IMRT-9F IMRT	0.906	0.092	0.583	0.327
NTCP	2 arcs- 3 arcs	0.009	0.284	0.437	0.388
	2 arcs- 7F IMRT	0.05	0.06	0.953	0.61
	2 arcs- 9F IMRT	0.154	0.034	0.673	0.433
	3 arcs-7F IMRT	0.021	0.031	0.411	1
	3 arcs-9F IMRT	0.026	0.003	0.607	0.814
	7F IMRT-9F IMRT	0.12	0.045	0.205	0.374
Effective Volume(cc)	2 arcs- 3 arcs	0	0	0.317	1
	2 arcs- 7F IMRT	0	0	0.887	0.719
	2 arcs- 9F IMRT	0	0	0.931	0.914
	3 arcs-7F IMRT	0	0	0.339	0.609
	3 arcs-9F IMRT	0	0	0.496	0.832
	7F IMRT-9F IMRT	0	0	0.581	0.48
EUD(cGy)	2 arcs- 3 arcs	0.409	0.388	0.433	0.272
	2 arcs- 7F IMRT	0.084	0.084	0.084	0.084
	2 arcs- 9F IMRT	0.328	0.328	0.328	0.328
	3 arcs-7F IMRT	0.182	0.182	0.182	0.272
	3 arcs-9F IMRT	0.433	0.433	0.433	0.456
	7F IMRT-9F IMRT	0.432	0.433	0.182	0.433
NTID	2 arcs- 3 arcs	0.032	0.14	0.084	0.875
	2 arcs- 7F IMRT	0.959	0.116	0.666	0.388
	2 arcs- 9F IMRT	0.371	0.004	0.117	0.209
	3 arcs-7F IMRT	0.084	0.008	0.195	0.583
	3 arcs-9F IMRT	0.329	0.003	0.937	0.272
	7F IMRT-9F IMRT	0.084	0.086	0.099	0.007

curve becomes saturated, increasing the likelihood that complications will arise as the effective volume increases. It was not statistically significant (p = 0.068) to compare the effective volumes of both parotids using all four planning methods.

Discussion

In this investigation, we examined the delivery of radiation dose to the target volumes and the surrounding normal structures and compared the SIB for HNC [24-26] plans using four different treatment planning techniques from Rapid arc [27, 28] and IMRT [29-32]. The constraints for the maximal dose to the brain stem and spinal cord were achieved with all planning techniques (p < 0.01). The brainstem and spinal cord normal tissue

Table 6. Mean and Standard Deviation of Treatment Parameters (monitor units) for the 2 arc, 3 arc, 7 F IMRT, and 9 F IMRT Treatment Methods

