Original Article

Evaluation and Comparison of the Dose Received by the Mandible, Maxilla, and Teeth in Two Methods of Three-dimensional Conformal Radiation Therapy and Helical Tomotherapy

Abstract

Background: Using three-dimensional conformal radiation treatment (3D-CRT) and helical tomotherapy (HT), this study examines and contrasts the dosage received by the mandible, maxilla, and teeth. **Methods:** Sixteen patients with head-and-neck cancer (H and NC) were the subject of treatment planning at the Seyyed Al-Shohada Hospital in Isfahan, Iran. This study examined target coverage quality, exposure of healthy tissue, and radiation delivery effectiveness. **Results:** In terms of a number of measures, including $D_{2\%}$, $D_{50\%}$, D_{mean}, $V_{95\%}$, conformity index (CI), and homogeneity index (HI) for the planning target volume (PTV) and $D_{2\%}$, $D_{98\%}$, D_{mean}, $V_{95\%}$, CI, and HI for the nodal PTV, HT showed considerable gains over 3D-CRT. The brainstem, D_{1cc}, and D_{10cc} received considerably lower maximum dosages in HT. Measurements of the right and left cochleas (D_{mean}, V55, and D_{max}) revealed decreases in HT, with D_{mean} revealing the most significant variations. The D_{mean} and D_{max} values for HT significantly decreased in constrictors as well. In terms of several HT-related indicators, the larynx, optic chiasm, optic nerves, oral cavity, mandible, thyroid, and parotid glands all showed considerable decreases. **Conclusion:** The findings of the comparison of the two treatment approaches revealed that the HT method was more than 50% more effective than the 3D-CRT method in sustaining organs at risk (OARs) and the target volume dose. In general, dosimetric coverage, homogeneity, conformity indices, and the absence of cold and hot patches showed that HT produced targets with greater accuracy than 3D-CRT. In addition, HT outperformed 3D-CRT in protecting important structures (OARs). HT as a result has the potential to be a more effective method of treatment for those with H and NC and involvement of regional lymph nodes.

Keywords: *Cancer, helical tomotherapy, radiotherapy, three-dimensional conformal radiation therapy*

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Introduction

The seventh-most frequent disease worldwide was reported to be head-and-neck cancer (H and NC).[1] H and NC includes cancers of the larynx, oropharynx, nasopharynx (NPC), oral cavity, lips, and hypopharynx.[2] Depending on the tumor's location, these malignancies are often treated with a combination of surgery, chemotherapy, and radiation treatment.[3-5]

The oral, jaw, and facial tissues are frequently severely affected by high-dose treatment, and some of these adverse effects might last an individual their entire life. Irradiation is the primary method of treatment for nonmetastatic NPC, one of the most prevalent H and NCs. In the early stages, irradiation is often effective in treating NPC. Due to their positioning inside the radiation field, the teeth, mandible, maxilla, and salivary glands in NPCs receive substantial doses of radiation. Loss of tooth enamel or dentin as well as decreased salivation have all been reported as side effects of high doses.[6] In addition, radiation exposure raises the incidence of osteoradionecrosis (ORN) of the jaw by interfering with bone homeostasis.[7] Consequently, dental implantation in the affected bone area becomes challenging, impacting the patient's quality of life after treatment.[8] Likewise, reduced saliva secretion and damage to the salivary glands (sublingual, parotid, and

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submandibular) caused by radiotherapy can lead to dental issues such as periodontal disease, tooth decay, and tooth loss.[9]

Today, radiotherapy techniques have significantly improved, allowing for more precise delivery of radiation beams to the target volume while minimizing the dose to organs at risk (OARs).[10] Modern radiation therapy techniques, such as stereotactic radiosurgery, intensity modulated radiation therapy (IMRT), and volumetric modulated arc therapy (VMAT), demand precise beam models in treatment planning systems, with a focus on small field dose assessments.[11,12]

One of the three-dimensional conformal radiation treatment (3D-CRT) radiotherapy techniques involves creating 3D volumes of the internal anatomy using computed tomography (CT)-based planning methods.[13,14] Another type of radiation therapy method is called cochlear helical tomotherapy (HT), which is a high-tech radiation dose delivery method used for IMRT.[15] HT utilizes a binary MLC that operates on a rotating fan beam around the patient while the couch moves at a constant speed through a gantry. This technique typically involves thousands of beams, making it suitable for delivering a highly precise dose to the planning target volume (PTV) while sparing critical OARs.[16]

Monadi *et al.*[17], studied on images of 20 patients with head and neck cancer by HT and 3D-CRT techniques. They found that HT technique has considerable promise to treatment head and neck cancer with the involvement of regional lymph nodes.

In a study, Santa Cruz *et al*.[18] treated 72 HNC patients with curative HT. The median follow-up period was 20 months, with 11 locoregional recurrences. In H and NC patients, IMRT combined with HT provided adequate locoregional control and overall survival.

