

## Original Research Article

# Comparison of dosimetry in head and neck cancer patients treated with intensity modulated radiation therapy and helical tomotherapy

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### ABSTRACT

**Background:** This study was conducted to compare dosimetric parameters and dose to specific organs at risk (spinal cord and parotids) between intensity modulated radiation therapy (IMRT) and helical tomotherapy (HT) in head and neck squamous cell carcinomas (HNSCC).

**Methods:** Thirty patients with histologically proven HNSCC were treated with chemo radiotherapy, to a dose of 60-70 Gray in 30-35 fractions. This study consists of two arms; IMRT arm and tomotherapy arm. Fifteen consecutive patients treated under IMRT and 15 patients were treated under helical tomotherapy, along with concurrent chemotherapy. PTV<sub>1</sub> encompasses low risk planning target volume (PTV) which receives 50 Gy; PTV<sub>2</sub> encompasses intermediate risk PTV which receives 54-60 Gy and PTV<sub>3</sub> encompasses high risk PTV which receives 66-70 Gy. After completion of planning, dose to the organs at risk (OARs) and targets, homogeneity index and conformity index were evaluated, and tabulated.

**Results:** On evaluation of plans we found that V95% in PTV<sub>1</sub>, PTV<sub>2</sub> and PTV<sub>3</sub> were 91.82%, 96.85% and 90.67% respectively for IMRT and 99.25%, 99.68% and 99.73% respectively for tomotherapy. For PTV<sub>3</sub>, V110% was 0.11% for IMRT and 0.01% for tomotherapy. Homogeneity index in IMRT arm was 0.285 and it was 0.206 in tomotherapy arm. Conformity index was found to be 1.04 for IMRT plans and 1.06 for tomotherapy plans. When mean dose to contra lateral parotids was evaluated, it was 26.91 Gy in IMRT arm and 25.97 Gy in tomotherapy arm. Max dose to spinal cord was better in tomotherapy (43.07 Gy in IMRT and 34.41 Gy in tomotherapy).

**Conclusions:** There was statistically significant reduction in spinal cord maximum dose and point doses in tomotherapy plans compared to IMRT plans. The decrease in spinal cord dose can increase the tolerance reserve which can be useful in dose escalation or re-irradiation if required. There was also decrease in contra lateral parotid doses (not statistically significant). There was significant improvement in V95% in tomotherapy arm compared to IMRT arm, indicating the significantly superior coverage of target volumes in helical tomotherapy plans compared to IMRT plans. V110% (hot spots) inside the target was very minimal in tomotherapy arm compared to IMRT arm. Conformity index, homogeneity index between two arms were comparable.

**Keywords:** Conformity index, Head and neck carcinoma, Homogeneity index, IMRT, OAR, PTV, Tomotherapy

### INTRODUCTION

One of the greatest challenge for radiation therapy or any cancer therapy is to attain the highest probability of cure

with the least morbidity. Theoretically spoken, the simplest way is to increase this therapeutic ratio with ionizing radiation is to encompass all cancer cells with sufficient doses of radiation during each fraction, while simultaneously sparing surrounding normal tissues.<sup>1</sup>

Radiotherapy has undergone a drastic change in terms of techniques used and as a result organ sparing became possible.<sup>2,3</sup> Radiotherapy for HNSCC in many sub sites, has shifted from three-dimensional conformal radiotherapy (3D-CRT) to intensity-modulated radiotherapy (IMRT), resulting in highly conformal and more homogenous dose administration to the target volumes and better sparing of the organs at risk (OARs). IMRT has the capability to generate steep dose gradients, improving PTV conformity and normal tissue complication probability (NTCP) by sparing OARs thereby leading to an improved therapeutic index.<sup>4-8</sup>

Going a step further, image guided radiotherapy (IGRT) was developed and this technique makes frequent imaging during treatment which helps in making treatment decisions based on these images.<sup>9</sup> IGRT takes into account the tumor motion and thereby helps in decreasing CTV to PTV margin which in turn facilitates sparing of critical organs at risk.<sup>9,10</sup>

Different systems are available for IGRT implementation. One of it being tomotherapy.<sup>11</sup> Computed tomography (CT) component of helical tomotherapy device allows on-line megavoltage CT imaging, which permits verification of patient positioning prior to and during treatment, reconstruction of delivered radiation dose, and target tumor/organ registration to account for internal motion and tumor shape or volume changes.<sup>12</sup> Patients with very long targets and proximity of organ at risk are better treated with this technique. The image guidance allows the safe application of highly conformal treatment plans with steep dose gradients.<sup>13</sup>

With this background we proposed to conduct a study which compared dose to specific organs at risk and dosimetric parameters in 15 consecutive head and neck cancer patients treated with linac based IMRT and 15 consecutive head and neck cancer patients treated with helical tomotherapy.