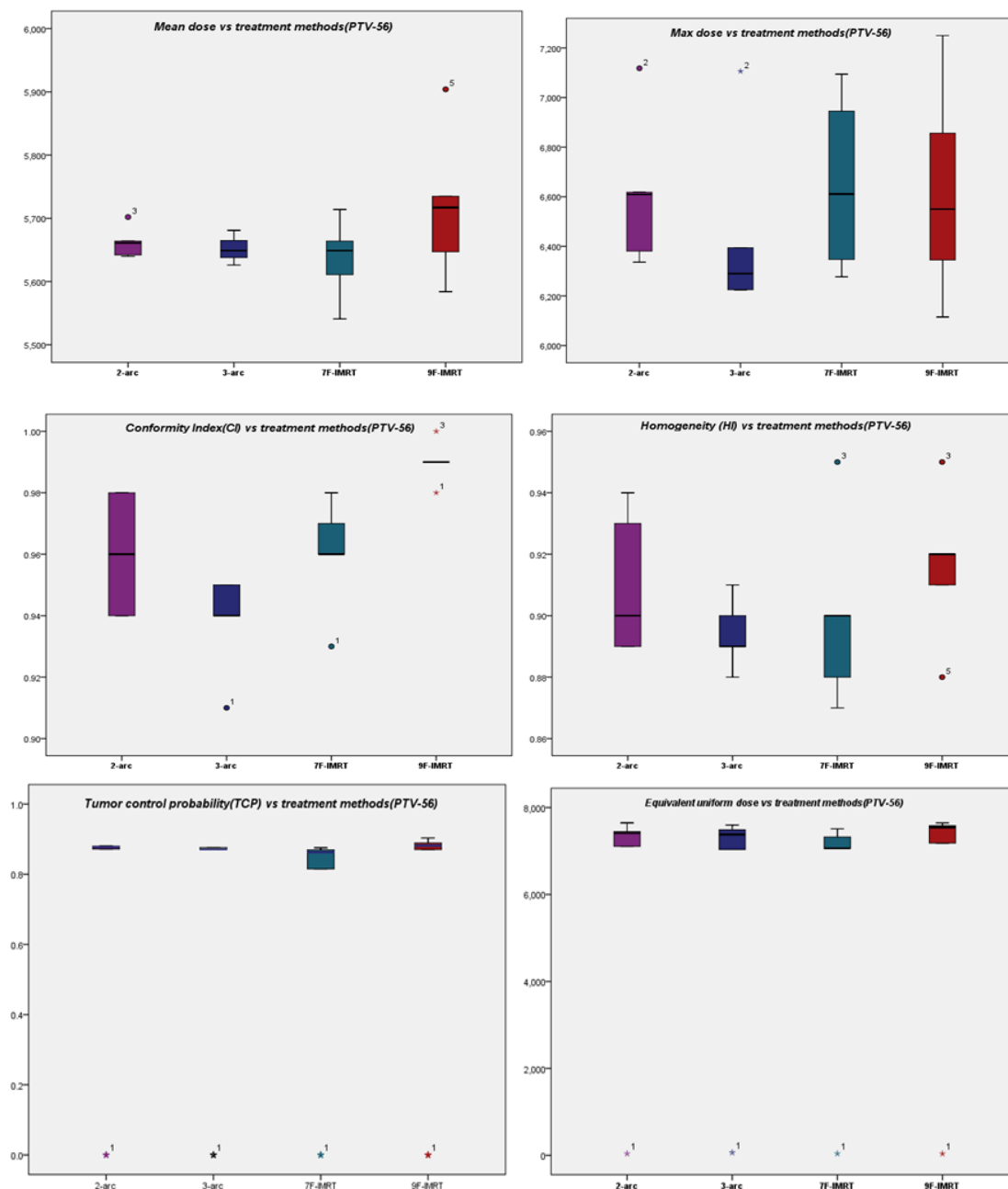| Treatment parameter	2- arcs	p value	3- arcs	p value	7F-IMRT	p value	9F-IMRT	p value
MU	986±217	<0.01	904±144	<0.01	1815±224	<0.01	2213±328	<0.01

Figure 4. Box-whisker plot of PTV-56 in 2-arc, 3-arc, 7F-IMRT and 9F-IMRT treatment methods for (a) mean dose, (b) max dose, (c) CI, (d) HI, (e) TCP and (f) EUD.

complication probability was less than 5% to 7% (p 0.01). The equivalent uniform dose for both the brain stem and spinal cord was 5.5 Gy to 6 Gy (p < 0.01). The normal tissue integral dose for the brain stem to the spinal cord was 3 to 7 cGy.Lit. The effective volume calculated from the LKB model was 0 cm3. This clearly shows the OAR sparing of both the brain stem and spinal cord based on the above dosimetric and radiobiological analysis.

The mean dose constraints to both the left and right parotids were not achieved in any of the planning methods (p < 0.01). The mean doses to both parotids for all four treatment planning methods were 32 Gy. The NTCP of the right parotid was 96 to 97% (p 0.01). This is more than the complications of the left parotid, 75 to 77% (p < 0.01). A right parotid EUD of 31 to 33 Gy (p 0.01) was lower than a left parotid EUD of 40 Gy (p 0.01). The normal

tissue integral dose for both parotids ranges from 17 to 24 cGy-lit. The effective volumes calculated from the LKB model were 1.9 and 0.9 cm3 for the right and left parotids, respectively. This clearly shows that OAR sparing is not possible for both parotids based on the above dosimetric and radiobiological analysis.

