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ORIGINAL ARTICLE

A Dosimetric Plan Study to Increase the Dose from 63 Gy to 70 Gy in Early-Stage Glottic Larynx Cancer

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OBJECTIVE
The present study aims to compare the treatment plan parameters of different radiotherapy techniques [3D-Conformal Radiotherapy (3D-CRT), Dynamic – Intensity Modulated Radiotherapy (D-IMRT), Intensity Modulated Arc Therapy (IMAT) and Helical Tomotherapy (HT)] in Early-Stage Glottic Larynx (EGL) cancer to increase the treatment dose from 63 Gy to 70 Gy.

METHODS
The dose prescription was defined as 2.12 Gy per fraction to a total of 33 fractions. 95% of Planning Treatment Volume-63 Gy (PTV-63) and Planning Treatment Volume-70 (PTV- 70) treatment volumes received the treatment dose of at least 63 and 70 Gy, respectively. The conventional-boost technique was used for 3D-CRT and the simultaneous integrated boost technique was used for other techniques.

RESULTS
The doses obtained from carotid arteries, thyroid and submandibular glands using IMRT, IMAT, and HT were significantly lower than 3D-CRT. The study results pointed out the possibility of giving a treatment dose of 70 Gy to the PTV of EGL with all planning techniques, with some advantages and disadvantages between them. All IMRT techniques provided superiority to 3D-CRT on the doses of the carotid artery, the thyroid gland, the submandibular glands, and the pharyngeal constrictor muscles with less variation between them.

CONCLUSION
The IMAT and 3D-CRT techniques yielded lower monitor unit values compared to other techniques. Normal tissue radiation exposure was lowest with the 3D-CRT technique. We recommend to increase the treatment dose from 63 Gy to 70 Gy in the radiotherapy of EGL cancer but to select the technique according to the patient's condition.

Keywords: Dynamic-IMRT; 3D-CRT; early-stage glottic laryngeal cancer; helical tomotherapy; IMAT.

Introduction

Laryngeal cancers constitute 1.1% (157.000 new cases) of all new cancer cases worldwide. Laryngeal cancers are more common in men than in women. The male/female ratio is 7/1.[1] Approximately 2/3 of the laryngeal cancers arises from the glottic region, while between 80% and 85% of glottic cancers are in the

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early-stage (T1-T2N0M0) at the time of diagnosis.[2] Providing larynx and voice preservation is an important factor in the choice of treatment.[3] In EGL cancer, surgical and radiotherapy treatment techniques give similar survival results, and their superiority over each other remains controversial.[4] However, to many patients, radiotherapy is recommended since it provides better voice preservation.[5] Patients with EGL cancer are under high risk of cardiovascular disease and metachronous secondary head and neck cancer since they have a smoking history.[6,7] These risks should be considered in the selection of radiotherapy techniques. Although using conventionally used parallel-opposed wedge field techniques (2 Dimensional Radiotherapy-2D RT, 3 Dimensional Conformal Radiotherapy- 3D-CRT), high local control rates can be reached, tissues around the tumor receive high doses uprising the risk of side effects due to irradiated the critical organs and their possible subsequent deterioration.[8,9] The re-irradiation of the neck may cause critical organ doses to exceed tolerance doses. Several studies showed that the traditionally used parallel-opposed field techniques produce high doses on carotid vessels and may cause late cerebrovascular diseases, vascular stenosis, and ischemic strokes.[10,11] As a part of the late side effects of radiation, hyperthyroidism and hypothyroidism may also be seen.[12] By the protection of the spinal cord and submandibular glands, the risk of myelopathy and dry mouth may be reduced.[13,14] Lower radiation exposure on these structures may reduce the radiation damage and side effects. Intensity Modulated Radiation Treatment modalities (such as Dynamic Intensity Modulated Radiotherapy (D-IMRT), Intensity Modulated Arc Radiotherapy (IMAT), Helical Tomotherapy (HT)) using more advanced technology can maintain high levels of local control with lower normal tissue exposure than conventional radiotherapy and provides sharp dose decreases at the target volume boundaries.[15] These modern techniques provide a more conformal dose distribution on tumor volume while providing low dose exposure on normal tissues, reducing the risk of normal tissue damage from high radiation exposure. However, healthy tissue volume with a low dose is particularly important for radiation-induced secondary cancer risk and an important concern for IMRT techniques is that they increase in normal tissue volume with low doses. It is estimated that the incidence of secondary cancers can be almost doubled with IMRT techniques compared to conventional techniques.[16]