### **Aims and objectives**

To compare dose to specific organs at risk (spinal cord and parotids) and dosimetric parameters between helical tomotherapy and IMRT in head and neck cancer patients.

## **METHODS**

### **Study design and study population**

The study was a prospective, single institute, observational, double arm, comparative study. This study was conducted in a tertiary cancer care hospital- Health Care Global Enterprises Ltd. (HCG hospital) in Bangalore, Karnataka, India, between the time period of June 2016 to May 2017.

Patients diagnosed with head and neck carcinoma and found to have locally advanced disease status and who

were suitable for radical radiotherapy with IMRT or tomotherapy, satisfying inclusion and exclusion criteria and those who consented for study were recruited.

### **Inclusion criteria**

Inclusion criteria were patients with histologically proven squamous cell carcinoma of head and neck (oral cavity, oropharynx, hypopharynx, nasopharynx, supraglottic larynx) with AJCC 7<sup>th</sup> edition TNM staging T3/T4 with N0, any N+, M0, patients suitable for concurrent chemo radiation, with age above 18 years and below 70 years, ECOG 1 and 2; patients with normal renal function tests and patients with or without surgery were considered for the study.

### **Exclusion criteria**

Exclusion criteria were patients not consenting for the study; patients with prior radiotherapy to head and neck; patients with evidence of distant metastasis, simultaneous secondary malignancy, recurrent disease or those who have received neo-adjuvant chemotherapy and female patients who are pregnant. Patients with thyroid carcinoma, vocal cord carcinoma, paranasal sinus carcinoma were also excluded from the study.

### **Sample size calculation**

Sample size was calculated using hypothesis testing of two means formula. As per Murthy et al, considering parotid mean dose, standard deviation in tomotherapy group was 2.75, and that of IMRT group was 14.98, mean difference was 12.22. Alpha error was 5%, power of the study was 80%. As per the formula, minimum sample required is 12 per arm.<sup>14</sup> Our study had two arms- standard IMRT arm and tomotherapy arm. Our study population was formed by 15 consecutive head and neck cancer patients in each arm.

*Formula:*

$$n = \frac{2s_p^2 \left[ z_{1-\frac{\alpha}{2}} + z_{1-\beta} \right]}{\mu_d^2}$$

Where,  $s_p^2 = \frac{s_1^2 + s_2^2}{2}$

$s_1^2$ : Standard deviation in the first group

$s_2^2$ : Standard deviation in the second group

$\mu_d^2$ : Mean difference between the samples

$\alpha$ : Significance level

$1-\beta$ : Power

$$n = [2 \times 108.42 (1.96 + 6.30)] / (12.22)^2;$$

$$n = 12$$

### Methodology

A complete clinical evaluation, required blood and imaging studies were carried out in all patients. A complete informed consent barring local language barriers was taken for immobilization device preparation, imaging, treatment planning and radiotherapy. Immobilization was done with patients positioned supine with head in neutral position with standard neck rest. Treatment planning computed tomography (CT) simulation performed with wide bore (80 cm) SEIMEN® CT scanner. A CT-scan of head and neck taken with 2.5 mm slice thickness from vertex down through the clavicles up to the carina using a contrast sequence. These images were transferred to digital imaging and communication (DICOM) format and sent to ECLIPSE® planning system (Version 11) (Varian medical systems)®.

The gross tumor volume (GTV), clinical target volume (CTV), and planning target volumes (PTV) were delineated on axial computed tomography (CT) images following International Commission on Radiation Units and Measurements (ICRU) report number 50 and 62.<sup>15</sup> Low risk target volume (low risk subclinical disease) were named as PTV<sub>1</sub>, intermediate risk target volumes (intermediate risk subclinical disease) were named as PTV<sub>2</sub>, and high risk volumes (gross disease and involved nodes) were named as PTV<sub>3</sub>. Organs at risk in head and neck malignancies like brainstem, spinal cord, parotid glands (bilateral), submandibular glands, cochlea (bilateral), oral cavity, mandible and temporomandibular joint, and brain (in cases of carcinoma nasopharynx), optic apparatus (in cases of carcinoma nasopharynx, nasal cavity) like eye ball, lens, optic chiasma and retina were contoured as per standard institutional protocol.