Comparisons of OAR with IMRT (7 fields and 9 fields)

The maximum dose for the brain stem and spinal cord [33, 34] and the mean dose for the parotids [35-38] were not statistically significant for either 7-field or 9-field IMRT (p > 0.05). The NTCP [39], effective volume, EUD, and NTID of the brainstem, spinal cord, and parotids were also not statistically significant (p > 0.05). The mean dose, NTCP, effective volume, EUD, and NTID of both parotids were not statistically significant (p > 0.05). The p values

Table 7. p value between 2arcs and 3 arcs, 2arcs and 7F IMRT, 2 arcs and 9F IMRT, 3 arcs and 7F IMRT,3 arcs and 9F IMRT, 7F IMRT and 9F IMRT for All Radiobiological and Dosimetric Parameter of PTV 70,63,60,56 and 54.

Radiological and Dosimetric parameter	Comparison of planning techniques	PTV 70 p value	PTV 63 p value	PTV 60 p value	PTV 56 p value	PTV 54 p value
Mean dose	2 arcs- 3 arcs	0.413	0.715	0.345	0.5	0.345
	2 arcs- 7F IMRT	0.005	0.5	0.225	0.686	0.042
	2 arcs- 9F IMRT	0.013	0.686	0.5	0.345	0.225
	3 arcs-7F IMRT	0.005	0.345	0.345	0.786	0.138
	3 arcs-9F IMRT	0.012	0.5	0.5	0.225	0.138
	7F IMRT-9F IMRT	0.959	0.5	0.08	0.138	0.043
Max dose	2 arcs- 3 arcs	0.878	0.225	0.08	0.138	0.686
	2 arcs- 7F IMRT	0.047	0.043	0.225	0.5	0.225
	2 arcs- 9F IMRT	0.575	0.225	0.5	0.893	0.08
	3 arcs-7F IMRT	0.074	0.043	0.138	0.225	0.345
	3 arcs-9F IMRT	0.575	0.043	0.138	0.345	0.043
	7F IMRT-9F IMRT	0.114	0.5	0.893	0.686	0.08
Conformity Index(CI)	2 arcs- 3 arcs	0.035	0.713	0.083	0.059	0.034
	2 arcs- 7F IMRT	0.011	0.279	0.276	1	0.157
	2 arcs- 9F IMRT	0.017	0.655	0.705	0.041	0.276
	3 arcs-7F IMRT	0.007	0.131	0.109	0.041	0.157
	3 arcs-9F IMRT	0.007	0.705	0.713	0.42	0.066
	7F IMRT-9F IMRT	0.785	0.144	0.066	0.39	0.066
Homogeneity Index(HI)	2 arcs- 3 arcs	0.01	0.157	0.063	0.063	0.705
	2 arcs- 7F IMRT	0.121	0.063	0.783	0.498	0.785
	2 arcs- 9F IMRT	0.027	0.285	0.414	0.683	0.414
	3 arcs-7F IMRT	0.011	0.063	0.257	0.705	0.705
	3 arcs-9F IMRT	0.007	0.176	0.102	0.176	0.593
	7F IMRT-9F IMRT	0.234	0.564	1	0.273	0.581
TCP	2 arcs- 3 arcs	0.23	0.465	0.225	0.273	0.343
	2 arcs- 7F IMRT	0.005	0.138	0.08	0.068	0.043
	2 arcs- 9F IMRT	0.009	0.465	0.684	0.144	0.225
	3 arcs-7F IMRT	0.005	0.176	0.138	0.144	0.08
	3 arcs-9F IMRT	0.007	0.343	0.893	0.144	0.138
	7F IMRT-9F IMRT	0.721	0.416	0.5	0.068	0.043
EUD	2 arcs- 3 arcs	0.085	0.5	0.225	0.345	0.225
	2 arcs- 7F IMRT	0.005	0.225	0.08	0.068	0.043
	2 arcs- 9F IMRT	0.013	0.345	0.465	0.225	0.138
	3 arcs-7F IMRT	0.005	0.08	0.138	0.138	0.08
	3 arcs-9F IMRT	0.007	0.345	0.5	0.225	0.138
	7F IMRT-9F IMRT	0.919	0.225	0.686	0.08	0.043

of all organs at risk are tabulated in Table 5.

