Short-term efficacy comparison between helical tomotherapy and intensity-modulated radiotherapy in patients with locally advanced nasopharyngeal carcinoma

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Abstract

Background: To evaluate short-term safety and efficacy of helical tomotherapy (HT) versus intensity-modulated radiotherapy (IMRT) in patients with nasopharyngeal carcinoma (NPC).

Methods: Retrospective analysis of locally advanced nasopharyngeal carcinoma treated with radiotherapy and concurrent platinum based neoadjuvant chemotherapy (cisplatin 80 mg/m2 every 3 weeks for 1 cycle) in our hospital from February 2017 to October 2019, including 70 patients in HT group and 70 in IMRT group. The target area of the tumor was delineated by magnetic resonance (MRI) imaging. The prescription doses delivered to the gross tumor volume (pGTVnx) and positive lymph nodes (pGTVnd), the high risk planning target volume (PTV1), and the low risk planning target volume (PTV2), were 69.96 Gy, 66-70 Gy, 60 Gy and 50-54 Gy, in 33 fractions, respectively. Acute reactions were evaluated according to the RTOG/EORTC criteria, whereas the therapeutic efficacy was assessed according to RECTST version 1.1 criteria in a 3-months period.

Results: The CI of PGTVnx, PGTVnd, PTV1 and PTV2, and HI of PGTVnx, PTV1 and PTV2 in HT group was significantly better than those in IMRT group. The OAR Dmax and Dmean in HT group were better than those in IMRT group with a significant difference (all $p < 0.05$). Patients in the HT group were significantly better than those in the IMRT group in the protection of acute parotid gland injury and hearing damage ($p < 0.05$), but not other acute adverse reaction. No significant difference was found on the short-term efficacy illustrated by ORR between HT group and IMRT group ($x2 = 0.119$; $p = 0.730$).

Conclusions: Compared with IMRT, HT has better radiophysical-related dosimetric advantages in radiotherapy for locally advanced nasopharyngeal carcinoma. Despite similar on short-term effects, HT has lower incidence of adverse reactions than IMRT.

Background

Nasopharyngeal carcinoma is one of the most common cancer type located in head and neck. In 2018, 130,000 people were diagnosed with nasopharyngeal carcinoma worldwide, and its incidence was as high as 9.8/100,000 in China, of which 70% of patients were locally advanced nasopharyngeal cancer [1, 2]. Due to the special anatomical structure of the nasopharynx and the radiation sensitivity property possessed in biological characteristics of nasopharyngeal carcinoma, radiotherapy is considered as the preferred treatment choice for nasopharyngeal carcinoma [3]. For locally advanced nasopharyngeal carcinoma, concurrent chemoradiotherapy is the standard treatment in clinical practice [4]. In recent years, with the rapid development of radiotherapy modality and radiotherapy technology, the 5-year overall survival of nasopharyngeal carcinoma radiotherapy has exceeded 80% [5]. However, adverse reactions resulted from radiotherapy (such as dry mouth etc) remain the main factors affecting the quality of life of patients with radiotherapy. Effectively reduction of the side effects generated by radiotherapy in the treatment nasopharyngeal carcinoma is one of the major concerns in clinical practice.

Helical tomotherapy (HT) is one of the most advanced intensity-modulated radiotherapy (IMRT) technologies used in current clinical practice. As a newly emerging IMRT technology, HT integrates IMRT, Image-Guided Intensity Modulated Radiotherapy (IGRT), and Dose-Guided Intensity Modulated Radiotherapy (DGRT) via combining 360°spiral tomography scan with straight accelerator in tumor radiotherapy, thereby realizing real dynamic intensity modulation. Regarding few study, small sample size and inconsistent results on the efficacy of HT in nasopharyngeal carcinoma radiotherapy in China and worldwide [6–8], elucidation of the role of HT in nasopharyngeal carcinoma treatment via a large sample study is required.

Here, we performed a retrospective study to evaluate the advantages of HT radiotherapy for locally advanced nasopharyngeal carcinoma via comparison of the differences in target conformation index, homogeneity index, acute adverse reactions, and short-term efficacy between the patients treated with HT and conventional IMRT.