In Lu *et al*.'s study,[19] 15 patients with stage III/IVA NPC who were treated from 2019 to 2020 were selected for this retrospective analysis and replanned for HT, VMAT, and fixed field-IMRT (FF-IMRT). For locally advanced NPC, the results showed that HT and VMAT had higher target homogeneity and conformity, resulting in a lower dose administered to OARs compared to traditional FF-IMRT, with HT having the greatest effect. VMAT had the shortest radiation delivery time of any of the techniques examined. This study's findings can help guide the selection of appropriate radiation technologies for treating patients with locally advanced NPC who are receiving concurrent chemoradiotherapy.

Considering the importance of preserving the received dose in the lower jaw, upper jaw, and teeth, as well as the significance of ORN prevention, this study aims to quantitatively compare the received dose of the lower jaw, upper jaw, and teeth between two radiation therapy methods, 3D-CRT and HT. The goal is to identify a better technique that can enhance the patient's quality of life.

Materials and Methods

Data collection

This retrospective cross-sectional experimental study (IR.MUI.MED.REC.1399.1130) was conducted at Seyyed Al-Shohada Hospital in Isfahan. Sixteen nasopharyngeal patients, with 81% of males and 19% of females, aged between 16 and 81 years (mean age: 42.7 ± 16.3), were randomly selected from those who sought treatment at the hospital between March 2021 and March 2023. None of the patients had a history of radiation therapy. Due to the limitations of administering multiple treatments to the patients, computed tomography (CT) scans and magnetic resonance imaging (MRI) scans were used to simulate treatment plans in two different ways. The oncologist determined the target volume of the areas at risk based on the guidelines of the International Commission on Radiological Units using the available tools in the treatment planning system.

After contouring, the treatment design was carried out to ensure that at least 95% of the PTV received a dose ≥95%. In addition, the dose to OARs was kept within tolerable limits. The dose limits for the OARs were classified in Table 1. The total dose administered to the patients was 70.2 g, delivered over 39 treatment sessions. The treatment design for 3D-CRT was performed using the Elekta Compact model and TiGRT software, while HT was planned using the Accuray X9 Radixact machine and Precision software. Both devices operated at an energy of 6 MV.

Data analysis was conducted using dose-volume histogram (DVH). Various parameters were calculated, including the mean dose (D_{mean}), minimum dose (D_{min}), and maximum dose (D_{max}) for the PTV, mandible, spinal cord, left parotid, right parotid, oral cavity, larynx, and thyroid. The following values were also collected: volume of PTV receiving 2% of the total dose ($D_{2\%}$), volume receiving 50% of the total dose ($D_{50\%}$), volume receiving 98% of the total dose ($D_{98\%}$), dose covering 95% of the volume ($V_{95\%}$), and total volume of PTV. Homogeneity index (HI) and conformity index (CI) were calculated using Equations 1 and 2, respectively.

Table 1: Summary of dose-volume constraints used in the plan optimization process for normal tissues in nasopharyngeal carcinoma patients[19]

Structures	Dose-volume constraints
Spinal cord	D_{max} ≤45 Gy
Mandible	D_{max} ≤70 Gy
TMJ	D_{max} ≤70 Gy
Parotid gland	D_{mean} ≤28 Gy
Larynx	D_{mean} ≤45 Gy

TMJ – Temporomandibular; D_{max} – $_{Max}$imum dose; D_{mean} – Mean dose

$$HI = (D_{2\%} - D_{98\%})/(D_{50\%}) \quad (1)$$

$$CI = (V_{95\%})/VPTV \quad (2)$$

The HI is a ratio used to assess the homogeneity of the PTV. A value closer to zero indicates better homogeneity. The CI is a ratio used to evaluate how well the PTV conforms to the prescribed isodose curve in the treatment design. A value closer to 1 indicates better conformity.

Delineation of contours

The OARs included in the DVH evaluation were the brainstem, spinal cord, optic nerve, optic chiasm, eyeball, lens, temporal lobe, parotid glands, auditory structures, contractile muscles, larynx, mandible, and maxilla. Axial CT slices were utilized to contour the upper and lower teeth.

Treatment planning

The treatment plans for all patients were developed by the radio-oncology department physicists. Dose limits for OARs within the nasopharyngeal carcinoma (NPC) range are provided in Table 1 as their values recommended by Lu *et al.*[19] Dose-volume histogram (DVH) analysis of patients undergoing radiation therapy using 3D-CRT and HT methods was conducted with TiGRT treatment planning systems using the full convolution scatter convolution algorithm and PRECISION utilizing the collapsed-cone convolution/superposition algorithm. The process involved fixation, imaging, image fusion, contouring, simulation, and treatment planning for all patients. Treatment was administered using 6 MV accelerator photons, with a total prescribed dose of 70.2 Gy.

Three-dimensional conformal radiation treatment

The treatment parameters were selected, and the treatment planning software was used to generate the dose distribution. The distribution of the generated dosage was then assessed. For all patients receiving 3D-CRT, four treatment zones were used. The anterior–posterior field had a collimator angle of 0 and a beam weight of 1.4, while the posterior–anterior field had a collimator angle of 180 and a beam weight of 0.6. Arc modulation was achieved by adjusting the left and right lateral fields with collimator angles of 90 and 270, respectively. To customize the dosage and deliver the required dose at particular depths into the tumor, wedges were used to curve the photon beams. For every treatment scenario, the dosage needed to cover the PTV and reduce exposure to OARs was estimated. The maximum dosage was kept under 115% of the prescription dose at all times, and treatment regimens were created to guarantee at least 95% coverage of the PTV at the specified dose.