Ekici et al. administer a treatment dose of 63 Gy to PTV in their study comparing four techniques for T1N0 EGL cancer radiotherapy. However, they did not perform any study to increase the dose beyond 63 Gy.[17] Using IMRT treatment techniques (D-IMRT, IMAT, HT), it is possible to increase the treatment dose of EGL. This study aims to investigate the treatment plan parameters and Organ at Risk (OAR) doses obtained by 3-D CRT, D-IMRT, IMAT and HT techniques to increase the treatment dose from 63 Gy to 70 Gy in the radiotherapy of EGL cancer.

Materials and Methods

DICOM sets of 15 previously treated early glottic laryngeal cancer (T1-T2, N0, M0) patients were obtained from the archives of our institute. This study was approved by the Ethics committee before the start (Date: 01.12.2017, Registration number: 2017/1399). Treatment volumes and critical organs were contoured by a radiation oncologist according to the guidelines of our institute. The planning target volume-70 Gy (PTV-70) was created by giving a 1-cm margin to the gross tumor volume (GTV) in all axes. A 5-mm margin was given to larynx in all axes to create the PTV-63 volume. Mean treatment volumes were 95.56 cm^3, 28.26 cm^3 for PTV-63 and PTV-70, respectively.

The prescription dose was defined as 2.12 Gy per fraction to a total of 33 fractions. At least 95% of the PTV-63 and PTV-70 treatment volumes ($D_{95\%}$) were normalized to be administered 63 Gy and 70 Gy, respectively. The dose homogeneity of treatment volumes was aimed to be between 95-107%. Conventional-boost technique (a sequential boost) was used for 3D-CRT plans and Simultaneous-Integrated-Boost (SIB) technique was used for D-IMRT, IMAT and HT plans. 3D-CRT, D-IMRT, and IMAT plans were performed using an Eclipse treatment planning software version 15.6 (Varian Medical Systems Inc., Palo Alto, CA). TomoHDA™ treatment planning software version 2.0 was used for HT plans.

For the 3D-CRT plans, parallel opposed-lateral fields (at 90^0 and 270^0) were used for PTV-63 volumes and wedge filters (35^0 and 45^0 angles) were used to provide dose homogeneity. After the PTV-63 plan was created, oblique fields from the anterior part of the neck (coplanar or noncoplanar) were used according to the PTV-70 position. PTV-63 and PTV-70 plans were combined to obtain cumulative-dose volume histograms (c-DVH). The c-DVHs and isodose lines were used to examine the plan sum. By examining the pa-

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rameters shown on the plan sum, PTV-63 and PTV-70 were normalized to the adequate isodose line so that 95% of the PTVs received the prescribed doses. A bolus was not necessary for these plans.

The 5-field D-IMRT plans 0^0, 51^0, 102^0, 255^0, 306^0 oblique fields were used for 14 patients, and the fields of 0^0, 40^0, 80^0, 120^0, 320^0 were used to remove the shoulders from the treatment fields for one patient.

Two full arcs were used in the IMAT plans. The first arc was started with 180.1^0-179.9^0 angles and the other arc was set to rotate on the same plane in the opposite direction (179.9^0-180.1^0) of the first arc. To avoid the interleaf leakage radiation, the primary and secondary fields were given a 300^0 and 330^0 collimation angle, respectively. A dose calculation algorithm was used for 3D-CRT, D-IMRT, and IMAT plans. Photon Optimizer (PO) and Progressive Resolution Optimizer (PRO) algorithms were utilized for the D-IMRT and IMAT, respectively.