Gross disease and involved nodes (PTV<sub>3</sub>) were prescribed 66-70 Gy in 33-35 fractions, intermediate risk PTV (PTV<sub>2</sub>) was prescribed 54-60 Gy, and low risk PTV (PTV<sub>1</sub>) was prescribed 50 Gy. Treatment was delivered in conventional 2 Gy/fraction, with daily fractionation, 5 fractions per week over 7 weeks. Patients in IMRT arm were planned accordingly with IMRT using an inverse planning algorithm with step and shoot technique on Eclipse® planning system (Version 11), for treatment on Siemens Artiste® linear accelerator (refer Figure 1) with MLC- 160 leaves, each with a width of 5 mm at the isocentre. Treatment was delivered using 6 MV photons. In the final plan, the optimal beam arrangement that delivers optimal tumor coverage and normal tissue sparing were selected after comparisons of various beam arrangements, which depend on the size and location of the tumor. All dose calculations and IMRT fluence optimizations were performed using the Varian Eclipse® treatment planning system. Dose constraints as advised by QUANTEC® was followed for the OAR structures during

planning. Prior to delivery, a fluence map check and other quality assurance checks was ensured before starting the treatment.



**Figure 1: Siemens Artiste linear accelerator.**

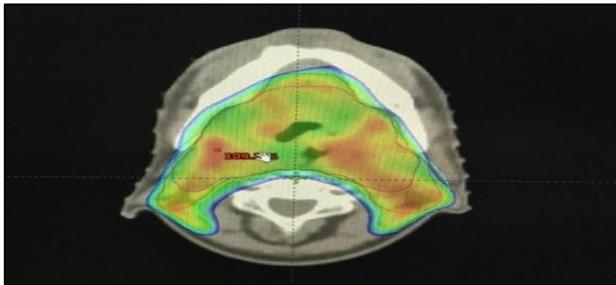


**Figure 2: Helical tomography machine- Accuray HAD.**

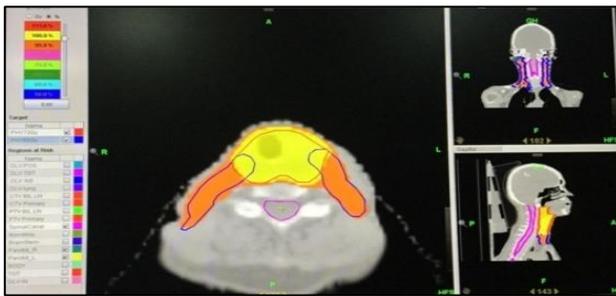
Patients in tomotherapy arm were planned using an inverse planning algorithm using dynamic delivery technique on Volo® treatment planning system version 5.1 for treatment on Accuray HAD® machine (refer Figure 2), with 64 binary MLCs of 0.625 cm each. All planning were done with plan field width of 2.5 cm, modulation factor of 2, and pitch depending on size of tumor. Treatment was delivered using 6 MV photons.

Each plan was evaluated both quantitatively and qualitatively. The plans were evaluated with the help of dose volume histogram (DVH). Quantitative evaluation involved an assessment of dose to GTV, CTV, PTV (PTV<sub>1</sub>, PTV<sub>2</sub>, PTV<sub>3</sub>), and doses received by the normal tissues. Qualitative evaluation involved a slice-by-slice evaluation of the dose conformity, and of all hot and cold spots. Mean, dose to 2%, 50% and 98% of PTV (i.e., D2%, D50% and D98% respectively) and volume of PTV receiving 95% of prescription dose (i.e., V95%) were assessed for all planning target volumes. Volume of PTV receiving 110% of prescription dose (i.e., V110%) was assessed for PTV<sub>3</sub>. Hot spot was analysed by comparing V110%. Parotid sparing was compared using mean doses,

volume of parotid receiving 30 Gy and 20 Gy (V30 Gy and V20 Gy) in both ipsilateral and contralateral parotids, and spinal cord sparing was compared using maximum and point doses (D0.1 cc, D0.5 cc, i.e., dose to 0.1 cc and 0.5 cc of OAR). Conformity index (CI) and homogeneity index (HI) were also assessed. Homogeneity index was calculated using the formula  $[D2\% - D98\%] / D50\%$ . Smaller values of HI correspond to a more homogeneous dose distribution in the PTV. A value of zero corresponds to absolute homogeneity of dose.<sup>16</sup>



**Figure 3: Example of dose distribution in an IMRT plan.**



**Figure 4: Example of dose distribution in a tomography plan.**

Concurrent chemotherapy administered weekly with Inj. Cisplatin 40 mg/m<sup>2</sup>. Injection carboplatin was used in

patients with compromised renal parameters (e.g. higher creatinine clearance) and/or where cisplatin was not expected to be tolerated. Dose of carboplatin calculated by area under curve (AUC) based on glomerular filtration rate (AUC-2).