Methods

1.1 Patient inclusion

From February 2017 to September 2019, 140 cases of stage IIIa-IVb locally advanced NPC treated in our department were collected. Inclusion criteria: (1) NPC with confirmed pathological diagnosis; (2) complete clinical data; (3) stage IIIa-IVb according to 8th edition of American Joint Committee on Cancer (AJCC) staging classifications; (4) The Karnofsky Performance Scale (KPS) ≥70 points; (5) no contraindication to radiotherapy and chemotherapy; (6) with written form of informed consent. The study was approved by the Ethical committee of the First Affiliated Hospital of Bengbu Medical College. Patients were divided into HT group and IMRT group according to radiotherapy methods, with 70 cases in each group. No significant difference was found on general information between the two groups (all $p > 0.05$) (Table 1).

1.2 CT scan for simulation and immobilization

The patient was placed in supine position and was fixed with a head-neck-shoulder thermoplastic mask before subjection to a Spiral computed tomography (CT) simulator. The scanning range was 5 cm length from head to subclavian, and the layer thickness is 3 mm.

1.3 Target area and organs at risk (OAR) delineation

Target area was delineated according to the International Commission on Radiation Units & Measurements (ICRU) Reports 50 & 62. The primary nasopharyngeal tumor was defined as GTVnx and metastatic lymph nodes as GTVnd. CTV1 was defined as the high-risk areas of microscopic extension encompassing the entire nasopharynx, parapharyngeal space, retropharyngeal lymph node area, skull base, clivus, sphenoid sinus, pterygopalatine fossa, nasal cavity and 5 mm anterior to the posterior wall

of the maxillary sinus, part of the oropharyngeal and superior neck lymph drainage area, including gross tumor (GTVnx) and regional metastatic nodes (GTVnd). CTV2 was defined as the low-risk region of inferior neck lymph drainage area below CTV1. PTV1 and PTV2 was respectively generated by 3 mm expansion outside of CTV1 and CTV2, and at least 3-mm distant away from the skin for protection purpose. OARs included brain stem, spinal cord, lens, optic nerves, optic chiasm, parotid glands, temporomandibular joints (TMJs), inner ear, parotid gland, oral cavity, spinal cord and other non-specified tissues. A re-delineation of the target area and OAR were processed when the larger volume of primary or metastatic lymph nodes were observed.

The Pinnacle 9.8 system was used for the target area and OAR delineation. IMRT plans and HT plans were respectively formulated on Pinnacle 9.8 system and TomoTherapy Hi-Art Planning Station by the same medical physicist.

1.4 Planning techniques

1.4.1 IMRT plan

IMRT plan were optimized by Dose Volume Optimize Version 11.0.31, and treatment dose was initially calculated using the Eclipse TPS algorithm. After interactively optimization by inverse planning software, the final dose was calculated using the Anisotropic Analytical Algorithm version 11.031 dose algorithm with a grid size of 2.5 mm.

1.4.2 HT plan

HT plan were optimized by TomoTherapy Hi-Art Software Version 2.07 (Accurray, Madison, WI, USA), and 3 major parameters were set as follows: 2.5 cm for field width, 0.287 for a pitch and 2.1-2.6 for modulation factor. Dose calculation was performed by a collapsed cone convolution model with a grid size of 1.95 mm.

1.5 Dose prescription

The prescribed dose was 69.96Gy/33F for PGTVnx, 66-70Gy/33F for PGTVnd, 60Gy/33F for PTV1, and 54Gy/33F for PTV2 respectively. Moreover, an at least 98% of the target area coverage, and >110% and > 93%of the prescribed dose was respectively cover <20% and <3% of planning target volume (PTV). OAR and target doses were restrained according to the protocol of Radiation Therapy Oncology Group (RTOG)-0615 as follows: parotid gland V30 <50%, temporal lobe <60Gy, brain stem <54Gy, spinal cord <45Gy, optic nerve and optic chiasm <54Gy, TMJ <60Gy, lens <5Gy, inner ear <50Gy.

1.6 Chemotherapy

In both HT and IMRT treatment groups, cisplatin-based concurrent chemotherapy was given during radiotherapy. The dose of cisplatin was 80 mg / m2 every 3 weeks for 1 cycle. During chemotherapy, symptomatic treatment was applied for anti-vomiting and the gastrointestinal mucosa protection.

1.7 Dosimetric comparisons

1.7.1 Conformity index (CI)

CI: measurement of how conformed the dose distribution is along target volume of PTV1 and PTV2. Formula: $CI = (TV_{PV} \times TV_{PV})/(VP_{TV} \times V_{TV})$, whereas the definitions of TV_{PV} , TV_{PV},VP_{TV} and V_{TV} were as follows: VP_{TV}: volume of PTV, V_{TV}: treatment volume of body receiving 95% of prescribed dose and TV_{PV}: volume of VP_{TV} within V_{TV}. The closer of the CI value to 1, the better conformity of the tumor target area.