Comparisons of OAR with Raid arc (2 arcs and 3 arcs)

The max dose, NTCP, and NTID of the brain stem were statistically significant (p < 0.05), but EUD was not significant (p > 0.05). The maximum dose, NTCP, and EUD of the spinal cord were not statistically significant (p > 0.05). All parotid dosimetric and radiobiological parameters were not statistically significant (p > 0.05) among the mean dose, NTCP, effective volume, EUD, and NTID. The p values of all organs at risk are tabulated in Table 5.

Comparisons of OAR with IMRT and Raid arc

The maximum dose and NTCP of the brain stem were statistically significant (p < 0.05), but EUD and NTID were not statistically significant (p > 0.05). The maximum dose, NTCP, and NTID of the spinal cord were statistically significant (p < 0.05), but EUD was not statistically significant (p > 0.05). The mean dose, NTCP, effective volume, EUD, and NTID were not statistically significant (p > 0.05). The p values of all organs at risk are tabulated in Table 5.

Comparison of MU for IMRT and Rapid arc

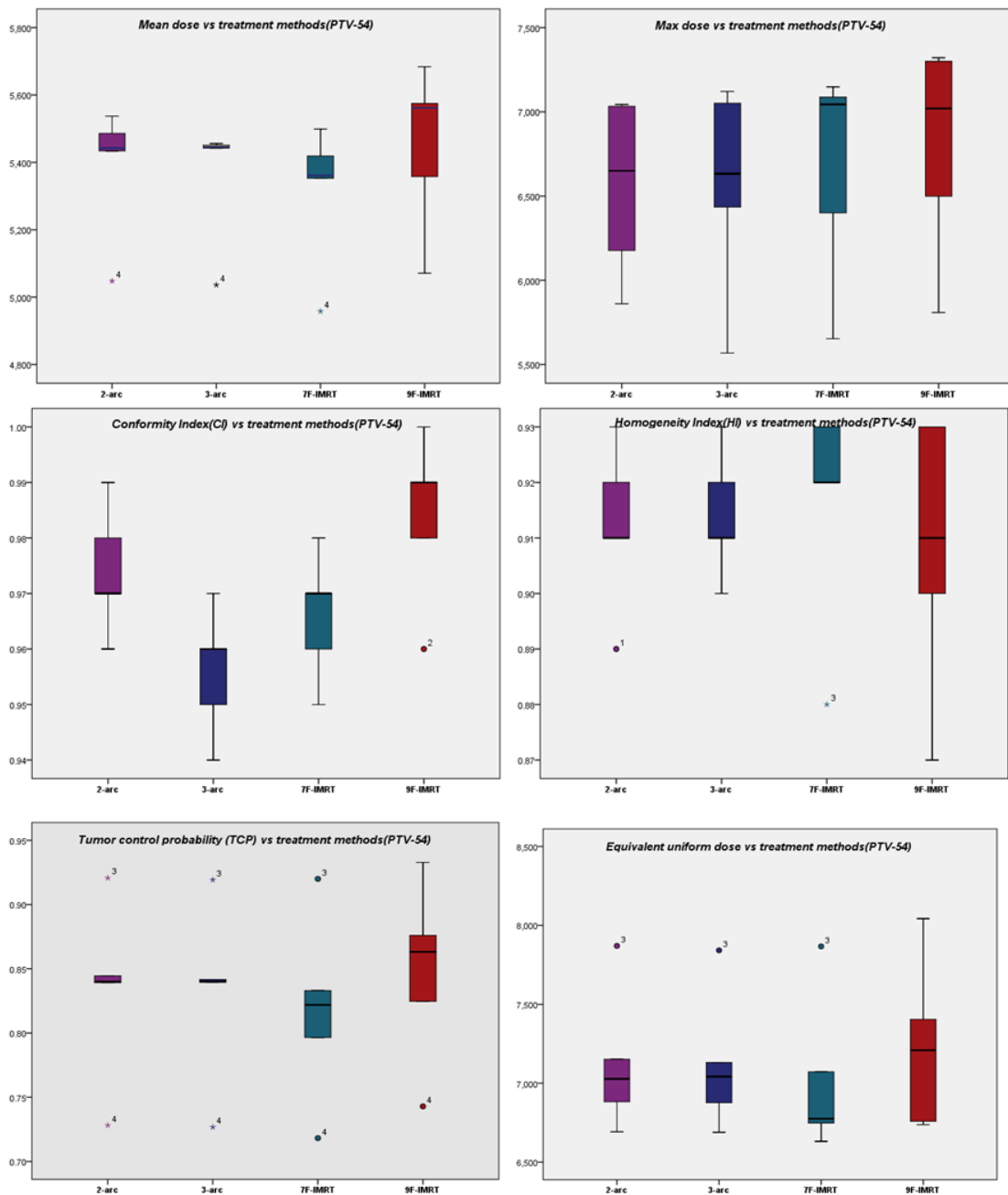The monitor units [4] were compared with 2 and