**Ethical approval**

Scientific review committee and Central ethics committee approvals were taken before starting the study. A complete informed consent barring local language barriers was taken from each patient.

**Statistical analysis**

All study data were manually entered into an electronic spread sheet. Data was analysed using SPSS-IBM® Software version 23 for Windows. The descriptive data statistics- frequency analysis, percentage analysis were used for categorical variables and the mean and standard deviation were used for continuous variables. Association between two variables was tested using Chi-square test. The results of tomotherapy and IMRT compared with the two sided Mann-Whitney U test. The threshold for statistical significance was  $p < 0.05$ .

**RESULTS**

In our study, patients of various ages ranging from 33-70 years were taken. Mean age being 48.67 years (range 33-70 years) in IMRT arm and 56.93 years (range 35-70 years) in tomotherapy arm. Male population was predominant in our study [IMRT- 11/15 (73.3%), tomotherapy- 14/15 (93.3%)]. All the sub sites of head and neck (hypopharynx, oral cavity and oropharynx) were included in our study, with maximum cases being oral cavity (IMRT- 11/15, tomotherapy 11/15). Sub sites were matched in both arms. All the patients included were locally advanced tumors and majority were of stage IVA.

**Table 1: Patient and tumor characteristics and radiation dose received in IMRT and tomotherapy arms.**

		IMRT		Tomotherapy	
		Number	Percentage	Number	Percentage
Age of the patients	31-40 years	5	33.3	1	6.7
	41-50 years	4	26.7	3	20
	51-60 years	3	20	5	33.3
	61-70 years	3	20	6	40
	Total	15	100	15	100
	Mean±SD	48.67±11.94		56.93±10.65	
Sex of the patients	Male	11	73.3	14	93.3
	Female	4	26.7	1	6.7
Subsite of disease	Hypopharynx	3	20	3	20
	Oral cavity	11	73.3	11	73.3
	Oropharynx	1	6.7	1	6.7
Group stage	III	2	13.33	7	46.66
	IVA	13	86.66	8	53.33

Continued.

		IMRT		Tomotherapy	
		Number	Percentage	Number	Percentage
Radiation dose	60 Gy	3	20	4	26.7
	66 Gy	7	46.7	9	60
	70 Gy	5	33.3	2	13.3

Table 2: Total number of cases in different stages in each sub site.

	IMRT			Tomotherapy		
	Total cases	Stage III	Stage IVA	Total cases	Stage III	Stage IVA
Hypopharynx	3	0	3	3	1	2
Oral cavity	11	2	9	11	5	6
Oropharynx	1	0	1	1	1	0

Majority of patients used cisplatin (IMRT- 13/15 and 12/15) for concurrent chemotherapy and the rest had carboplatin. Prescription dose ranged from 60-70 Gy in 30-35 fractions, with majority of patients having prescription dose of 66 Gy [IMRT- 7/15 (46.7%) and tomotherapy 9/15 (60%)]. Overall treatment time for majority of patients was between 50-56 days. All the patients received bilateral neck irradiation. Patient and tumor characteristics are detailed in Table 1 and Table 2.

**Dosimetric analysis**

In PTV<sub>1</sub> (low risk PTV), V95% increased from 91.82% in IMRT to 99.25% in tomotherapy indicating significantly better coverage in tomotherapy (p=0.018). There was no statistically significant difference in D2%, D98%, D50% and mean doses between two groups (Table 3).

In PTV<sub>2</sub> (intermediate risk PTV), V95% increased from 96.85% in IMRT to 99.68% in tomotherapy showing improved coverage in tomotherapy (p=0.031). D2% (dose maximum according to ICRU 83) was 71.61 Gy in IMRT and 68.90 Gy in tomotherapy (p=0.033). There was no statistically significant difference in D98%, D50% and mean doses between two groups (Table 4).

In PTV<sub>3</sub> (high risk PTV), V95% increased from 90.67% in IMRT to 99.73% in tomotherapy representing improved target coverage in tomotherapy (p=0.034). V110% inside the target decreased from 0.11% in IMRT to 0.01% in tomotherapy (p=0.021), showing less hot spots within the target in tomotherapy plans than IMRT plans. There was no statistically significant difference in D2%, D98%, D50% and mean doses between two groups (Table 5).

