Dosimetric variations of target volumes and organs at risk in nasopharyngeal carcinoma intensity-modulated radiotherapy

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Objective: The aim of this study was to evaluate the actual dose variability to the targets and organs at risk (OARs) during nasopharyngeal carcinoma (NPC) intensity-modulated radiotherapy (IMRT) and to investigate the significance of replanning.

Methods: 11 NPC patients were included in this study. Each patient had both a planning CT and weekly repeated CT. Simulated plans that were generated by using the same beam configurations mapped to the repeated CT represented the actual delivered doses to the target volumes and OARs. An IMRT replanning was performed with the fifth week CT scan. Doses among the initial plan, the simulated plans and replanning were compared.

Results: There were no significant dosimetric differences in the gross tumour volume, clinical target volume (CTV) 1 or CTV2 for either the simulated plans or the replanning compared with the initial plan. Dosimetric variability of both parotid glands and the brain stem were unique to each individual, and doses to the spinal cord were always maintained within the limit. Replanning in the fifth week had significantly decreased the doses delivered to both parotids (*p*-values of the mean dose were 0.015 and 0.026 for the left and right parotid, respectively), whereas it did not reduce the doses to the brain stem and spinal cord. There was no relationship between dose variability and weight loss.

Conclusions: There are no significant dose changes for target volumes and spinal cord, and doses to the brain stem and both parotid glands changed individually during NPC IMRT. Replanning helps to spare bilateral parotids.

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Nasopharyngeal carcinoma (NPC) is common in China. Radiotherapy (RT) is the primary treatment modality, and the chance of recovery is highly dependent on tumour stage and delivered doses. Recently, intensity-modulated RT (IMRT) has become widely adopted in the treatment of NPC because of its capacity to provide more conformal dose distributions with steep dose gradients and to spare the surrounding organs at risk (OARs). For these reasons, it may achieve excellent local control and decrease toxicity [1, 2]. However, many authors have reported that head and neck cancer patients undergo significant anatomical changes during a 6–7 week treatment course, which may be related to a series of factors, including tumour shrinkage and weight loss. Barker et al [3] reported on the geometric and volumetric changes of 14 head and neck cancer patients during the course of RT with frequent CT imaging. Obvious measurable anatomic changes occurred throughout IMRT. Gross tumour volumes decreased at a median rate of 0.2 cm³ per treatment day, while parotid glands decreased at a median rate of 0.19 cm³ per day and shifted medially because of weight loss due to treatment. Robar et al [4] documented that both parotid glands showed a median translation of 0.85 mm per week, and

glands shrank by 4.9% per week. In the study by Kuo et al [5], the lymph nodes in head and neck cancer underwent a volume reduction of more than 50% after 45 Gy of treatment, which may increase actual radiation doses to the parotid glands. These anatomical changes would probably cause overdose to the OARs and underdose to targets, which would negate the benefits of IMRT. Whether replanning during the treatment will ensure the prescription doses to both targets and OARs is unknown. We therefore conducted this pilot study to investigate the dosimetric changes in target volumes and OARs using frequent CT images throughout the NPC IMRT treatment course. This study will also further clarify the significance of replanning.

Methods and materials

Patient sample

Consecutive patients with NPC were selected. All were treated between August 2007 and January 2009 at the radiation oncology department of the Cancer Hospital of the Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. To be included in this study, patients were required to have obvious gross nasopharyngeal masses, definitely receive concurrent chemotherapy and radiation treatment, and accept consecutive weekly CT scans during the treatment course. All of the patient treatments involved concurrent radiation therapy using IMRT and chemotherapy with

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Table 1. Patient sample

Patient number	Sex	Age (years)	Diagnosis	Stage (2002 UICC/AJCC)	Chemotherapy	Weight loss (%)	IMRT (GTV doses/fractions)
1	M	41	NPC	T2N2	Yes	5.3	69.96/33
2	M	48	NPC	T3N1	Yes	5.3	73.92/33
3	F	54	NPC	T3N1	Yes	4.1	73.92/33
4	F	38	NPC	T4N2	Yes	3.7	73.92/33
5	F	40	NPC	T4N2	Yes	0	73.92/33
6	M	46	NPC	T4N0	Yes	1	73.92/33
7	M	39	NPC	T2N2	Yes	4.7	69.96/33
8	F	50	NPC	T4N0	Yes	2.3	73.92/33
9	M	40	NPC	T3N2	Yes	7.7	73.92/33
10	M	58	NPC	T3N0	Yes	6	73.92/33
11	M	46	NPC	T4N1	Yes	11	73.92/33

F, female; GTV, gross tumour volume; IMRT, intensity-modulated radiotherapy; M, male; NPC, nasopharyngeal carcinoma, non-keratinising, undifferentiated subtype.

cisplatin at a weekly dose of 30 mg m⁻². The weekly total body weight of each patient was recorded on the same weekday. The study was approved by the institutional review board and informed consent was obtained from each patient before treatment.