Figure 5. Box-whisker plot of PTV-54 in 2-arc, 3-arc, 7F-IMRT and 9F-IMRT treatment methods for (a) mean dose, (b) max dose, (c) CI, (d) HI, (e) TCP and (f) EUD.

3 arcs of the Rapid arc and 7 and 9 fields of IMRT planning methods. Box plots are plotted as shown in Supplementary Figure 11 (a), and line graph comparisons with MU and PTV volumes are shown in Supplementary Figure 11 (b) and data in Table 6. It is apparent from the tabulated values that the 3 arc Rapid arc had a significantly lower MU than the other three planning methods.

Comparisons of the target volume with IMRT

The p values of mean dose, max dose, conformity index, homogeneity index, tumor control probability, and equivalent uniform dose of planned target volumes [40, 41] from 7 fields and 9 fields IMRT are greater than 0.05, which is statistically not significant and shown in Table 7. The dosimetric and radiobiological parameters from both

treatment planning methods were comparable.

Comparison of the target volume with RapidArc

The p values of mean dose, max dose, tumor control probability, and equivalent uniform dose of the target volume from 2 arcs and 3 arcs RapidArc were greater than 0.05, which is statistically not significant, but p values of conformity and homogeneity index are less than 0.05, which is statistically significant and shown in Table 7.

Comparison of target volume from IMRT and RapidArc

The p values of the mean dose, conformity index, homogeneity index, tumor control probability, and equivalent uniform dose were statistically significant (p < 0.05), except for the maximum dose, which was not

statistically significant (p > 0.05). The p values of the results are shown in Table 7.

The conformity and homogeneity index [23, 24, 42] for the 3 arc Rapid arc is significantly superior to the other three planning methods, while EUD and TCP are not significant. This is shown in Supplementary Figure 12, and it is apparent that the 3 arc rapid arc provides higher tumor control than the other planning methods. The monitor units calculated from all four planning methods clearly show that the 3 arc Rapid arc is the least.

The NTCP of the brain stem and spinal cord was significantly less than that of the other three planning methods, while the NTCP of the right and left parotids were significantly the same in all four treatment planning methods, as shown in the 3D bar chart in Supplementary Figure 13. It is evident that OAR sparing is possible for the brain stem and spinal cord, as the NTCP is less than 5%, while both of the parotids are not spared, as the complication was more than 75%.

Treatment times

Typical 7-9 fileds HNC IMRT requires dramatically increased treatment times of 12-18 minutes [28]. However, arc rapid arc methods can result in short treatment times of approximately 2-6 minutes. The treatment times are proportional to the calculated monitor units and treatment field mode up times.In this study, it is clear that the equivalent uniform dose of the target volume for Rapid arc was statistically significant (p < 0.05) and far better than IMRT, which is responsible for the enhanced conformity and homogeneity index, but the same time, rapid 2 arcs and 3 arcs were not statistically significant (p > 0.05), which generates similar effects, except for the maximum dose of all other radiobiological and dosimetric parameters in this approach.