1.7.2 Homogeneity Index (HI)

Formula: HI = D5 / D95. In the formula, D5 is the lowest dose that covers the 5% PTV, and D95 is the lowest dose that covers the 95% PTV. The closer of the value to 1, the better conformity of the tumor target area.

1.8 Clinical monitoring

During the treatment, all patients were required to undergo blood routine tests every week, liver and kidney function tests every 2-3 weeks, head and neck enhanced magnetic resonance imaging and upper abdomen ultrasound examination 3 months after radiotherapy to evaluate the patients' short-term efficacy.

1.9 Evaluation of radiotherapy-related adverse reactions

The most commonly used American Radiation Therapy Oncology Group (RTOG)/European Organization for Research on Treatment of Cancer (EORTC) standards [9]were used here for evaluation.

1.10 Short-term efficacy evaluation

According to the solid tumor evaluation standard Response evaluation criteria in solid tumors (RECIST) 1.1 [10], the complete response (CR), partial remission (PR), stable disease (SD), progress disease (PD), and objective response (ORR), and the incidence of adverse reactions were used for between group

comparison. ORR = (number of CR cases + number of PR cases) / total number of cases × 100%; observation period of the short-term efficacy was from the first day of the radiotherapy to 3 month after the end of the radiotherapy.

1.11 Statistical methods

Data were processed using SPSS version 19.0 software. The measurement data was expressed as mean ± standard deviation, and the t-test was used for between-group comparisons for the data with normal distribution, whereas the count data was expressed as the rate and compared using $\chi 2$ test. The category data was compared using Wilcoxon rank-sum test. $p < 0.05$ was taken as statistically significant.

Results

Comparison of CI and HI between HT group and IMRT group

As shown in Table 2, the CI of PGTVnx, PGTVnd, PTV1 and PTV2 in HT group was superior to that in IMRT group, which exhibited a significant difference (all $p < 0.05$). The number of HI of PGTVnx, PTV1 and PTV2 was lower in HT group than those in IMRT group (all $p < 0.05$), whereas PGTVnd is higher in HT group than that in IMRT group (all $p < 0.05$). These results indicated that better CI and HI could be achieved by HT than IMRT.

Comparison of OAR Dmax and Dmean between HT group and IMRT group

For the OAR, except optic nerve, optic chiasm and mandible, the OAR Dmax and Dmean in HT group was better than those in IMRT group with a significant difference (all $p < 0.05$, Table 3).

Comparison of acute adverse reactions between HT group and IMRT group

According to the RTOG / EORTC acute radiotherapy reaction criteria and shown in Table 4, the acute adverse reactions that occurred in both groups of patients, including oral mucosa and salivary glands, were mainly grades 1–2, and very few patients had grade 3 adverse reactions. Leukopenia and skin reactions are the main manifestations of severe grade 3 and grade 4 adverse reactions. Patients in the HT group were better than those in the IMRT group in the protection of acute parotid gland injury and hearing damage, and the difference was statistically significant ($p < 0.05$). There were no significant differences in other acute adverse reactions between the two groups of patients (p□0.05).

Comparison of short-term efficacy between HT group and IMRT group

All patients were carried out with the head and neck enhanced magnetic resonance imaging at three months after radiotherapy completion radiotherapy for short-term efficacy evaluation. In the HT group, CR cases were 44, PR were 22 cases, SD were 4 cases, PD was 0 and ORR was 94.29%; In the IMRT group, CR cases were 40, PR were 25, SD were 4, PD was 1 and ORR was 92.86%. No statistical significance were found on ORR between these 2 groups (P = 0.730, Table 5)