The brainstem, optic nerve, optic chiasm, and eye each received a maximum allowable dose of 54 Gy; the spinal cord received a maximum legal dose of 45 Gy; and the jaw, maxilla, and teeth received a maximum permissible dose of 70 Gy. To make sure that the radiation exposure to these crucial structures stays within reasonable limitations and does not go over the predetermined thresholds, these dosage limits were developed. To decrease any potential risks and side effects of radiation therapy, it is critical to adhere to these acceptable limitations.

Tomotherapy

In the design of radiation therapy treatments, the three most important factors are pitch, modulation factor, and field width. The size and form of the treatment region in HT are significantly influenced by the field width. The three field widths used by 1, 2.5, and 5 cm are necessary for the helical nature of HT therapy. A 2.5 cm field width is typically regarded as the best choice for head-and-neck treatments. A linear accelerator used in HT radiation treatment may constantly revolve 360°. The transmission of radiation beams from 51 optimized angles is made possible by this rotational capacity in conjunction with a mobile treatment table.

Statistical analysis

The dose-volume histogram (DVH) methods were used to collect and analyze the data. PTV, maxillary, mandibular, teeth, spinal cord, left parotid, and right parotid were among the several locations, for which mean dose (D_{mean}), minimum dose (D_{min}), and maximum dose (D_{max}) in Gy were computed. We also calculated the percentages for D_2, D_{50}, D_{95}, and D_{98} to calculate the HI and CI. We used the Statistical Package for the Social Sciences (SPSS) software, version 26.0 (SPSS Inc., Chicago, IL, USA), to analyze the data. The quantitative variables were presented using measures such as mean, standard deviation, median, and range (minimum value minus maximum value). The normality of the data was assessed using the Shapiro–Wilk test. If the data violated the assumption of normality, the Wilcoxon signed-rank test was used to compare the differences between the related groups. In cases where the data followed a normal distribution, the paired samples *t*-test was utilized to evaluate the mean differences. $P < 0.05$ was considered statistically significant.

Results

Figure 1 illustrates the dose distribution color wash for a representative NPC patient, highlighting the disparities between the HT and 3D-CRT techniques. The evaluation of both radiation techniques was conducted for a total of 16 patients. In each case, both techniques met the planning objectives in terms of dose requirements.

Target dose optimizing

Table 2 demonstrates that both HT and 3D-CRT radiation techniques met the prescribed targets. However, when considering target coverage, HT plans exhibited superior dosimetric parameters for the PTV compared to 3D-CRT plans. Figure 2a shows that the mean dose covering 2% of the PTV in HT plans (107.14% ±7.60%) was significantly higher than in 3D-CRT plans (100.00% ± 0.00%), indicating a 7.1% increase in dose coverage for HT plans ($P < 0.001$). In addition, the D95% of the PTV was significantly higher in HT plans, with a 4.9% increase ($P < 0.01$). However, the average D50% of both HT and 3D-CRT techniques achieved similar dose coverage and did not show a significant difference ($P = 0.605$). Similarly, the differences in dose coverage for 98% of the PTV between HT and 3D-CRT plans were not statistically significant (93.38% and 92.24%, respectively). Figure 2b illustrates that the maximum, mean, and minimum doses of the PTV were not significantly different between HT and 3D-CRT plans ($P > 0.05$ for all comparisons). Moving on to plan quality indices in Figure 2b, the CI and HI were significantly higher in HT plans compared to 3D-CRT plans (CI: 0.13 vs. 0.05, $P = 0.006$; HI: 1.01 vs. 0.98, $P = 0.002$). Moreover, the average HI for HT plans (100.74) was significantly higher than for 3D-CRT plans (98.23). These results are summarized in Table 2 and depicted in Figure 2.

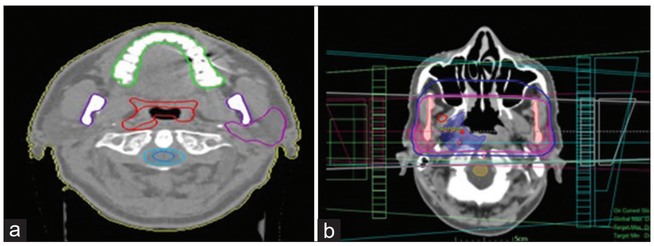

Figure 1: Dose distribution color wash for a representative nasopharyngeal carcinoma patient, highlighting the disparities between; (a) helical tomotherapy and (b) three-dimensional conformal radiation treatment techniques

Organs at risk dose comparison

Table 3 provides a summary of the dosimetric parameters for all OARs, including D_{mean}, D_{min}, D_{max}, D_2, D_{50}, D_{95}, and D_{98}.