For HT in all plans, the width of the field was 2.5 cm, the modulation factor was 2.5, and the pitch factor was 0.446. The dose calculations for HT plans were performed using the Convolution/Superposition algorithm. All plans were generated with 6-MV photons using a multileaf collimator. Planning parameters for critical organs in the process of optimization for D-IMRT, IMAT and HT techniques: Spinal cords D_{max}<20 Gy, Carotid arteries D_{mean}<35 Gy and V35,50,63Gy <35, 50, 63(%), Thyroid glands D_{mean}<30 Gy and V30,50Gy< 30,50(%), Submandibular glands D_{mean}<39 Gy were used. As an example of treatment plans, the dose distribution of an individual patient plan obtained from the four treatment modalities is shown in Figure 1.

$D_{2\%}$ (near-max), $D_{98\%}$ (near-min) and D50% (dose-mean) were analyzed in evaluation of PTV volumes (doses received by 2%, 98% 50% of the treatment volumes) as described in ICRU 83 guidelines. For Homogeneity Index (HI); $HI=(D_{\%2}-D_{\%98})/D_{\%50}$ formula and for Conformity Index (CI); $CI=V_{ri}/TV$ (Where V_{ri} is the volume of reference isodose and TV is the treatment volume covered by reference isodose line) formula were used. HI values approximating to zero indicate a more homogeneous dose distribution in the target volume (zero is the ideal value). The ideal CI value is equal to 1.[18]

For the statistical comparison, the One-Way ANOVA test was employed when parametric conditions were provided; otherwise, the Kruskal-Wallis test was used. When parametric conditions were provided for pair-wise comparisons, the Bonferroni test was used; otherwise, the Mann-Whitney U test was used.

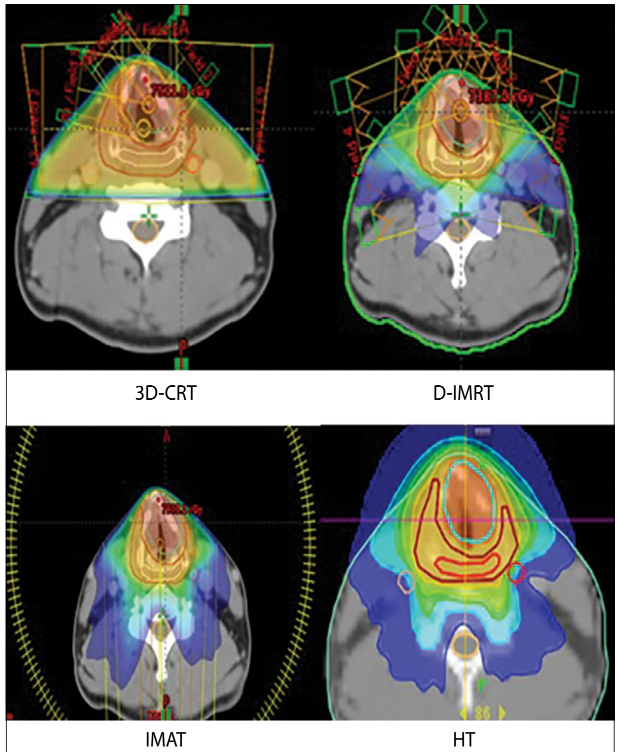

Fig. 1. The dose distribution of an individual patient plan obtained from the four treatment modalities.

The P-value of <0.05 is considered statistically significant. The IBM SPSS 24.0 version (SPSS Inc., IL, USA) was applied for statistical comparison. Table 1 and Table 2 indicate comparison and analysis data of PTVs, OARs, and MU.

Results

Evaluation of Treatment Plan Parameters for PTV

The results of the PTV comparison of four different techniques are shown in Table 1. When PTV-70 volume was evaluated concerning $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ values, D-IMRT, IMAT and HT techniques were found to be significantly more optimal than the 3D-CRT technique. There was no significant difference between intensity-modulated techniques (p>0.05). Between IMAT and HT techniques, significantly differences were observed for D%2 of PTV-63. The IMAT was superior to the HT. No significant differences were found between IMAT vs. D-IMRT and D-IMRT vs. HT. There was no statistically significant difference between $D_{98\%}$ for PTV-63 volumes of 4 techniques (p>0.05).