Discussion

Nasopharyngeal carcinoma is one of the most common head and neck cancer type in China, with a particularly high incidence in Southern China [1]. With the development of radiotherapy technology and modality, the 5-year survival rate of nasopharyngeal carcinoma has reached more than 80% [5]. Target area conformity and homogeneity indexes are the key factors that determine the efficacy of radiotherapy. Complications caused by radiotherapy such as radiation parotid injury are the main factors affecting the quality of life of patients after radiotherapy. Effective improvement of the CI and HI of the target area could reduce radiotherapy related side effects, thereby improving the quality of life of patients after radiotherapy is the major concern in the treatment of nasopharyngeal carcinoma in current clinical practice. Puebla [11] conducted a study of 17 patients with locally advanced nasopharyngeal carcinoma who underwent HT radiotherapy and the results showed that HT had better target area CI and HI than conventional IMRT in dosimetry, which could result in significantly decreased dose exposure on the vital organs. Zhang et al [12] compared the Three-dimensional Conformal Radiotherapy (3D-CRT) plan with the HT plan dosimetry for patients with locally advanced nasopharyngeal carcinoma, and the results showed that the use of spiral tomography in HT can further improve the CI and HI of the target area, thereby achieving a better protection of normal tissue. However, relative a lower number of patients were included in these study for HT radiotherapy. In this study, we analyzed the HT radiotherapy results of 70 patients. The results of our study were consistent with these previous reported studies. The target area CI and HI of the HT group were better than those from IMRT group. At the same time, we also compared the difference between OAR Dmax and Dmean in the HT group and the IMRT group according to the radiation treatment plan. In addition to the optic nerve, optic chiasm and mandible, there were no significant abnormalities on OAR between the two groups. The HT group was better than the IMRT group on OAR Dmax and Dmean comparison. It is suggested that HT has a greater radiation-related dosimetric advantage over conventional IMRT in nasopharyngeal carcinoma radiotherapy.

So far, a high tumor control rate could be achieved by radiotherapy in the treatment of nasopharyngeal carcinoma. Therefore, how to better protection of the normal tissues and organs around the tumor in the target area and reduction the adverse reactions to radiotherapy to improve the quality of life after radiotherapy is of great significance. Compared with conventional two-dimensional radiotherapy, the

emergence of three-dimensional conformal radiotherapy and intensity-modulated radiotherapy has greatly improved the protection of OAR and reduced the adverse reactions to radiotherapy. The results from this study showed that the acute adverse reactions that occurred in most organs such as oral mucosa and salivary glands in both groups were mainly grade 1–2, and very few patients had grade 3 reactions, all of which were under control. Leukopenia and skin injury are the main manifestations of severe grade 3 and 4 adverse reactions and were only presented in a small number of patients. Radiation injury of the parotid gland can affect the secretory function of the parotid glands, cause symptoms such as dry mouth, and is the main reason that result in quality of life decreasing after radiotherapy for nasopharyngeal carcinoma. Therefore, it is particularly important to protect the parotid gland[13]. HT may further reduce the exposure dose of parotid glands. Studies on head-and-neck cancer spiral tomography such as nasopharyngeal carcinoma have been reported in the study of OAR protection. It has been found that tomotherapy can reduce radiation dosage exposure at OAR, such as the parotid gland, with affecting clinically required target dose [7, 14]. Leung [15] et al analyzed the treatment results of 72 cases of locally advanced nasopharyngeal carcinoma with HT, and only 2 patients had grade 2 dry mouth adverse reaction, suggesting that HT has a good parotid gland protective effect. The results of this study showed that 61 patients in the HT group and 70 patients in the IMRT group with grade 1–2 parotid gland injury, which had significant statistical differences for between group comparison ($p < 0.05$). It is suggested that HT radiotherapy does further reduce the incidence and degree of parotid injury. Although HT radiotherapy showed good dosimetric advantages and good protection of the parotid gland, the incidence of acute radiation parotid gland injury in patients with locally advanced nasopharyngeal carcinoma was not low.

In fact, the volume of the parotid gland changes greatly after radiation exposure, and the parotid gland shrinks by more than 30% in the later stage of radiotherapy [16, 17]. The reduced volume of parotid gland could result in its shifting to the midline of the body, thereby resulting in the actual radiation dosage on the parotid gland could excess the planned dosage. Therefore, although HT has better protection on the parotid gland, it is currently unrealistic to completely avoid the occurrence of acute radioactive mumps. Because nasopharyngeal carcinoma radiotherapy usually resulting in exposure of the inner ear in higher doses field, different degrees of hearing damage are the more common side effects caused by nasopharyngeal carcinoma radiotherapy. Moreover, concurrent chemotherapy can also increase the incidence of hearing loss. The study by Bhandare et al.[18] showed that the incidence of sensorineural hearing loss in patients with nasopharyngeal carcinoma undergoing concurrent chemoradiation could increase from 8–30%. Therefore, reduction of the exposure dose of the inner ear is of great significance for hearing impairment protection. There is still a great difference on the dose restriction for the inner ear. Dmean < 50Gy is currently the most commonly used restriction dose[19]. Our results showed that the average inner ear dose of patients in the HT group was 38.900 ± 3.470 Gy, while in the IMRT group was 47.625 ± 3.651 Gy, indicating that HT has a better advantage in hearing protection ($p < 0.05$). However, HT did not show obvious advantages on oral mucosal reaction and throat pain, which may be related to lower threshold on radiation dose of oral and throat mucosal inflammation. Concurrent chemoradiotherapy is the standard treatment option for locally advanced nasopharyngeal carcinoma, however, concurrent chemoradiation could also aggravates the adverse reactions to radiotherapy [12].