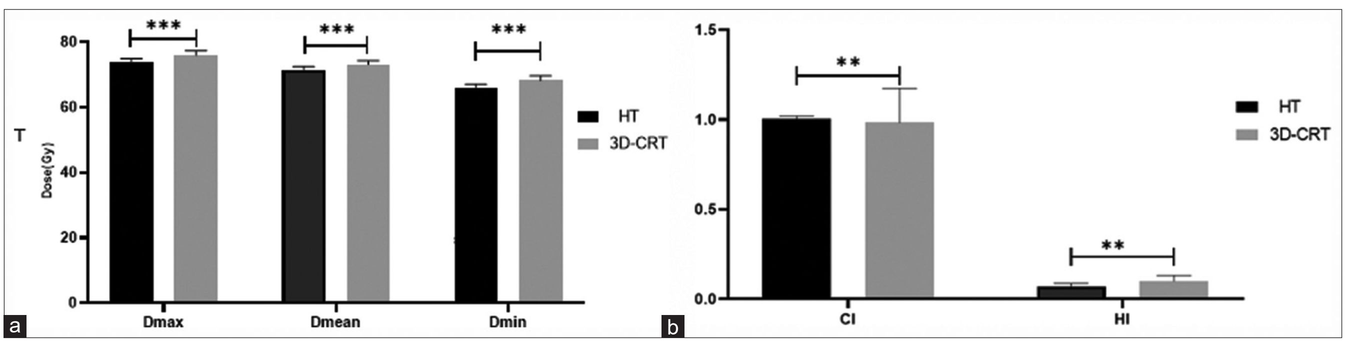

Figure 2: (a) Helical tomotherapy (HT) and three-dimensional conformal radiation treatment (3D-CRT): planning target volume (PTV) dosimetric comparison of PTV (D_{max}, D_{mean}, and D_{min}). (b) Comparison of quality indices (homogeneity index and conformity index between HT and 3D-CRT techniques in NPC patients. mean ± standard deviation, **$P < 0.01$, ***$P < 0.001$, and nonsignificant ($P > 0.05$). HT: Helical tomotherapy, 3D-CRT: Three-dimensional conformal radiation treatment, HI: Homogeneity index, CI: Conformity index

Table 2: Dose comparison of planning target volume between helical tomotherapy and three-dimensional conformal radiotherapy techniques in nasopharyngeal carcinoma patients

Index	HT		3D-CRT		*P*
	Mean±SD	Median (range)	Mean±SD	Median (range)	
PTV					
D_2 (%)	107.14±7.60	105.70 (133.30–100.56)	100.00±0.00	100.00 (100.00–100.00)	<0.001[b,*]
D_{50} (%)	104.85±7.33	103.38 (130.80–98.48)	100.00±0.00	100.00 (100.00–100.00)	0.001[b,*]
D_{95} (%)	101.11±7.23	100.04 (125.30–91.70)	99.31±1.83	100.00 (100.00–92.90)	0.605[b]
D_{98} (%)	93.38±23.59	98.35 (123.90–10.24)	95.24±14.90	100.00 (100.00–40.10)	0.326[b]
D_{max} (Gy)	75.05±2.38	75.00 (79.46–71.98)	74.03±2.39	73.91 (77.61–69.09)	0.193[a]
D_{mean} (Gy)	71.58±1.97	71.10 (76.13–68.19)	70.38±2.24	70.98 (73.27–64.62)	0.118[a]
D_{min} (Gy)	58.53±8.15	59.99 (70.43–40.23)	57.67±8.38	57.95 (69.96–40.23)	0.715[b]
HI	0.13±0.22	0.07 (0.93–0.03)	0.05±0.15	0.00 (0.60–0.00)	0.006[b,*]
CI	1.01±0.01	1.00 (1.04–0.99)	0.98±0.02	0.99 (1.00–0.95)	0.002[b,*]
$V_{95\%}$ (CC)	100.74±1.38	100.00 (104.20–99.30)	98.23±1.92	98.60 (100.00–94.92)	0.002[b,*]

*Statistically significant at the level of 5%, [a]Using the paired samples *t*-test (for two experimental groups with normally distributed data), [b]Using Wilcoxon's nonparametric test (for at least one experimental group with the abnormally distributed data). HT – Helical tomotherapy; 3D-CRT – 3D conformal radiotherapy; PTV – Planning target volume; $D_{2\%}$ – Dose covering 2% of PTV, representing the near maximal dose; $D_{50\%}$ – Dose covering 50% of PTV; $D_{95\%}$ – Dose covering 95% of PTV; $D_{98\%}$ – Dose covering 98% of PTV; D_{max} – Maximum dose; D_{mean} – Mean dose; D_{min} – Minimum dose; $V_{95\%}$ – The PTV volume receiving 95% of the prescribed dose. Range – Maximum value minus minimum value; 3D – Three dimensional; HI – Homogeneity index; CI – Conformity index; SD – Standard deviation

Table 3: Dosimetric parameter comparisons of organs at risks between helical tomotherapy and three-dimensional conformal radiotherapy techniques in nasopharyngeal carcinoma patients (*n*=16)