In conclusion, optimization of radiotherapy plans and therapeutic decisions can benefit from radiobiological models. This study shows that Rapid arc (3 arcs) is more effective than Rapid arc (2 arcs), 7-field IMRT, and 9-field IMRT. The rapid arc (3 arcs) resulted in significantly better OAR sparing and had the least number of complications against normal tissue. The findings indicate that the Rapid arc (3 arcs) plan improves tumor control, dose homogeneity, and conformity in the target volume compared with IMRT. However, the tumor control probability obtained for the two planned techniques, Rapid arc (2 arcs) and IMRT (7 fields), was analogous. The treatment time and monitor units for the Rapid arc (3 arcs) were better than IMRT planning methods, which are standard in head & neck radiotherapy.

Author Contribution Statement

All authors contributed equally in this study.

Acknowledgements

None.

References

1. Stromberger C, Wlodarczyk W, Marnitz S, Jamil B, Budach V, Raguse JD, et al. Simultaneous integrated boost (sib): Rapidarc and tomotherapy plan comparison for unilateral and bilateral neck irradiation. Anticancer Res. 2015;35(5):2991-7.
2. Teh BS, Woo SY, Butler EB. Intensity modulated radiation therapy (imrt): A new promising technology in radiation oncology. Oncologist. 1999;4(6):433-42.
3. Grégoire V, Lefebvre JL, Licitra L, Felip E. Squamous cell carcinoma of the head and neck: Ehns-esmo-estro clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010;21 Suppl 5:v184-6. https://doi.org/10.1093/annonc/mdq185.
4. Dirix P, Nuyts S, Van den Bogaert W. Radiation-induced xerostomia in patients with head and neck cancer: A literature review. Cancer. 2006;107(11):2525-34. https://doi.org/10.1002/cncr.22302.
5. Pignon JP, le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (mach-nc): An update on 93 randomised trials and 17,346 patients. Radiother Oncol. 2009;92(1):4-14. https://doi.org/10.1016/j.radonc.2009.04.014.
6. Abel E, Silander E, Nyman J, Bove M, Johansson L, Björk-Eriksson T, et al. Impact on quality of life of imrt versus 3-d conformal radiation therapy in head and neck cancer patients: A case control study. Adv Radiat Oncol. 2017;2(3):346-53. https://doi.org/10.1016/j.adro.2017.05.002.
7. Buzalaf MA, Hannas AR, Kato MT. Saliva and dental erosion. J Appl Oral Sci. 2012;20(5):493-502. https://doi.org/10.1590/s1678-77572012000500001.
8. Deasy JO, Moiseenko V, Marks L, Chao KS, Nam J, Eisbruch A. Radiotherapy dose-volume effects on salivary gland function. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S58-63. https://doi.org/10.1016/j.ijrobp.2009.06.090.
9. Niemierko A, Goitein M. Calculation of normal tissue complication probability and dose-volume histogram reduction schemes for tissues with a critical element architecture. Radiother Oncol. 1991;20(3):166-76. https://doi.org/10.1016/0167-8140(91)90093-v.
10. Gabryś HS, Buettner F, Sterzing F, Hauswald H, Bangert M. Parotid gland mean dose as a xerostomia predictor in low-dose domains. Acta Oncol. 2017;56(9):1197-203. https://doi.org/10.1080/0284186x.2017.1324209.
11. Dashnamoorthy S, Rajamanickam K, Jeyasingh E, Pandey V, Nachimuthu K, Ahmed I, et al. Comparison of dose statistics of intensity-modulated radiation therapy plan from varian eclipse treatment planning system with novel python-based indigenously developed software. Prog Med Phys. 2022;33:25-35. https://doi.org/10.14316/pmp.2022.33.3.25.
12. Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R, et al. Radiation therapy oncology group: Radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys. 1993;27(5):1231-9. https://doi.org/10.1016/0360-3016(93)90548-a.
13. Anonymous. Prescribing, recording and reporting photon beam therapy (supplement to icru report 50). Report 62, international ommission on radiation units and measurements. Washington;1999.
14. Carrie C, Ginestet C, Bey P, Aletti P, Haie-Meder C, Briot E, et al. [conformal radiation therapy. Fédération nationale des centres de lutte contre le cancer (fnclcc)]. Bull Cancer. 1995;82(5):325-30.
15. Niemierko A. Reporting and analyzing dose distributions: A concept of equivalent uniform dose. Med Phys.