In the comparison of HI and CI, three intensity-modulated modalities (D-IMRT, IMAT, HT) were

Table 1 $D_{2\%}$, $D_{98\%}$, D50%, HI, CI and MU values for PTV-63 Gy and PTV-70 Gy and their statistical results (The values are the average data of the 15 patients)

Parameters	3D-CRT		D-IMRT		IMAT		HT		3D-CRT vs. D-IMRT	3D-CRT vs. IMAT	3D-CRT vs. HT	D-IMRT vs. IMAT	D-IMRT vs. HT	IMAT vs. HT
	Mean	SD	Mean	SD	Mean	SD	Mean	SD						
PTV-70 Gy														
$D_{2\%}$	74.74	±0.53	73.6	±0.63	73.49	±0.33	73.47	±0.67	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
$D_{98\%}$	68.89	±0.17	69.31	±0.11	69.5	±0.89	69.49	±0.06	0.01	0.003	0.002	>0.05	>0.05	>0.05
$D_{50\%}$	72.61	±0.43	72.05	±0.38	71.85	±0.24	71.95	±0.37	0.001	<0.001	<0.001	>0.05	>0.05	>0.05
PTV-63 Gy														
$D_{2\%}$	70.12	±0.18	67.42	±0.60	66.93	±0.43	67.81	±0.63	<0.001	<0.001	<0.001	>0.05	>0.05	0.02
$D_{98\%}$	62.29	±0.45	62.33	±0.46	62.36	±0.37	62.31	±0.50	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
$D_{50\%}$	66.68	±0.48	65.07	±0.48	64.83	±0.19	64.98	±0.40	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
HI														
PTV-70	0.08	±0.01	0.059	±0.01	0.055	±0.01	0.054	±0.01	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
CI														
PTV-70	1.49	±0.02	1.076	±0.04	1.023	±0.04	0.982	±0.02	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
MU	476	±11	649	±112	459	±40	2181	±260	<0.001	0.01	<0.001	<0.001	<0.001	<0.001

*>0.05 statistically not significant; SD: Standart devision

found to be statistically more optimal than 3D-CRT and HI index of D-IMRT, IMAT and HT were found as 0.059, 0.055 and 0.054, respectively. The lowest HI was obtained by HT. The nearest result to the desired CI value was obtained with the IMAT, and the worst was with 3D-CRT. The maximum Monitor Unit (MU) value was with HT (2181±260) against LINAC-based modalities (3D-CRT, D-IMRT, IMAT). The minimum MU was with IMAT.

Evaluation of OAR Doses Parameters

The statistical comparison of the critical organ values [Dose Maximum (D_{max}), Mean (D_{mean}) and Dose volumes ($V_{Gy\%}$)] obtain by four different technique is given in Table 2.

The average D_{max} (Gy) values of the spinal cord were significantly lower with the 3D-CRT technique compared to D-IMRT, IMAT and HT techniques. Although there was no statistically significant difference between D-IMRT, IMAT and HT techniques, better values were provided with the D-IMRT technique.

The evaluation of D_{mean} (Gy), D_{max} (Gy) and volume-based criteria ($V_{35\%}$, $V_{50\%}$ and $V_{63\%}$) values for the right and left carotid arteries showed that three different intensity modalities were statistically significantly superior to 3D-CRT in dose sparing of the carotid arteries. No statistically significant differences were found between the IMRT techniques in the comparison of carotid artery dose values. The lowest D_{mean} (Gy) values were obtained with HT for bilateral carotid arteries.

The results found in the evaluation of D_{mean} (Gy) of submandibular glands were similar to carotid arteries. While IMRT techniques provide statistically significantly superiority compared to 3D-CRT, no statistically differences were found among the IMRT techniques. Looking at the average D_{mean} (Gy), IMAT yielded smaller dose values than D-IMRT and HT. When the thyroid gland doses were evaluated, the IMRT techniques exhibited statistically significantly superiority to 3D-CRT concerning the average D_{mean} (Gy), V30% and $V_{50\%}$. The average D_{mean} (Gy) dose values to the thyroid glands were 29.28, 20.16, 18.31 and 20.54 Gy for 3D-CRT, D-IMRT, IMAT and HT plans, respectively. There was no statistically significant difference among the IMRT techniques. Similar results were observed when volume-based criteria ($V_{30\%}$ and $V_{50\%}$) were examined. IMAT provided superior values compared to D-IMRT and HT for sparing the thyroid gland.