OAR	Index	HT		3D-CRT		*P*
		Mean±SD	Median (range)	Mean±SD	Median (range)	
Mandible	$D_{2\%}$ (%)	86.67±7.14	86.47 (98.60–74.70)	100.00±0.00	100.00 (100.00–100.00)	<0.001[a,*]
	$D_{50\%}$ (%)	56.88±12.50	57.45 (74.50–34.90)	73.91±18.65	76.30 (97.90–40.00)	<0.001[a,*]
	$D_{95\%}$ (%)	30.17±8.30	31.05 (51.50–17.84)	25.86±19.86	28.40 (57.40–0.00)	0.404[a]
	$D_{98\%}$ (%)	26.41±7.30	26.40 (46.00–15.68)	20.06±16.95	19.48 (52.80–0.00)	0.177[a]
	D_{max} (Gy)	67.21±6.48	67.50 (78.10–56.83)	66.84±4.90	68.65 (72.69–56.83)	0.708[a]
	D_{mean} (Gy)	39.58±6.48	37.81 (50.24–31.39)	40.28±6.12	41.10 (50.24–30.44)	0.288[a]
	D_{min} (Gy)	12.57±4.86	13.30 (25.30–4.46)	13.10±4.88	13.56 (25.30–4.70)	0.293[a]
Spinal cord	$D_{2\%}$ (%)	60.85±6.19	59.59 (81.50–55.28)	90.78±8.15	91.75 (100.00–77.60)	<0.001[b,*]
	$D_{50\%}$ (%)	35.48±11.52	37.48 (52.80–18.16)	40.98±26.86	34.49 (88.20–5.50)	0.312[a]
	$D_{95\%}$ (%)	1.55±0.95	1.35 (3.90–0.60)	14.48±31.25	0.00 (85.10–0.00)	0.234[b]
	$D_{98\%}$ (%)	1.34±0.86	1.16 (3.40–0.50)	14.39±31.07	0.00 (84.80–0.00)	0.234[b]
	D_{max} (Gy)	44.66±2.59	44.76 (51.06–40.55)	49.24±10.82	45.86 (78.48–41.57)	0.225[b]
	D_{mean} (Gy)	21.86±4.11	21.50 (28.60–15.36)	24.66±9.78	21.50 (50.39–17.37)	0.225[b]
	D_{min} (Gy)	0.83±0.56	0.68 (2.19–0.33)	0.93±0.61	0.68 (2.19–0.34)	0.223[b]
Maxilla	$D_{2\%}$ (%)	89.93±8.26	90.10 (99.30–65.20)	100.00±	100.00 (100.00–100.00)	<0.001[b,*]
	$D_{50\%}$ (%)	53.82±12.99	55.50 (74.50–30.10)	71.36±20.88	68.05 (100.00–25.70)	0.003[a,*]
	$D_{95\%}$ (%)	35.45±6.68	35.55 (45.30–18.90)	25.72±25.04	25.25 (100.00–0.00)	0.030[b,*]
	$D_{98\%}$ (%)	33.70±6.59	34.55 (44.10–17.60)	21.56±25.21	19.80 (100.00–0.00)	0.013[b,*]
	D_{max} (Gy)	69.33±7.06	70.69 (77.48–47.72)	68.80±6.97	70.69 (74.89–46.53)	0.144[b]
	D_{mean} (Gy)	40.27±7.85	42.34 (49.62–24.06)	42.21±7.16	43.97 (49.62–23.32)	0.465[b]
	D_{min} (Gy)	22.37±4.57	21.82 (31.19–11.15)	23.71±5.49	22.63 (32.21–10.97)	0.209[a]
Teeth upper jaw	$D_{2\%}$ (%)	71.88±17.06	76.90 (91.40–43.30)	100.00±0	100.00 (100.00–100.00)	<0.001[b,*]
	$D_{50\%}$ (%)	42.26±7.71	40.65 (57.70–30.00)	45.18±15.29	49.05 (63.80–0.00)	0.326[b]
	$D_{95\%}$ (%)	31.52±5.53	31.30 (43.52–20.70)	8.18±10.65	5.05 (32.70–0.00)	0.001[b,*]
	$D_{98\%}$ (%)	29.41±6.54	30.15 (42.64–15.10)	4.02±4.74	2.65 (16.70–0.00)	<0.001[b,*]
	D_{max} (Gy)	52.60±13.46	57.26 (68.80–30.71)	57.28±12.49	62.07 (68.80–30.71)	0.225[b]
	D_{mean} (Gy)	30.48±5.78	31.00 (43.09–22.73)	33.10±7.13	32.53 (45.66–20.50)	0.123[a]
	D_{min} (Gy)	19.22±4.71	19.88 (30.91–10.08)	20.81±6.83	19.97 (34.77–10.08)	0.178[a]
Teeth lower jaw	$D_{2\%}$ (%)	61.12±17.87	59.45 (82.70–31.30)	100.00±0.00	100.00 (100.00–100.00)	<0.001[b,*]
	$D_{50\%}$ (%)	39.76±9.62	37.85 (59.30–25.20)	46.70±33.16	39.90 (100.00–0.00)	0.348[a]
	$D_{95\%}$ (%)	31.84±6.03	31.75 (44.30–22.20)	4.36±7.90	0.00 (25.50–0.00)	<0.001[b,*]
	$D_{98\%}$ (%)	31.29±5.95	31.10 (43.10–22.00)	3.03±5.97	0.00 (20.10–0.00)	<0.001[b,*]
	D_{max} (Gy)	46.93±13.81	50.27 (62.97–22.39)	48.28±13.79	52.44 (64.51–22.30)	0.622[a]
	D_{mean} (Gy)	29.15±7.01	28.00 (42.95–18.48)	30.83±9.21	28.82 (47.88–16.84)	0.351[a]
	D_{min} (Gy)	20.70±4.51	19.73 (30.38–14.79)	22.53±7.78	19.73 (40.49–13.92)	0.686[b]
Left parotid gland	$D_{2\%}$ (%)	75.75±8.68	74.75 (88.90–60.80)	100.00±0	100.00 (100.00–100.00)	<0.001[b,*]
	$D_{50\%}$ (%)	31.74±8.10	31.90 (52.50–20.64)	38.38±18.66	34.30 (73.20–6.70)	0.109[a]
	$D_{95\%}$ (%)	16.34±4.48	16.65 (27.50–10.60)	9.53±10.34	5.70 (32.00–0.00)	0.023[b,*]
	$D_{98\%}$ (%)	15.45±4.19	15.85 (25.80–9.50)	7.18±7.70	4.75 (23.50–0.00)	0.002[b,*]
	D_{max} (Gy)	65.06±6.86	62.44 (77.43–56.84)	70.69±16.08	64.58 (110.90–56.84)	0.686[b]
	D_{mean} (Gy)	26.25±5.31	25.67 (37.67–16.44)	27.74±7.75	27.50 (42.51–15.09)	0.349[a]
	D_{min} (Gy)	9.50±2.76	9.47 (16.59–5.67)	10.03±3.56	9.47 (16.88–5.67)	0.465[b]
Right parotid gland	$D_{2\%}$ (%)	85.42±9.59	84.70 (98.20–62.00)	100.00±0.00	100.00 (100.00–100.00)	<0.001[b,*]
	$D_{50\%}$ (%)	37.27±13.13	30.70 (57.10–19.10)	41.98±22.41	35.55 (96.10–5.90)	0.215[b]
	$D_{95\%}$ (%)	17.62±6.19	16.50 (28.60–10.72)	16.53±17.54	14.58 (68.10–0.00)	0.320[b]
	$D_{98\%}$ (%)	15.64±5.60	14.45 (26.60–9.66)	13.04±16.13	11.15 (66.20–0.00)	0.063[b]
	D_{max} (Gy)	65.39±6.96	63.25 (78.57–56.49)	65.10±6.30	63.95 (75.53–56.32)	0.699[a]
	D_{mean} (Gy)	32.00±12.52	28.40 (69.72–15.76)	30.56±12.06	28.39 (69.72–14.35)	0.116[b]
	D_{min} (Gy)	12.91±13.13	9.85 (60.27–6.10)	13.64±13.37	9.75 (60.27–6.10)	0.500[b]
Oral cavity	$D_{2\%}$ (%)	96.59±9.51	97.18 (119.10–81.40)	96.01±24.08	100.47 (110.12–7.00)	0.379[b]
	$D_{50\%}$ (%)	66.46±19.06	71.75 (96.50–40.90)	73.55±34.85	87.81 (95.80–1.72)	0.234[b]