The most severe manifestation is leukopenia, although only a few patients have grade III-IV leukopenia. Therefore, patients with weak or older locally advanced nasopharyngeal carcinoma failed to complete concurrent chemotherapy according to the current established protocol. With the application of granulocyte colony-stimulating factor, all patients could complete the radiotherapy plan. In this study, no significant adverse reactions were observed on the gastrointestinal tract, liver and kidney function, and leukocyte toxicity caused by concurrent chemotherapy (p 0.05). Patients in the HT group have certain advantages in reducing adverse reactions, which improves patient compliance during radiotherapy. In this study, 9 patients in the IMRT group did not complete all chemotherapy, while only 5 patients in the HT group did not complete the planned concurrent chemotherapy, and the difference was statistically significant ($p < 0.05$). Simultaneously, there was no significant difference in fatigue and weight loss between the two groups after radiotherapy. The analysis showed that fatigue and weight loss were mainly related to the diet, while oral ulcer reactions and gastrointestinal reactions caused by chemotherapy in both group showed no significant difference.

In terms of short-term efficacy, the difference between these two groups of patients was not statistically significant (p 0.05), and the results were consistent with those reported in previous literature [20]. These results indicated that the advantages of HT in dosimetry and OAR protection have not been translated into short-term efficacy improvement. After radiotherapy, the KPS score of patients in the HT group was improved compared with those in conventional IMRT group. This may be related to the fact that less harmful of OAR such as the parotid gland and other organs in the HT group, and more faster recovery of the patient physical condition after radiotherapy.

There are several limitations in present study. First, due to the short follow-up time, data on progression-free survival (PFS) and overall survival (OS) are not yet available. Second, this study was relative a small sample size. In the future, we will continue to expand the sample size, further observe the late adverse reactions and long-term effects of patients, thereby more objectively evaluation of the value of HT in the nasopharyngeal carcinoma treatment.

Conclusions

In summary, compared with conventional IMRT, HT has a greater advantage in locally advanced nasopharyngeal carcinoma radiotherapy. In terms of radiophysics, it mainly has better dosimetry advantages. HT can effectively reduce the exposure doses to the organs at risk, such as the parotid gland and inner ear, and reduce the incidence of acute adverse reactions, which could be helpful in the improvement of the quality of life of the patients.

Abbreviations

AJCC: American Joint Committee on Cancer, CI: Conformity index, CR: complete response, HI: Homogeneity Index, HT:helical tomotherapy, IGRT: Image-Guided Intensity Modulated Radiotherapy, IMRT:intensity-modulated radiotherapy, MRI: magnetic resonance imaging, NPC: nasopharyngeal

carcinoma, OAR: organ at risk, PD: progress disease, $pGTV_{nx}$: gross tumor volume, $pGTV_{nd}$: positive lymph nodes, PR: partial remission, PTV1:the high risk planning target volume, PTV2: the low risk planning target volume, RECIST: Response evaluation criteria in solid tumors, RTOG/ EORTC: American Radiation Therapy Oncology Group /European Organization for Research on Treatment of Cancer, SD: stable disease.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical committee of the First Affiliated Hospital of Bengbu Medical College, and written informed consent was provided by all the included patients.

Consent for publication

All authors approved the manuscript

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

ZC, JL, QS, HJ conceived the study and managed it. ZC, JL, QS, CW, MF, ZH, DL, HJ performed the data analysis. ZC, JL, QS, CW, MF, ZH, DL, HJ collected the data and built the database. ZC, JL, QS, HJ drafted the manuscript.