CT imaging and treatment planning

After patients were immobilized with a head and neck thermoplastic mask (MedTech, Orange, CT), a CT scan was acquired for initial IMRT planning. In addition, weekly CT scans were acquired for each patient until the fifth week of the treatment course. Each patient received the repeated scans on the same weekday throughout the treatment. All the CT scans were obtained on a helical CT scanner (BrillianceTM CT; Philips Medical Systems, Cleveland, OH) with 3 mm slice space, using the same patient set-up. The scan started from the vertex to 3 cm inferior to the clavicles. Both the initial CT scan and the fifth-week scan were contrast enhanced, whereas the other weekly scans were not. One planning set of images plus 5 weekly images totalled 6 CT scans for each of the 11 patients, resulting in a total of 66 images acquired for this analysis.

Both target volumes—gross tumour volume (GTV) and clinical target volumes 1 and 2 (CTV1 and CTV2)—and organs at risk (OARs; bilateral parotids, spinal cord and brain stem) were contoured on the axial slices of the planning CT scan by a resident physician and approved by an attending physician. According to the International Commission on Radiation Units and Measurements (ICRU) reports 50 and 62 [6, 7], the GTVs were composed

of visible tumour and/or enlarged or suspicious lymph nodes; CTV1 included the high-risk regions surrounding the primary tumour and the upper neck nodes at risk; CTV2 included the mid-lower nodes at risk. The planning target volumes (PTVs) were generated by adding a 3 mm margin to the CTVs. The planning organ at risk volumes (PRVs) were generated for the brain stem and spinal cord by adding 3 mm and 5 mm margins, respectively.

All of the IMRT plans were created on the Pinnacle³ treatment planning system (Philips/ADAC, Milpitas, CA) using nine coplanar beams with 6 MV photons. The simultaneous intensity boost (SIB) technique was used to deliver higher doses to primary tumours at the same time. All PTVs were covered by the 95% isodose. The GTVs received doses of 69.96 Gy in 33 fractions for T1–T2 tumours, and 73.92 Gy in 33 fractions for T3–T4 tumours, while PTV1 received 60.06 Gy in 33 fractions and PTV2 received 50.96–56 Gy in 28 fractions. Doses of OARs were subject to the following restrictions: spinal cord <45 Gy, brain stem <54 Gy and at least 50% of the parotids <30–35 Gy.

Recontouring and dosimetric comparisons

Recontouring of the target volumes and OARs was performed on the repeated CT scans. This was completed by the same physicians in order to minimize the delineation variability between observers. In our centre, the method for recontouring GTVs was somewhat different from that reported by the University of California–San Francisco, in which the original size of GTVs was maintained so as to ensure an adequate dose to

Table 2. Dosimetric parameters of gross tumour volume comparisons (mean ± standard deviation)

Time	Dmean (Gy)	D95 (Gy)	D90 (Gy)	D10 (Gy)	D5 (Gy)	V100 (%)
Pre-week	15.88 ± 0.26	15.42 ± 0.28	15.56 ± 0.28	16.24 ± 0.26	16.34 ± 0.26	97.6 ± 2.2
Week 1	15.92 ± 0.41	15.29 ± 0.40	15.49 ± 0.38	16.36 ± 0.44	16.48 ± 0.44	94.0 ± 5.8
Week 2	15.83 ± 0.30	15.17 ± 0.32	15.38 ± 0.34	16.25 ± 0.32	16.34 ± 0.32	96.6 ± 2.8
Week 3	15.85 ± 0.32	15.16 ± 0.32	15.37 ± 0.35	16.30 ± 0.30	16.40 ± 0.30	95.3 ± 4.1
Week 4	15.86 ± 0.35	15.16 ± 0.34	15.38 ± 0.36	16.31 ± 0.32	16.41 ± 0.32	96.7 ± 3.4
Week 5	15.94 ± 0.28	15.33 ± 0.34	15.45 ± 0.34	16.34 ± 0.17	16.44 ± 0.19	97.3 ± 4.3
F-value	0.095	0.617	0.283	0.135	0.143	0.720
p-value	0.992	0.688	0.919	0.983	0.981	0.614

D5, dose to 5% of the volume; D10, dose to 10% of the volume; D90, dose to 90% of the volume; D95, dose to 95% of the volume; Dmean, mean dose; V100, volume of receiving prescription dose.