Table 3: Dosimetric evaluation of PTV<sub>1</sub> in IMRT and tomotherapy plans.

PTV <sub>1</sub>	IMRT		Tomotherapy		P value
	Mean±SD	Median (Q3-Q1)	Mean±SD	Median (Q3-Q1)	
Mean	60.18 Gy±2.45	60.61 Gy (62.08-58.45)	60.29Gy ± 2.78	59.51Gy (62.25-58.31)	0.983
D2%	67.05 Gy±3.08	67.79 Gy (69.69-64.3)	65.94Gy ± 4.47	67.35Gy (68.29-62.0)	0.407
D98%	47.49 Gy±11.41	49.99 Gy (56.12-45.72)	51.72Gy ± 2.53	51.38Gy (53.58-50.35)	0.494
D50%	60.33 Gy±3.48	60.39 Gy (62.22-59.54)	61.14Gy ± 5.11	61.79Gy (65.2-58.06)	0.272
V95%	91.82%±22.85	99.04% (99.73-94.9)	99.25% ± 0.899	99.79% (99.93-98.33)	0.018*

where Q1- first quartile; Q3- third quartile; SD- standard deviation; D2%, D50% and D98%- dose to 2%, 50% and 98% of PTV respectively; V95%- volume of PTV receiving 95% of prescription dose; \*- statistical significance

Table 4: Dosimetric evaluation of PTV<sub>2</sub> in IMRT and tomotherapy plans.

PTV <sub>2</sub>	IMRT		Tomotherapy		P value
	Mean±SD	Median (Q3-Q1)	Mean±SD	Median (Q3-Q1)	
Mean	67.38 Gy±1.35	67.12 Gy (68.20-66.64)	66.04 Gy±2.25	66.24 Gy (67.09-65.68)	0.131
D2%	71.61 Gy±2.60	70.31 Gy (74.20-69.84)	68.90 Gy±3.39	68.13 Gy (71.10-67.37)	0.033*
D98%	61.81 Gy±1.07	62.25 Gy (62.64-60.77)	60.52 Gy±3.55	61.28 Gy (62.77-60.06)	0.424
D50%	65.82 Gy±5.66	67.43 Gy (68.32-66.07)	66.63 Gy±2.23	66.69 Gy (67.57-66.31)	0.374
V95%	96.85%±7.67	99.78% (99.96-98.42)	99.68%±0.95	99.98% (100-99.97)	0.031*

where Q1- first quartile; Q3- third quartile; SD- standard deviation; D2%, D50% and D98%- dose to 2%, 50% and 98% of PTV respectively; V95%- volume of PTV receiving 95% of prescription dose; \*- statistical significance

**Table 5: Dosimetric evaluation of PTV<sub>3</sub> in IMRT and tomotherapy plans.**

PTV <sub>3</sub> Parameter	IMRT		Tomotherapy		P value
	Mean±SD	Median (Q3-Q1)	Mean±SD	Median (Q3-Q1)	
Mean	67.19 Gy±14.47	67.96 Gy (69.75-63.39)	67.08 Gy±4.14	67 Gy (71.62-61.82)	0.541
D2%	70.80 Gy±3.95	70.39 Gy (75.01-67.49)	68.49 Gy±4.42	67.88 Gy (73.35-63.14)	0.150
D98%	56.99 Gy±14.47	64.29 Gy (67.48-46.77)	64.95 Gy±3.77	65.9 Gy (67.78-59.97)	0.206
D50%	66.50 Gy±6.34	68.28 Gy (72.4-62.8)	67.17 Gy±4.20	67 Gy (71.83-61.97)	0.541
V95%	90.67%±23.69	99.18% (99.97-92.20)	99.73%±0.38	99.97% (100-99.47)	0.034*
V110%	0.11%±0.215	0% (0.1-0)	0.01%±0.039	0% (0-0)	0.021*

where Q1- first quartile; Q3- third quartile; SD- standard deviation; D2%, D50% and D98%- dose to 2%, 50% and 98% of PTV respectively; V95%- volume of PTV receiving 95% of prescription dose; V110%- volume of PTV receiving 110% of prescription dose; \*- statistical significance

**Table 6: Homogeneity index and conformity index in IMRT and tomotherapy plans.**

Parameters	IMRT			Tomotherapy			Mean difference	P value
	Mean±SD	Range		Mean±SD	Range			
		Max.	Min.		Max.	Min.		
Homogeneity index	0.285±0.22	0.645	0.059	0.206±0.09	0.29	0.06	0.079	0.395
Conformity index	1.04±0.23	1.23	0.39	1.06±0.32	1.07	0.22	0.287	0.845