Contd...

Table 3: Contd...

OAR	Index	HT		3D-CRT		*P*
		Mean±SD	Median (range)	Mean±SD	Median (range)	
	$D_{95\%}$ (%)	42.63±17.65	42.60 (78.80–18.80)	35.61±28.77	29.34 (88.94–2.40)	0.381[a]
	$D_{98\%}$ (%)	37.24±15.79	37.90 (75.10–16.72)	14.21±16.92	8.91 (70.15–2.53)	0.006[b,]*
	D_{max} (Gy)	71.55±2.29	72.51 (74.82–67.10)	68.43±13.55	70.61 (78.45–18.40)	0.679[b]
	D_{mean} (Gy)	47.96±7.89	48.51 (66.50–31.21)	46.38±16.35	51.70 (64.66–1.42)	0.796[b]
	D_{min} (Gy)	22.06±8.87	20.67 (46.43–11.00)	8.59±20.84	3.92 (86.26–0.00)	0.007[b,]*
Larynx	$D_{2\%}$ (%)	75.24±15.83	71.25 (102.30–52.80)	86.62±20.59	92.94 (98.90–13.49)	0.070[b]
	$D_{50\%}$ (%)	49.67±14.34	46.67 (85.40–26.50)	62.30±27.07	67.65 (89.43–6.94)	0.056[b]
	$D_{95\%}$ (%)	34.09±16.28	29.56 (62.30–4.50)	36.46±26.66	34.90 (87.75–3.18)	0.706[a]
	$D_{98\%}$ (%)	33.20±15.97	29.86 (61.20–4.20)	28.93±26.69	14.24 (80.49–3.01)	0.438[b]
	D_{max} (Gy)	54.69±7.53	52.88 (72.49–44.23)	60.99±11.41	64.97 (70.48–22.64)	0.070[b]
	D_{mean} (Gy)	34.62±8.69	34.61 (51.66–21.26)	42.33±16.23	43.93 (62.85–4.20)	0.106[a]
	D_{min} (Gy)	20.17±11.00	19.62 (41.53–2.69)	27.72±27.20	16.02 (99.83–2.18)	0.438[b]