Table 3. Dosimetric parameters of clinical target volume 1 comparisons (mean $\pm$ standard deviation)

Time	Dmean (Gy)	D95 (Gy)	D90 (Gy)	D10 (Gy)	D5 (Gy)	V100 (%)
Pre-week	14.45 $\pm$ 0.47	13.37 $\pm$ 0.25	13.55 $\pm$ 0.28	15.53 $\pm$ 0.57	15.86 $\pm$ 0.35	99.2 $\pm$ 0.4
Week 1	14.43 $\pm$ 0.49	13.25 $\pm$ 0.29	13.51 $\pm$ 0.36	15.57 $\pm$ 0.54	15.92 $\pm$ 0.36	96.8 $\pm$ 3.2
Week 2	14.34 $\pm$ 0.45	13.13 $\pm$ 0.25	13.39 $\pm$ 0.28	15.48 $\pm$ 0.57	15.84 $\pm$ 0.36	96.7 $\pm$ 4.4
Week 3	14.25 $\pm$ 0.54	13.15 $\pm$ 0.22	13.67 $\pm$ 0.55	15.17 $\pm$ 0.70	15.50 $\pm$ 0.68	96.5 $\pm$ 4.4
Week 4	14.37 $\pm$ 0.50	13.11 $\pm$ 0.34	13.39 $\pm$ 0.36	15.50 $\pm$ 0.56	15.85 $\pm$ 0.36	95.3 $\pm$ 6.2
Week 5	14.39 $\pm$ 0.49	13.18 $\pm$ 0.28	13.42 $\pm$ 0.31	15.50 $\pm$ 0.55	15.87 $\pm$ 0.34	96.8 $\pm$ 4.2
F-value	0.149	0.698	0.513	0.354	0.745	0.528
p-value	0.979	0.629	0.764	0.876	0.596	0.753

D5, dose to 5% of the volume; D10, dose to 10% of the volume; D90, dose to 90% of the volume; D95, dose to 95% of the volume; Dmean, mean dose; V100, volume of receiving prescription dose.

this high-risk volume [8]. The new GTVs were generated by removing the air cavity that was formed by tumour shrinkage while maintaining the other dimensions of the primary GTVs [9]. The new CTVs and PTVs were generated by maintaining the original contours, but with modifications that made sure they did not extend beyond the skin contour or into adjacent normal structures. OARs were again contoured on the repeated CT scans slice by slice. The new parotid volumes were recontoured based on the volumetric changes.

The grey value registration was used to ensure the same isocentre between the initial helical CT and weekly CTs. After recontouring, the initial treatment plan was mapped to the repeated CT scans with the same beam configurations. These plans were referred to as “simulated plans”, and they represented actual delivered doses to the target volumes and OARs. In addition, a new “replanning” plan was created using the fifth-week images and contours with the same optimization parameters. To determine the effect of anatomic changes on doses, the original plan was compared with the weekly simulated plans. To determine whether replanning is beneficial, the fifth-week simulated plan was also compared with the replanning plan. The dosimetric changes of the target volumes were compared using common dose–volume parameters such as the mean dose (Dmean), dose to 95% of the volume (D95), dose to 90% of the volume (D90), dose to 10% of the volume (D10), dose to 5% of the volume (D5) and V100 (volume of receiving prescription dose). For the OARs, comparisons were quantified using the dose to 1% of the volume (D1) and the maximum dose (Dmax) for brain stem and spinal cord, and Dmean, V20 and V30 for bilateral parotids. Since the simulated plans and replanning were within the scope of the study, patients were still treated on the initial plan.

Statistical analysis

Comparisons between the primary prescribed doses to the target volumes and OARs and the weekly actual delivered doses were evaluated using analysis of variance. Dose comparisons between the replanning and the fifth-week simulated plan were performed by analysis of paired samples *t*-test. All *p*-values are two-sided. A value of *p* < 0.05 was considered statistically significant. The correlation between dose changes and weight losses was determined using two-tailed Spearman correlation analysis. All statistics were calculated using SPSS® for Windows v. 13.0 (SPSS Inc., Chicago, IL).