**Table 7: Dose to ipsilateral parotids in IMRT and tomotherapy plans.**

Structure	Parameter	IMRT	Tomotherapy	Mean difference	P value
		Mean±SD	Mean±SD		
I/L parotid	I/L mean	35.50 Gy±10.61	42.13 Gy±16.03	6.63	0.277
	I/LV30 Gy	68.42%±22.50	69.53%±27.01	1.11	0.916
	I/LV20 Gy	78.89%±19.59	76.34%±21.76	2.55	0.983

Where SD- standard deviation

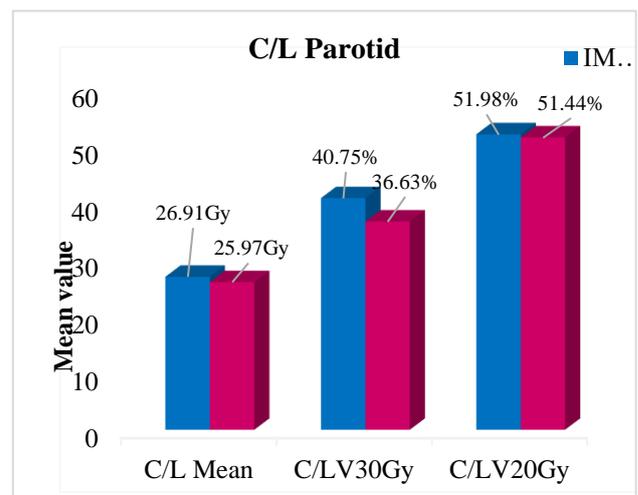
Homogeneity index (HI) for IMRT was 0.285 and for tomotherapy plans it was 0.206. The conformity index (CI) for IMRT was 1.04 and for tomotherapy plans it was 1.06. We did not find any statistical significance for HI and CI between two groups (p value- 0.395 and 0.845 respectively for homogeneity index and conformity index) (Table 6).

**Dose distribution to the organs at risk**

Ipsilateral parotid mean dose was 35.50 Gy in IMRT plans and that of tomotherapy plans was 42.13 Gy. V30 Gy was 68.42% in IMRT plans and 69.53% in tomotherapy. Similarly 78.89% of parotid in IMRT plans was receiving 20 Gy (V20 Gy) and 76.34% of parotid in tomotherapy plans was receiving 20 Gy (V20 Gy). In ipsilateral parotids, there was no statistically significant difference in mean dose, V30 Gy and V20 Gy between two groups (Table 7).

In contra lateral parotid, mean dose reduced from 26.91 Gy in IMRT to 25.97 Gy in tomotherapy. Though there was only 1 Gy difference, literature says it has clinical significance. Contra lateral parotid V30 Gy was 40.75%

in IMRT and 36.63% in tomotherapy. V20 Gy was 51.98% in IMRT and 51.44% in tomotherapy. There was no statistically significant difference between two groups (Table 8).



**Figure 1: The dose to contra lateral (C/L) parotids in IMRT and Tomotherapy plans.**

**Table 8: Dose to contralateral parotids in IMRT and tomotherapy plans.**

Structure	Parameter	IMRT	Tomotherapy	Mean difference	P value
		Mean±SD	Mean±SD		
C/L parotid	C/L mean	26.91 Gy±3.80	25.97 Gy±3.83	0.94	0.494
	C/LV30 Gy	40.75%±7.79	36.63%±9.02	4.12	0.221
	C/LV20 Gy	51.98%±11.49	51.44%±8.26	0.54	0.694