*Statistically significant at the level of 5%, [a]Using the paired samples *t*-test (for two experimental groups with normally distributed data), [b]Using Wilcoxon's nonparametric test (for at least one experimental group with the abnormally distributed data). HT – Helical tomotherapy; 3D-CRT – 3D conformal radiotherapy; OAR – Organs at risk; PTV – Planning target volume; $D_{2\%}$ – Dose covering 2% of PTV, representing the near maximal dose; $D_{50\%}$ – Dose covering 50% of PTV; $D_{95\%}$ – Dose covering 95% of PTV; $D_{98\%}$ – Dose covering 98% of PTV; D_{max} – Maximum dose; D_{mean} – Mean dose; D_{min} – Minimum dose; Range – Maximum value minus minimum value; 3D – Three dimensional; SD – Standard deviation

In general, most dose parameters were lower for HT plans compared to 3D-CRT plans. Figure 3 illustrates the changes in OARs' dose parameters between the two techniques. In HT plans, significant decreases of 13.3%, 29.9%, 10.1%, 28.1%, 38.9%, 24.3%, and 14.6% were seen in the D_{mean} of the mandible, spinal cord, upper and lower jaw teeth, as well as the left and right parotid glands ($P < 0.001$) for all. In addition, the D_{mean} of the mandible and maxilla decreased by 17.0% and 17.5% ($P < 0.01$) in HT plans, respectively. On the other hand, in HT plans, the D_{mean} of the maxilla, upper and lower jaw teeth, and left parotid gland increased by 9.7%, 23.3%, and 27.5% ($P < 0.05$). With increases of 12.1%, 25.4%, 28.3%, 8.3%, and 23.0% ($P < 0.05$), the D_{max} of the maxilla, upper and lower jaw teeth, left parotid gland, and oral cavity was also significantly greater in HT plans. In addition, the HT plans significantly increased the oral cavity's minimum dosage (D_{min}) by 13.5% ($P < 0.01$). The variations in dose levels between the two radiation procedures were, however, clinically negligible ($P > 0.05$) for the remaining dosimetric parameters. These results are given in Table 3 and Figure 3.

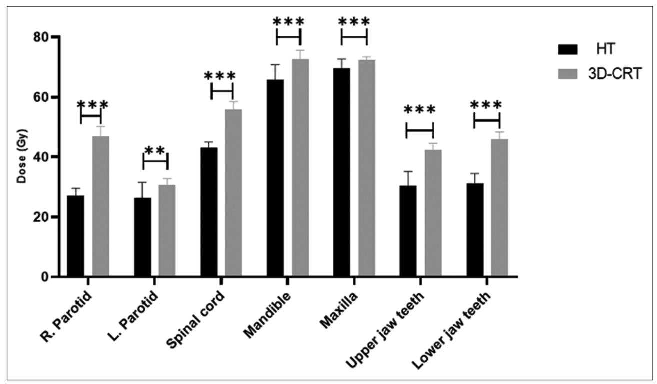

Figure 3: Dosimetric parameter comparisons of organs at risk (D_{max}, D_{mean}, and D_{min}) between helical tomotherapy (HT) and three-dimensional conformal radiation treatment plans in NPC patients, including the mandible, spinal cord, maxilla, tooth upper jaw, tooth lower jaw, left parotid gland, right parotid gland, oral cavity, and larynx. Mean dose (Gy) ± standard deviation (Gy), **$P < 0.01$, ***$P < 0.001$ and ns: Nonsignificant ($P > 0.05$). HT: Helical tomotherapy, 3D-CRT: Three-dimensional conformal radiation treatment

Discussion

The intricate anatomy of the head-and-neck region often leads to sensitive organs receiving high doses of radiation during H and NC radiotherapy, particularly in the treatment of nasopharyngeal cancer. This radiation exposure has been linked to adverse effects such as decreased salivation, degradation of enamel and dentin, and reduced blood supply to the irradiated bones. These factors directly or indirectly contribute to significant long-term complications.[6] As the survival rates for patients with H and NC improve, the importance of maintaining oral and dental health becomes increasingly evident. Radiation therapy can disrupt the balance of bone homeostasis and raise the risk of developing a condition known as ORN.[7] The ORN of the jaw is recognized as one of the most costly and debilitating complications resulting from radiation therapy.[19,20] When higher doses of radiation are administered to the posterior areas of the lower jaw, it can lead to not only ORN but also fibrosis and dysfunction of the temporomandibular joint.[6]

Several studies have indicated that the risk of ORN is higher for the lower jaw when doses exceed 60 Gy, while lower doses below 50 Gy are associated with a reduced risk of ORN.[21-23] Another study predicted the likelihood of this complication occurring with doses exceeding 60–75 Gy.[6,24] Oral and intraoral implants have become increasingly popular in recent years for prosthetic repair.