1997;24(1):103-10. https://doi.org/10.1118/1.598063.

16. Gay HA, Niemierko A. A free program for calculating eud-based ntcp and tcp in external beam radiotherapy. Phys Med. 2007;23(3-4):115-25. https://doi.org/10.1016/j.ejmp.2007.07.001.

17. Burman C, Kutcher GJ, Emami B, Goitein M. Fitting of normal tissue tolerance data to an analytic function. Int J Radiat Oncol Biol Phys. 1991;21(1):123-35. https://doi.org/10.1016/0360-3016(91)90172-z.

18. Lyman JT. Complication probability as assessed from dose-volume histograms. Radiation Research. 1985 Nov 1;104(2s):S13-9.

19. Puzhakkal N, Kochunny A, Padannayil N, Singh N, Chalil J, Umer J. Comparison of treatment plans: A retrospective study by the method of radiobiological evaluation. Polish J Med Phys Eng. 2016;22. https://doi.org/10.1515/pjmpe-2016-0011.

20. Shi C, Peñagarícano J, Papanikolaou N. Comparison of imrt treatment plans between linac and helical tomotherapy based on integral dose and inhomogeneity index. Med Dosim. 2008;33(3):215-21. https://doi.org/10.1016/j.meddos.2007.11.001.

21. Yadav S, Singh OP, Choudhary S, Saroj DK, Yogi V, Goswami B. Estimation and comparison of integral dose to target and organs at risk in three-dimensional computed tomography image-based treatment planning of carcinoma uterine cervix with two high-dose-rate brachytherapy sources: (60)co and (192)ir. J Cancer Res Ther. 2021;17(1):191-7. https://doi.org/10.4103/jcrt.JCRT_199_19.

22. Hall EJ, Wuu CS. Radiation-induced second cancers: The impact of 3d-crt and imrt. Int J Radiat Oncol Biol Phys. 2003;56(1):83-8. https://doi.org/10.1016/s0360-3016(03)00073-7.

23. D'Souza WD, Rosen, II. Nontumor integral dose variation in conventional radiotherapy treatment planning. Med Phys. 2003;30(8):2065-71. https://doi.org/10.1118/1.1591991.

24. Vanhavere F, Huyskens D, Struelens L. Peripheral neutron and gamma doses in radiotherapy with an 18 mv linear accelerator. Radiat Prot Dosimetry. 2004;110(1-4):607-12. https://doi.org/10.1093/rpd/nch135.

25. Podgorsak EB, Rawlinson JA, Johns HE. X-ray depth doses from linear accelerators in the energy range from 10 to 32 mev. Am J Roentgenol Radium Ther Nucl Med. 1975;123(1):182-91. https://doi.org/10.2214/ajr.123.1.182.

26. Broggi S, Perna L, Bonsignore F, Rinaldin G, Fiorino C, Chiara A, et al. Static and rotational intensity modulated techniques for head-neck cancer radiotherapy: A planning comparison. Phys Med. 2014;30(8):973-9. https://doi.org/10.1016/j.ejmp.2014.07.001.

27. Van Gestel D, van Vliet-Vroegindeweij C, Van den Heuvel F, Crijns W, Coelmont A, De Ost B, et al. Rapidarc, smartarc and tomohd compared with classical step and shoot and sliding window intensity modulated radiotherapy in an oropharyngeal cancer treatment plan comparison. Radiat Oncol. 2013;8:37. https://doi.org/10.1186/1748-717x-8-37.

28. Wiezorek T, Brachwitz T, Georg D, Blank E, Fotina I, Habl G, et al. Rotational imrt techniques compared to fixed gantry imrt and tomotherapy: Multi-institutional planning study for head-and-neck cases. Radiat Oncol. 2011;6:20. https://doi.org/10.1186/1748-717x-6-20.

29. Holt A, Van Gestel D, Arends MP, Korevaar EW, Schuring D, Kunze-Busch MC, et al. Multi-institutional comparison of volumetric modulated arc therapy vs. Intensity-modulated radiation therapy for head-and-neck cancer: A planning study. Radiat Oncol. 2013;8:26. https://doi.org/10.1186/1748-717x-8-26.