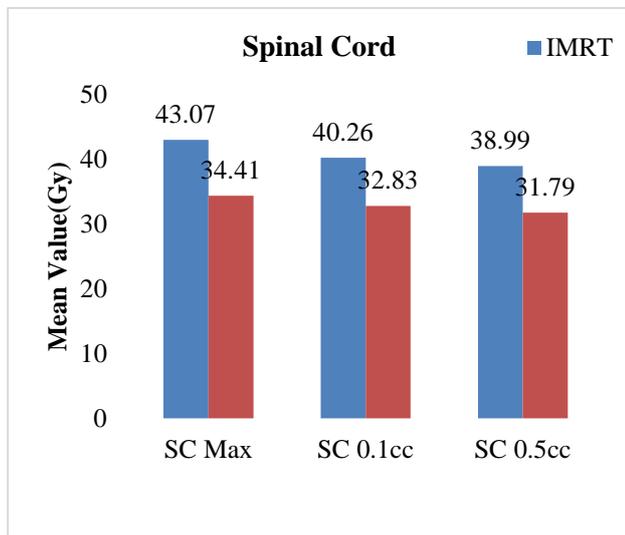
Where SD- standard deviation

**Table 9: Dose to spinal cord in IMRT and tomotherapy plans.**

Structure	Parameter	IMRT	Tomotherapy	Mean difference	P value
		Mean±SD	Mean±SD		
Spinal cord	SC max	43.07 Gy±3.83	34.41 Gy±4.88	8.66	P<0.001***
	SC 0.1 cc	40.26 Gy±3.21	32.83 Gy±5.06	7.43	P<0.001***
	SC 0.5 cc	38.99 Gy±2.87	31.79 Gy±5.26	7.29	P<0.001***

where SD- standard deviation; SC- spinal cord; \*- statistical significance

Spinal cord max dose reduced from 43.07 Gy in IMRT arm to 34.41 Gy in tomotherapy arm. 0.1 cc of spinal cord received 40.26 Gy in IMRT arm and 32.83 Gy in tomotherapy arm. 0.5 cc of spinal cord received 38.99 Gy in IMRT arm and 31.79 Gy in tomotherapy arm and there was statistically significant (p<0.001) difference between two arms in our study. The decrease in spinal cord dose can increase the “tolerance reserve” which can be useful in dose escalation or re-irradiation, if required (Table 9).



**Figure 2: The dose to spinal cord in IMRT and Tomotherapy plans (SC - spinal cord).**

Figure 2 shows significant reduction in spinal cord max and point doses in tomotherapy group than IMRT group.

**DISCUSSION**

In our present study, dosimetric outcome of the IMRT and helical tomotherapy plans were compared quantitatively and qualitatively in terms of target coverage, dose homogeneity and OAR sparing. Helical

tomotherapy plans showed superior target coverage, significant spinal cord sparing and minimal hotspots.

Murthy et al conducted a trial in which 12 patients of head and neck cancer who were previously treated with IMRT were replanned on helical tomotherapy using same CT database.<sup>14</sup> Helical tomotherapy plans showed improvement in target coverage and homogeneity, and less organ at risk doses compared to step and shoot IMRT. In another study by Fiorino et al, compared LINAC IMRT technique against two different HT planning approaches in five patients with advanced HNSCC.<sup>17</sup> In first approach (Tomo-a), similar constraints used for LINAC based IMRT were used; while in the second approach (Tomo-b), parotids and mandible were tried to be spared while maintaining similar PTV coverage and spinal cord D<sub>max</sub> in both the arms.

In Murthy et al study, the mean V95% did not show any significant difference between IMRT and HT.<sup>14</sup> In their study, for PTV 66, the mean V99% was improved by 14.65% in helical tomotherapy than IMRT (p=0.02). In contrary, Fiorino et al study, V95% increased from 89.6% (IMRT) to 97.3% (Tomo-a) and 96.2% (Tomo-b) in PTV<sub>1</sub>, showing better coverage (p value- 0.04).<sup>17</sup> Similarly, in our study, V95% was statistically significant in all PTVs (p value- 0.018, 0.031 and 0.034 respectively for PTV<sub>1</sub>, PTV<sub>2</sub> and PTV<sub>3</sub>), indicating the significant superior coverage of target volumes in helical tomotherapy plans compared to IMRT plans. Studies by Murthy et al and Fiorino et al, found a decrease in hot spots inside the target (V107%) in tomotherapy plans.<sup>14,17</sup> Murthy et al, study showed decrease in V107% in IMRT than tomotherapy (2.4% versus 1.21%). But it was not statistically significant. On the other hand in Fiorino et al study, V107% between tomotherapy and IMRT was statistically significant (0% versus 2.2%).<sup>17</sup> Similarly in our study also, there was considerable reduction in hot spots in tomotherapy plans. In our study, hot spots were analyzed considering V110%. It was 0.11% for IMRT

and 0.01% for tomotherapy plans ( $p=0.021$ ), indicating significant reduction in hot spots inside the target in tomotherapy plans.