This is because advances in restorative materials and surgical methods have improved patients' quality of life after radiation therapy, especially when radiation therapy has affected the oral architecture to the point where standard detachable prostheses are no longer practical.[25] For patients who have had radiation therapy in the afflicted bone region, high-dose radiation therapy can obstruct or even prohibit normal bone repair around the implanted implant. Implants have the potential to become unstable and give the patient great suffering.[8] It was found that dosages of 50 Gy and 65 Gy had no negative impact on the osseointegration of dental implants. This indicates that radiation therapy at these dosage ranges does not prevent dental implants from successfully fusing with the surrounding bone tissue.[26]

Tanaka[27] conducted a study and reported that placing dental implants in the anterior mandible after 12 months of radiation therapy with a cumulative dose below 50 Gy resulted in a favorable survival rate for the implants.[28] On the other hand, a different study found that the survival rate of dental implants decreased at radiation doses of more than 50 Gy. Furthermore, Schoen *et al*.[29] showed that bone regeneration is difficult at a radiation dosage of 40 Gy. In the present study, the cumulative radiation doses were reported as 72.36–72.73 Gy for 3D-CRT and 65.89–69.64 Gy for the HT treatment technique. These findings indicate that the HT technique performed better than 3D-CRT in terms of the radiation doses delivered.

An investigation by Benevides[30] suggested that patients with H and NC who get radiation therapy may have changes in the properties of the dentine collagen and periodontal ligament in their teeth, which may increase the risk of tooth decay. According to their study findings, the form and general integrity of the dentine collagen structure are altered when it is subjected to radiation dosages between 30 and 60 Gy. In the current evaluation, the radiation dosage supplied using the HT approach varied between 30.47 and 31.27 Gy, whereas the radiation dose delivered using the 3D-CRT technique varied between 42.31 and 45.81 Gy. Despite the potential advantages of the HT technique over 3D-CRT, its application in H and NC treatment remains a topic of debate due to the proximity of critical OARs and their potential overlap with the target volume. The complexity of the head-and-neck region poses challenges when determining the optimal treatment approach.

Studies that reduced radiation-induced toxicity showed that H and NC can be effectively treated using IMRT-based methods.[31,32] On the other hand, there are studies that have suggested that IMRT does not necessarily improve tumor control compared to other treatment modalities.[33,34] The HT and the 3D-CRT approach were done by Xianfeng Liu *et al*. on patients with nasal natural killer T-cell lymphoma. The outcomes showed that the CI and HI of HT showed improvements, suggesting improved dosage distribution within the target region. The coverage of the PTV was also increased by HT. However, there were often no appreciable differences between the HT and 3D-CRT approaches in terms of OARs.[35]

Elsewhere, Jaws-only IMRT (JO-IMRT) and 3D-CRT were evaluated in research by Tai *et al.* on patients with nasopharyngeal cancer. According to the study's findings, JO-IMRT performed better than 3D-CRT in terms of target volume coverage, HI, and CI. In addition, JO-IMRT drastically decreased the dosage given to the parotid gland compared to 3D-CRT. In addition, when JO-IMRT was used instead of 3D-CRT, the normal tissue complication probability for the parotid glands, brainstem, and spinal cord was decreased.[36]

Teng *et al*.[37] examined the impact of the HT technique for patients with H and NC on lowering the complication of xerostomia by protecting the bilateral parotid glands, mandibular submandibular glands, and lateral salivary glands in the oral cavity. According to the study's findings, HT lessens xerostomia by lowering the D_{mean} of the aforementioned glands without raising the chance of local recurrence. There is still debate regarding whether this technology is preferable to 3D-CRT since the dose achieved by these glands is higher than their tolerated dose. The results of the present study demonstrate that the HT technique provides superior preservation of the mandible, maxilla, and teeth compared to the 3D-CRT technique. HT shows significant improvements over 3D-CRT in terms of target volume coverage, dose uniformity within the target, and overall treatment efficacy.[38,39] As a result, HT is currently being utilized in the treatment of various cancer types, including NPC.

Conclusion

Comparing the use of 3D-CRT and HT in H and NC patients with regional lymph node involvement revealed that HT demonstrated notable improvements in target quality compared to 3D-CRT. These improvements include enhanced dosimetric coverage of target volumes, improved homogeneity and conformity indices, and a reduction in the volume of areas with insufficient and excessive radiation doses. Furthermore, HT outperformed 3D-CRT in effectively protecting critical structures known as OARs. Therefore, radiotherapy utilizing the HT technique can be considered a favorable approach for treating patients with H and NCs that involve regional lymph nodes.

Author contributions

Conceptualization, D.S.-G.; Methodology, Z.P., N.N.; Validation, D.S.-G., Z.P., N.N., M.S.; Investigation, Z.P., P.M.; Resources, D.S.-G.; Data Curation, Z.P., B.M.; Writing – Original Draft Preparation, Z.P., B.M., P.M.; Writing – Review and Editing, D.S.-G, P.M.; Supervision, D.S.-G.; Project Administration, D.S.-G.; and Funding Acquisition, D.S.-G. All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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