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Tables

Table 1. Basic characteristics of patients

Characteristics	n	HT group	IMRT group	*Chi-square*	*p*
Sex				0.041	0.839
male	109	54	55		
female	31	16	15		
Age (yrs)	51.41±13.75	49.63±14.70	53.19±12.58	1.539	0.126
Histology				0.522	0.770
squamous cell	18	10	8		
differentiated non-keratinizing	48	25	23		
non-keratinizing undifferentiated	74	35	39		
Stage				0.463	0.496
III	78	37	41		
IVa	62	33	29		

Table 2. Dosimetric data comparisons of target volumes between HT group and IMRT group

	HT group	IMRTgroup	*t*	*p*
PGTVnx				
CI	0.911±0.012	0.899±0.032	2.938	0.004
HI	1.055±0.006	1.059±0.013	2.337	0.021
PGTVnd				
CI	0.906±0.016	0.877±0.041	5.513	0.000
HI	1.084±0.040	1.023±0.031	10.085	0.000
PTV1				
CI	0.898±0.021	0.863±0.032	8.123	0.000
HI	1.186±0.020	1.205±0.026	4.846	0.000
PTV2				
CI	0.885±0.025	0.836±0.016	13.812	0.000
HI	1.082±0.018	1.089±0.023	2.005	0.047

PGTVnd = prescription doses delivered to the positive lymph nodes; pGTVnx = prescription doses delivered to the gross tumor volume

Table 3. Comparison of dosage data of organs at risk between HT group and IMRT group

Organ	Dmax			Dmean		
	HT	MRT	*p* value	HT	IMRT	*p* value
Eyeball	20.260±6.211	22.920±7.216	<0.05	5.021±1.420	6.046±2.098	<0.05
Lens	3.920±1.781	4.675±0.452	<0.05	2.846±1.327	4.543±0.754	<0.01
Optic nerve	31.579±14.650	32.877±7.908	0.05	24.543±8.806	26.650±7.098	0.05
optic chiasm	33.321±12.780	34.869±16.761	0.05	27.763±9.908	28.322±12.421	0.05
Brainstem	51.078±5.257	54.097±2.547	<0.01	34.564±5.356	37.120±6.096	<0.05
Spinal cord	37.076±3.215	41.879±2.037	<0.01	27.017±5.039	30.065±2.107	<0.01
Parotid gland	71.457±2.984	74.024±2.890	<0.01	35.768±3.553	39.089±2.021	<0.01
Inner ear	54.190±3.365	56.090±2.213	<0.01	38.900±3.470	47.625±3.651	<0.01
Oral cavity	61.900±11.134	67.290±9.780	<0.05	31.180±7.064	39.620±6.347	<0.01
Mandible	61.450±7.650	63.650±5.901	0.05	46.190±8.768	43.713±6.665	0.05

Dmean = mean dose (Gy); Dmax = maximum dose (Gy)

Table 4. Adverse reactions comparison between HT group and IMRT group.

	HT group					IMRT group					uc	p
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4		
Mucositis	0	11	43	16	0	0	18	31	20	1	0.154	0.878
Hearing loss	56	3	1	0	0	48	7	4	1	0	2.174	0.030
parotid glands injury	9	45	16	0	0	0	28	42	0	0	4.867	0.000
Skin reaction	1	8	48	12	1	0	11	48	11	0	0.600	0.548
Dysphagia	5	60	4	1	0	4	55	9	2	0	1.419	0.156
gastrointestinal reaction	4	51	12	3	0	5	46	17	2	0	0.467	0.640
Leucopenia	26	9	22	10	3	20	7	25	11	7	1.454	0.146
Thrombocytopenia	52	12	4	2	0	49	15	5	1	0	0.493	0.622
liver function damage	62	6	2	0	0	65	2	3	0	0	0.817	0.417
Kidney impariment	68	2	0	0	0	67	2	1	0	0	0.467	0.641
fatigue	4	42	24	0	0	3	50	17	0	0	1.043	0.297
Weight loss	20	30	12	8	0	15	25	12	0	0	0.680	0.497

Table 5: Comparison of short-term efficacy between HT group and IMRT group

Group	n	CR	PR	SD	PD	ORR(%)	x^2	*P value*
HT group	70	44	22	4	0	94.29	0.119	0.730
IMRT group	70	40	25	4	1	92.86		

CR = complete response; PR = partial response; ORR = overall response rate; SD = stable disease; PD = progressive disease