30. Peters S, Schiefer H, Plasswilm L. A treatment planning study comparing elekta vmat and fixed field imrt using the varian treatment planning system eclipse. Radiat Oncol. 2014;9:153. https://doi.org/10.1186/1748-717x-9-153.

31. Clemente S, Wu B, Sanguineti G, Fusco V, Ricchetti F, Wong J, et al. Smartarc-based volumetric modulated arc therapy for oropharyngeal cancer: A dosimetric comparison with both intensity-modulated radiation therapy and helical tomotherapy. Int J Radiat Oncol Biol Phys. 2011;80(4):1248-55. https://doi.org/10.1016/j.ijrobp.2010.08.007.

32. Stieler F, Wolff D, Schmid H, Welzel G, Wenz F, Lohr F. A comparison of several modulated radiotherapy techniques for head and neck cancer and dosimetric validation of vmat. Radiother Oncol. 2011;101(3):388-93. https://doi.org/10.1016/j.radonc.2011.08.023.

33. Lu SH, Cheng JC, Kuo SH, Lee JJ, Chen LH, Wu JK, et al. Volumetric modulated arc therapy for nasopharyngeal carcinoma: A dosimetric comparison with tomotherapy and step-and-shoot imrt. Radiother Oncol. 2012;104(3):324-30. https://doi.org/10.1016/j.radonc.2011.11.017.

34. Rao M, Yang W, Chen F, Sheng K, Ye J, Mehta V, et al. Comparison of elekta vmat with helical tomotherapy and fixed field imrt: Plan quality, delivery efficiency and accuracy. Med Phys. 2010;37(3):1350-9. https://doi.org/10.1118/1.3326965.

35. Tai DT, Oanh LT, Son ND, Loan TT. Evaluation of jaws-only intensity modulated radiation therapy treatment plans using Octavius 4D system. Polish Journal of Medical Physics and Engineering. 2018 Jun 1;24(2):75-8.

36. Tai DT, Oanh LT, Son ND, Loan TTH, Chow JCL. Dosimetric and monte carlo verification of jaws-only imrt plans calculated by the collapsed cone convolution algorithm for head and neck cancers. Rep Pract Oncol Radiother. 2019;24(1):105-14. https://doi.org/10.1016/j.rpor.2018.11.004.

37. Tai DT, Son ND, Loan TTH, Anson HPW. Quality assurance of the jaws only-intensity modulated radiation therapy plans for head-and-neck cancer. Phys Med. 2017a;38:148-52. https://doi.org/10.1016/j.ejmp.2017.05.059.

38. Tai DT, Son ND, Loan TT, Trang NT. Initial experiences of applying the jaws-only IMRT technique in Dong nai general hospital, Vietnam. In6th International Conference on the Development of Biomedical Engineering in Vietnam (BME6) 6 2018 (pp. 335-339). Springer Singapore.

39. Duong TT, Nguyen SD, Truong LT, Nguyen TT. Evaluation and comparison of dose distributions for nasopharyngeal carcinoma patients treated by Jaws-Only IMRT technique and by 3D-CRT technique at Dong Nai General Hospital. VNUHCM Journal of Natural Sciences. 2017 Dec 31;1(T4):79-87.

40. Mesbahi A, Rasouli N, Motlagh B, Mohammadzadeh M. Radiobiological model-based comparison of three-dimensional conformal and intensity-modulated radiation therapy plans for nasopharyngeal carcinoma. Iranian J Med Phys. 2017;14:190-6. https://doi.org/10.22038/ijmp.2017.22508.1213.

41. Anjum MN, Parker W, Aldahlawi I, Ruo R, Afzal M. Evaluation of treatment planning system monitor unit calculations for three intensity modulated radiotherapy delivery techniques. Int J Radiat Res. 2011;9(3):145-50.

42. Thilmann C, Zabel A, Grosser KH, Hoess A, Wannenmacher M, Debus J. Intensity-modulated radiotherapy with an integrated boost to the macroscopic tumor volume in the treatment of high-grade gliomas. Int J Cancer. 2001;96(6):341-9. https://doi.org/10.1002/ijc.1042.