The average mean dose values of the Pharyngeal Constrictor Muscles (PCM) were 32.76, 30.38, 29.33, and 29.49 Gy for 3D-CRT, D-IMRT, IMAT and HT

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Table 2 OAR dose parameter values and their statistical results for the four treatment techniques (The values are the average of 15 patients' data)

Parameters	3D-CRT		D-IMRT		IMAT		HT		3D-CRT vs. D-IMRT	3D-CRT vs. IMAT	3D-CRT vs HT	D-IMRT vs. IMAT	D-IMRT vs. HT	IMAT vs. HT
	Mean	SD	Mean	SD	Mean	SD	Mean	SD						
Spinal Cord.														
D_{max} (Gy)	4.96	±2.07	20.66	±1.26	20.71	±0.73	20.75	±0.67	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
Right Carotid A.														
D_{max} (Gy)	70.66	±2.43	67.51	±2.08	67.31	±2.45	66.5	±0.87	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
D_{mean} (Gy)	49.94	±7.63	33.52	±4.30	31.21	±4.26	29.68	±4.34	<0.001	<0.001	<0,001	>0.05	>0.05	>0.05
V_{35}	73.49	±11.64	44.84	±10.06	44.53	±10.16	39.73	±9.56	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
V_{50}	69.76	±11.90	28.82	±13.29	26.07	±11.92	21.98	±9.48	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
V_{63}	62.47	±2.07	10.57	±2.67	7.12	±2.15	6.41	±2.35	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
Left Carotid A.														
D_{max} (Gy)	70.32	±1.98	67.54	±2.73	66.83	±2.25	66.6	±2.34	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
D_{mean} (Gy)	47.55	±8.2	32.37	±4.15	30.6	±4.11	28.43	±3.61	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
V_{35}	70.26	±12.12	46.06	±7.54	44.17	±7.72	38.44	±7.27	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
V_{50}	66.63	±12.37	28.33	±11.20	26.32	±11.7	20.64	±6.61	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
V_{63}	56.12	±13.09	9.43	±8.19	6.94	±4.75	6.53	±4.53	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05
Thyroid Gland														
D_{mean} (Gy)	29.28	±10.55	20.16	±10.59	18.31	±2.63	20.54	±2.72	0.015	0.006	0.019	>0.05	>0.05	>0.05
V_{30}	41.25	±4.28	27.09	±3.57	23.39	±3.79	27.93	±3.65	0.007	0.001	0.008	>0.05	>0.05	>0.05
V_{50}	32.06	±17.98	21.55	±15.29	18.36	±14.63	21.45	±15.01	0.019	0.003	0.01	>0.05	>0.05	>0.05
R.Submand. Gl.														
V_{5Gy}	35.78	±13.83	22.18	±8.60	18.27	±8.27	23.61	±10.39	0.005	<0.001	0.01	>0.05	>0.05	>0.05
L.Submand. Gl.														
V_{5Gy}	34.92	±15.65	22.56	±10.94	18.36	±9.97	23.09	±11.97	0.04	0.003	>0.05	>0.05	>0.05	>0.05
Pharyngeal C.M.														
V_{5Gy}	32.76	±1.53	30.38	±1.37	29.33	±1.44	29.49	±1.42	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Normal Tissue.														
V_{5Gy}	3.55	±0.53	8.35	±1.44	8.76	±1.55	9.1	±1.65	<0.001	<0.001	<0.001	>0.05	>0.05	>0.05

*>0.05 statistically not significant; SD: Standart devision

plans, respectively. Although there was no statistically significant difference to the results of the comparison of four techniques, the IMRT techniques have lower PCM (Gy) values compared to 3D-CRT. The lowest average values were reached by the IMAT technique.

When the volumes of normal tissue of receiving 5 Gy (V_{5Gy}) were evaluated, the average mean volumes to 5 Gy were 3.55, 8.35, 8.76 and 9.10 cc for 3D-CRT, D-IMRT, IMAT and HT, respectively. There were statistically significant differences among the IMRT techniques. The 3D-CRT plans compared to intensity-modulated techniques (D-IMRT, IMAT, HT) had a lower average V_{5Gy}.