Results

The patient sample was highly homogeneous in terms of site, stage and treatment modality (Table 1). Of the 11 patients, 4 patients were female and 7 were male, all patients had locally advanced non-metastatic stage III–IV NPC. All patients completed at least 6 weeks concomitant chemotherapy according to our study protocol and no one missed the CT scans. Compliance was excellent.

Dosimetric comparisons

Target volumes

There were no significant dosimetric differences between the initial IMRT plan and the subsequent simulated plans for GTV, CTV1 or CTV2 (Tables 2–4). Similarly, dose differences between the fifth-week simulated plan and the replanning were also of no significance (Table 5). The *p*-values for all the parameters were >0.05. That is, although tumours gradually shrank through the RT

Table 4. Dosimetric parameters of clinical target volume 2 comparisons (mean $\pm$ standard deviation)

Time	Dmean (Gy)	D95 (Gy)	D90 (Gy)	D10 (Gy)	D5 (Gy)	V100 (%)
Pre-week	13.67 $\pm$ 0.15	13.20 $\pm$ 0.10	13.31 $\pm$ 0.12	14.05 $\pm$ 0.19	14.16 $\pm$ 0.20	99.6 $\pm$ 0.2
Week 1	13.26 $\pm$ 1.15	13.15 $\pm$ 0.37	13.31 $\pm$ 0.35	14.20 $\pm$ 0.37	14.31 $\pm$ 0.38	97.5 $\pm$ 3.3
Week 2	13.64 $\pm$ 0.30	13.05 $\pm$ 0.24	13.22 $\pm$ 0.25	14.14 $\pm$ 0.33	14.26 $\pm$ 0.33	97.4 $\pm$ 2.7
Week 3	13.64 $\pm$ 0.29	13.06 $\pm$ 0.23	13.22 $\pm$ 0.24	14.13 $\pm$ 0.30	14.26 $\pm$ 0.30	97.6 $\pm$ 2.1
Week 4	13.65 $\pm$ 0.28	12.94 $\pm$ 0.35	13.16 $\pm$ 0.30	14.15 $\pm$ 0.29	14.28 $\pm$ 0.29	95.8 $\pm$ 3.4
Week 5	13.67 $\pm$ 0.19	13.05 $\pm$ 0.12	13.22 $\pm$ 0.15	14.55 $\pm$ 0.95	14.70 $\pm$ 0.98	97.8 $\pm$ 1.3
F-value	0.463	0.586	0.258	0.675	0.737	1.182
p-value	0.8	0.711	0.932	0.646	0.603	0.347

D5, dose to 5% of the volume; D10, dose to 10% of the volume; D90, dose to 90% of the volume; D95, dose to 95% of the volume; Dmean, mean dose; V100, volume of receiving prescription dose.

Table 5. Dose comparisons between the fifth-week simulated plan and replanning

Objects	Parameters	Simulated plan (5th week)	Replanning	p-value
GTV	Dmean	15.94 ± 0.28 Gy	15.87 ± 0.21 Gy	0.332
	D95	15.33 ± 0.34 Gy	15.03 ± 0.53 Gy	0.093
	D5	16.44 ± 0.19 Gy	16.39 ± 0.22 Gy	0.054
CTV1	Dmean	14.39 ± 0.49 Gy	14.35 ± 0.53 Gy	0.119
	D95	13.18 ± 0.28 Gy	13.24 ± 0.27 Gy	0.063
	D5	15.87 ± 0.34 Gy	15.92 ± 0.32 Gy	0.249
CTV2	Dmean	13.67 ± 0.19 Gy	13.67 ± 0.18 Gy	0.934
	D95	13.05 ± 0.12 Gy	13.08 ± 0.13 Gy	0.557
	D5	14.70 ± 0.98 Gy	14.73 ± 1.01 Gy	0.443
Pd-L	Dmean	36.78 ± 3.5 Gy	31.51 ± 3.5 Gy	0.008
	V30	54.6 ± 8.0%	41.9 ± 8.1%	0.002
	V20	85.6 ± 6.8%	70.4 ± 14.7%	0.016
Pd-R	Dmean	34.85 ± 5.7 Gy	31.02 ± 2.3 Gy	0.041
	V30	48.2 ± 13.2%	40.4 ± 6.1%	0.05
	V20	79.1 ± 10.1%	68.3 ± 9.7%	0.016
Spinal cord	D1	28.49 ± 0.55 Gy	27.27 ± 0.42 Gy	0.391
	Dmax	33.2 ± 0.58 Gy	30.23 ± 0.33 Gy	0.065
Brain stem	D1	42.1 ± 0.79 Gy	35.92 ± 0.58 Gy	0.241
	Dmax	49.46 ± 0.83 Gy	43.56 ± 0.55 Gy	0.236