Above 2 studies also showed substantial reduction in mean parotid dose and spinal cord doses in tomotherapy plans compared to IMRT.<sup>14,17</sup> In Murthy et al study, in tomotherapy plans there was reduction of about 18.28 Gy in ipsilateral parotids ( $p=0.003$ ) and about 12.66 Gy in contra lateral parotids ( $P=0003$ ) compared to IMRT.<sup>14</sup> Likewise in Fiorino et al study also, the mean parotid dose decreased from 26.3 Gy in IMRT to 24.5 Gy (Tomo-a) and 20.8 Gy (Tomo-b) ( $p=0.01$ ).<sup>17</sup> On the contrary, in our study there was no statistically significant decrease in ipsilateral mean parotid doses in tomotherapy plans compared to IMRT plans. But there was slight decrease in mean dose of contra lateral parotids in tomotherapy plans than IMRT plans (26.91 Gy in IMRT versus 25.97 Gy in tomotherapy). The difference did not show statistical significance ( $p=0.494$ ), although it may be clinically relevant. Though there was only 1 to 2 Gy difference in parotid mean doses, Blanco et al in their study reported that there is exponential loss of about 5% of salivary function for every added Gray in mean dose.<sup>18</sup> There was a recovery of parotid function that occurs by 2 years and recovery of salivary gland function rates decreases by 5% for every one gray increase in mean dose.

In Fiorino et al study, there was significant reduction in spinal cord max dose in tomotherapy plans (26.4 Gy Tomo-a and 24.5 Gy Tomo-b) compared to IMRT (31.6 Gy) ( $p=0.04$ ).<sup>17</sup> In the same way, Murthy et al study also showed reduction in the max dose of spinal cord from 43.37 Gy (IMRT) to 31.30 Gy (tomotherapy) ( $p=0.002$ ).<sup>14</sup> Similarly, in our study there was reduction in spinal cord max and point doses in tomotherapy group than IMRT group. Spinal cord max dose reduced from 43.07 Gy in IMRT arm to 34.41 Gy in tomotherapy arm. 0.1 cc of spinal cord received 40.26 Gy in IMRT arm and 32.83 Gy in tomotherapy arm. 0.5 cc of spinal cord received 38.99 Gy in IMRT arm and 31.79 Gy in tomotherapy arm and there was statistically significant ( $p<0.001$ ) difference between two arms in our study. The decrease in spinal cord dose can increase the “tolerance reserve” which can be useful in dose escalation or re-irradiation, if required. Tomotherapy plans could achieve a higher degree of sparing for critical organs abutting the target, due to its capability of producing sharper dose gradients.

Papiu et al, in 2019 evaluated the efficiency of tomotherapy HD system on treatment of different cancer localization. In their study, in a locally advanced case of nasopharynx, primary tumor received 70 Gy in 35 fractions and bilateral (B/L) neck received 60 Gy in 30 fractions. Plans were evaluated for HI, mean and max doses for OAR. The spinal cord max dose was found to be 31.03 Gy in their study. In left parotid,  $D_{mean}$  was 23.46 Gy, D33% was 24.15 Gy and D66% was found to be 17.85Gy. In right parotid,  $D_{mean}$  was 24.57 Gy, D33%

was 26.44 Gy and D66% was found to be 17.26 Gy. Their study showed high conformity and homogeneity of doses in the target. OAR's received much lower values than recommended by RTOG.<sup>19</sup>

In a study by Yu et al, 15 patients of nasopharyngeal carcinoma (NPC) were chosen for retrospective analysis and replanned for helical tomotherapy (HT), volume-modulated arc therapy (VMAT), and fixed field IMRT (FF-IMRT). Their study results showed that HT and VMAT possessed better sparing of OAR's compared to conventional FF-IMRT. HT plans reduced the maximum doses of most organs such as brainstem, spinal cord, and optic nerves in NPC and significantly reduced the volume of high dose region.<sup>20</sup> Study by Liu et al, in the treatment of locally advanced NPC by HT showed that HT can achieve promising disease control and survival in the treatment of locally advanced NPC patients with mild acute and late toxicity profiles.<sup>21</sup>

Limitation of our study was smaller sample size and possible interpersonal variation in contouring.

## CONCLUSION

From the present study, we conclude that there was an improvement in spinal cord maximum dose (IMRT-43.07 Gy versus TOMO- 34.41 Gy,  $p$  value =0.001) and point doses in helical tomotherapy plans compared to IMRT plans, at the same time maintaining the contra lateral parotid doses to the acceptable level. The decrease in spinal cord dose can increase the “tolerance reserve” which can be useful in dose escalation or re-irradiation if required. There was slight decrease in contra lateral parotid doses which is not statistically significant. However literature shows that a drop as low as 1 Gy mean dose can cause reduction in incidence of xerostomia. There was significant improvement in V95% in helical tomotherapy arm compared to IMRT arm indicating the superior target coverage in tomotherapy. V110% (hot spots) inside the target was very minimal in tomotherapy arm compared to IMRT arm. Conformity indices and homogeneity indices between two arms were comparable.

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