Discussion

In the treatment of EGL cancer, high cure rates can be obtained with both surgery and radiotherapy. Although these treatment modalities offer similar treatment outcomes, many factors, such as the location of the tumor, the degree of the disease, the physician and patient's choice, are important in the choice of the modality.[19] With radiotherapy, the 5-year local control is at >90% and 80% for T1 and T2 disease, respectively.[8] The controversy continues between the modalities of surgery and radiotherapy in the treatment of EGL cancer, while the researches on the dose/fractions schemes, treatment contouring and techniques in the radiotherapy of EGL also continue. Several institutions use different dose/fraction schemes with different radiotherapy techniques. While EGL cancer can be treated using standard dose/fractions schemes daily 2 Gy dose total 66-70 Gy, there are studies on hypo-fraction schemes (2.25x28=63 Gy) and stereotactic dose fraction schemes (4.50x10=45 Gy), including our institute.[20,21] A few studies have indicated that local control is more optimal with higher doses per fraction, specifically when ≥2.25 Gy per fraction is used.[21] Radiation therapy has been delivered using lateral-opposed field, low energy photon fields that cover the whole larynx. The parallel-opposed fields (2D-RT and 3D-CRT) are used and given high survival rates in EGL radiotherapy before the advancement of radiotherapy techniques. Some authors have suggested that conventional lateral opposed fields RT for EGL cancer should be avoided because conventional lateral technique increases the dose of carotid arteries. IMRT based techniques decrease dose to the nearby critical structures of target volüme.[15]

In this work, we compared four different RT modalities for EGL cancer of 15 patients who were treated before. Our goal was to determine the capability of each modality, how to provide PTV coverage and evaluate the data of critical organ doses.

As shown in Table 1, our data suggest that three different IMRT techniques (D-IMRT, IMAT, HT) better than 3D-CRT concerning PTV doses, HI and CI. These IMRT techniques (D-IMRT, IMAT, HT) show similar results about PTV doses, CI and HI values. HT had much more MU than other techniques. High MU values are suspected to increase the risk of secondary cancer since the volume of normal tissue receiving low doses increased due to scattering and leakage caused by scattering leaf intervals in the IMRT techniques. The minimum MU values were achieved with the IMAT technique. A reduction in beam-on time may reduce radiation failure stemmed from organ and patient's movements.[16]

The stroke can be seen as the most important toxicity in EGL radiotherapy. Several studies show that irradiation of neck increases the paralysis incidence and cerebrovascular diseases.[10,11] Dorresteijn et al.[10] reported that ischemic paralysis risk after radiotherapy of the neck was 10 times greater than the general population under 60 years old. We determined that the carotid dose is lower in three IMRT techniques than a 3D-CRT technique for EGL cancer. Many studies have suggested the use of a dangerous dose-response value instead of a carotid artery threshold dose. Martin et al.[22] suggested that thickness intima-media was statistically significant for the dose ≥35-50 Gy. As shown in Table 2, in this work, the most suitable $V_{35\%}$ and $V_{50\%}$ values were obtained from three different IMRT techniques compared to 3D-CRT. These values in our study were determined higher than literature values. This may be due to the higher PTV volumes and higher treatment dose in our study.

In the study, IMAT plans had the lowest $V_{30\%}$, $V_{50\%}$ and the lowest mean dose for the thyroid glands. The IMRT techniques had lower thyroid gland doses than 3D-CRT. It has been shown that head and neck cancer radiotherapy causes side effects, such as hypothyroidism, hyperthyroidism, Graves' disease and thyroid malignancies on thyroid glands.[12] It has been reported that 25 to 50% of patients undergoing head and neck radiotherapy have some reduction in thyroid function and 6 to 15% have hypothyroidism.[23] The dose given to the thyroid gland has critical importance in EGL cancer radiotherapy. IMRT techniques may provide a clinical benefit in lowering the adverse effects of thyroid function because of the capability of delivering a lower dose to the thyroid than the 3D-CRT.[24]

Submandibular glands are another significant organ

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near PTV. When evaluated concerning dose-response, Murdoch-Kinch et al. show that submandibular gland–stimulated salivary function decreased remarkably after a mean dose of >40 Gy. In this work, the IMRT techniques were provided much more sparing than 3D-CRT in left-right submandibular glands with lower D_{mean} doses.