CTV, clinical target volume; D1, dose to 1% of the volume; D5, dose to 5% of the volume; D95, dose to 95% of the volume; Dmax, maximum dose; Dmean, mean dose; GTV, gross tumour volume; L, left; Pd, parotid; wk, week; R, right. A value of $p < 0.05$ was considered statistically significant.

treatment course, the primary IMRT plan could still offer adequate coverage to the target volumes.

Bilateral parotid glands

Bilateral parotid glands in this study shifted medially during the course of RT. It was interesting to note that the volumes of both parotids decreased to a plateau at weeks 4–5 (Figure 1). Table 6 demonstrates the dosimetric changes of both parotids during the RT course. Mean doses of both parotids showed a tendency to increase (Figures 2 and 3); however, they differed among individual patients (Table 6). That is, patients 1–4 had significant Dmean changes of the left parotids, whereas patients 9–11 experienced significant Dmean changes of the right parotids. The changes in parameters V20 and V30 were similar to those seen in Dmean. Meanwhile, replanning in the fifth week significantly decreased the doses delivered to both parotids (p -values of Dmean were 0.008 and 0.041 for the left and right parotid, respectively; Table 5).

Brain stem and spinal cord

Dosimetric variability in the brain stem was large. It was seen from the simulated plan DVHs that approximately

11.8% of D1 and 19.6% of Dmax parameters were out of dose constraint on the brain stem compared with the initial plans. However, replanning did not reduce the doses to the brain stem and spinal cord (p -values of Dmax were 0.065 and 0.236 for the brain stem and spinal cord, respectively; Table 5). Whereas the brain stem had some outliers, doses to the spinal cord always remained within the limits for both D1 and Dmax (Figures 4–7).

Correlation between dosimetric variability of organs at risk and weight loss

All of the patients except one lost weight during the concurrent chemoradiotherapy treatment course. The median weight loss was 4.6%, with ranges from 0% to 11%. To clarify the relationship between dosimetric variability of OARs and weight loss, a two-tailed Spearman correlation was calculated. Weight loss was not correlated with either small or large OAR dose changes (the Spearman correlation coefficients and p -values were -0.247 and 0.465 for the left parotid Dmean, -0.116 and 0.75 for the right parotid Dmean, 0.213 and 0.53 for the spinal cord D1, and -0.352 and 0.289 for the brain stem D1, respectively).

Figure 1. Total parotid volume changes during nasopharyngeal carcinoma intensity-modulated radiotherapy.

Table 6. Mean dose changes of both parotids

Patient number	Left parotid		Right parotid	
	Mean $\pm$ SD	Max-min	Mean $\pm$ SD	Max-min
1	1.14 $\pm$ 0.13	1.37–1.01	1.07 $\pm$ 0.06	1.16–0.98
2	1.14 $\pm$ 0.15	0.9–1.3	0.94 $\pm$ 0.1	1.1–0.84
3	1.14 $\pm$ 0.04	1.2–1.1	1 $\pm$ 0.05	1.1–0.96
4	1.17 $\pm$ 0.06	1.22–1.09	1.04 $\pm$ 0.11	1.2–0.88
5	1.06 $\pm$ 0.13	1.16–0.82	1.01 $\pm$ 0.04	1.09–0.95
6	1.05 $\pm$ 0.07	1.17–0.98	0.99 $\pm$ 0.1	1.12–0.87
7	1 $\pm$ 0.02	1.04–0.95	1.02 $\pm$ 0.21	1.39–0.85
8	0.97 $\pm$ 0.06	1.01–0.86	1.04 $\pm$ 0.01	1.06–1.01
9	1.06 $\pm$ 0.12	1.26–0.94	0.86 $\pm$ 0.11	1.07–0.78
10	1.08 $\pm$ 0.11	1.21–0.95	1.19 $\pm$ 0.17	1.45–1.05
11	0.97 $\pm$ 0.06	1.05–0.88	0.79 $\pm$ 0.03	0.73–0.82

Max, maximum; min, minimum; SD, standard deviation.