In conventional fractionation treatments, the tolerance dose for the spinal cord is about 50 Gy.[25] Spinal cord doses above 60 Gy can cause very serious side effects known as chronic progressive radiation myelopathy.[14,26] Our results indicate that 3D-CRT has lower spinal cord D_{max} doses than the IMRT techniques. Although there was no statistically significant difference among the 3 IMRT techniques, some values obtained by the D-IMRT technique were better. The technique that keeps the spinal cord doses at the lowest level is the 3D-CRT. The use of the 3D-CRT technique can be considered in cases for whom a low dose of the spinal cord is desired in re-irradiation.

Radiotherapy for head and neck cancer may cause increased side-effects, including dysphagia and aspiration. Feng et al.,[27] in a study of the pharyngeal constrictors of the average dose (D_{mean}) <60 Gy, if the limit is below this to no patients have suggested that no aspiration. Based on the videofluoroscopy findings, Eisbruch et al.[28] suggested that the average dose of PCM was significantly associated with the occurrence of late dysphagia and aspiration at doses >50 Gy. The average mean dose values to the PCM were 32.76, 30.38, 29.33, and 29.49 Gy for 3D-CRT, D-IMRT, IMAT and HT plans, respectively. Although there was no statistically significant difference to the results of comparison of 4 techniques, D-IMRT, IMAT and HT techniques have lower PCM D_{mean} (Gy) values compared to 3D-CRT.

Low-dose on healthy tissue outside the treatment area is particularly important for radiation-induced secondary cancers. An important concern for IMRT techniques is that low doses of radiation increase the scattering over normal tissue volume and potentially increase the risk of secondary cancer. It is estimated that the incidence of secondary cancers can be almost doubled with IMRT techniques compared to conventional techniques.[16] When the volumes of normal tissue of receiving 5 Gy (V_{5Gy}) were evaluated, 3D-CRT plans compared to the IMRT techniques had a lower average of V_{5Gy}. Although no statistically significant differences were found among the IMRT techniques, Helical Tomotherapy (HT) plans had more V_{5Gy} than other IMRT techniques.

When using a 63 Gy treatment dose by Ekici et al.,[17] HT treatment planning has been shown to be the most effective method for lowest right carotid, left carotid, submandibular and thyroid doses. In our study, where we prescript a 70 Gy dose to PTV, we found that HT treatment planning was the most effective method for the lowest right carotid, left parotid, submandibular and thyroid doses. On the other hand, we found that IMAT planning provided the lowest right and left submandibular (V_{5Gy}), thyroid (V_{5Gy}) and PCM (V_{5Gy}) doses. The results of our study suggest that HT and IMAT planning are the most appropriate methods to increase the treatment dose from 63 Gy to 70 Gy.

Conclusion

The findings obtained in this study suggest that it is possible to administer a treatment dose of 70 Gy to the PTV of EGL with all planning techniques used in this work. However, it is observed that there are advantages or disadvantages among each other. Based on the dosimetric findings in this study, D-IMRT, IMAT and HT treatment plans that were created using the SIB technique were superior to the 3D-CRT plans created using conventional boost technique concerning the PTV (coverage), CI and HI values of the treatment volumes. With the 3D-CRT technique, it is difficult to achieve sharp dose drops in treatment volumes with overlapping PTV. However, this technique that keeps the spinal cord doses at the lowest level is. The use of the 3D-CRT technique can be considered in organs where low doses preferred to where complications of re-radiotherapy should be taken account in advance, such as spinal cord. Three different IMRT techniques provided superiority with less variation among themselves compared to 3D-CRT plans concerning carotid artery, thyroid gland, submandibular glands and PCM doses. IMAT and 3D-CRT techniques yielded minimum MU values compared to other techniques. On the other hand, in the case of normal tissue doses, which are important for secondary cancers, the 3D-CRT technique is superior to the IMRT techniques.

We recommend to increase the treatment dose from 63 Gy to 70 Gy in the radiotherapy of EGL cancer but to select the technique according to the patient's condition. Patient age, treatment volumes, and critical organ protection should be taken into consideration for patient-specific decision-making.

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Ethics Committee Approval: This study was conducted in accordance with local ethical rules. (Date: 01.12.2017, Registration number: 2017/1399)

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