Data were collected by calculating the ratio of weekly parotid mean dose to plan mean dose. A ratio of more than 1.1 was considered to be large.

Discussion

This study demonstrates the dosimetric variability of target volumes and OARs during an NPC IMRT course,

including GTV, CTV1/2, parotid, brain stem and spinal cord, as well as the significance of replanning at the fifth week. Our results reveal that there are no significant dose changes of target volumes and spinal cord. For

Figure 2. Mean dose changes (Dmean) of the left parotid during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

Figure 3. Mean dose changes (Dmean) of the right parotid during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

other OARs, such as the brain stem and both parotids, while some experienced large dose variability, others varied only slightly. This dosimetric variability of OARs had no correlation with weight loss, which was different from Lee et al's report. Median weight change of their patients was only 3.3%; however, a correlation did exist. Another important finding of this study is related to replanning, which reduced the actual delivered doses to the parotid glands. Based on our findings, we believe that there is a benefit to bilateral parotids through replanning, which may further improve xerostomia and quality of life in patients with NPC. In addition, since the primary plan always covered the target volumes, we may expect that there is no need for replanning in response to target volumetric changes. Our results are consistent with the literature.

Because the nasopharynx is such an anatomically challenging region, owing to its location near a series of critical normal organs such as the brain stem, spinal cord and optic chiasm, IMRT is ideal for delivering a high

dose to the nasopharynx while sparing the surrounding OARs. However, patients receiving RT to the head and neck region always experience significant anatomical changes during the treatment course, including tumour and/or nodal shrinkage, contour changes due to weight loss, and fluid shifts, which probably result in deviation of the doses to both targets and OARs from the prescribed doses. Thus, increasing interest regarding dosimetric changes during head and neck IMRT has been provoked in recent years. The earliest study was reported by Hansen et al in 2006 [8]. A total of 13 patients were enrolled in their analysis, comprising 6 NPCs, 6 oropharyngeal carcinomas and 1 unknown primary site carcinoma. Owing to tumour shrinkage and weight loss during the treatment course, a second IMRT plan was generated based on the second CT scan that was performed on an average number of 19($\pm$ 6) fractions. At the same time, a hybrid IMRT plan was also generated by applying the beam configurations of the first IMRT plan to the anatomy of the second CT scan. Then, doses to target volumes and OARs were compared

Figure 4. Maximum dose (Dmax) changes of spinal cord during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

Figure 5. Dose to 1% (D1) volumes of spinal cord changes during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

between the replanning and hybrid plan. The results demonstrated that IMRT replanning could significantly increase doses to target volumes and decrease doses to OARs. In a study [4] of head and neck cancer patients with different primary sites, as well as different treatment modalities, at least three repeated CT scans were acquired for each patient 1 week into treatment, and weekly thereafter. After the initial plan was recalculated on all the CT sets, a significant dose variability was described in the left parotid and inferior spinal cord but not in the right parotid, brain stem and superior spinal cord. However, individual patients might have large dose changes in these organs. For example, an individual patient might have a mean difference of the maximal dose as great as 5–7%, whereas the mean maximal dose of the entire sample was within 1%. The advent of deformable image registration makes assessing the dosimetric variations with cumulative doses more accurate. Lee et al [10] reported on a series of 10 head and neck cancer patients. They observed that the daily mean parotid dose differed from the plan dose by an average of 15%; however, 3 patients received a mean parotid dose 33% higher than the originally planned dose.

Although these authors reached different conclusions regarding the dosimetric changes of target volumes and OARs, they held the same opinions that multiple factors might have contributed to the dosimetric variability, including relative locations of target volumes and OARs, different shrinkage rates of tumour masses and parotid glands, different weight changes, variability of selected margins, variable target delineations and beam arrangements, and proximal dose gradients [4, 8, 10, 11]. Based on this analysis, we found the studies mentioned above highly heterogeneous. That is, different sites and stages were involved in these studies, as well as primary and recurrent tumours and post-operative treatment, which affected doses to OARs to some extent. With this in mind, we therefore enrolled 11 patients who were diagnosed with locally advanced

NPC and all of them were treated with IMRT combined with concurrent chemotherapy.

There is little in the literature regarding dosimetric changes of target volumes. Wu et al [12] presented an analysis of 11 head and neck cancer patients for whom weekly helical CT scans were performed. The deformable registration technique was used to compute the cumulative doses. Compared with the original treatment plan, cumulative doses to the target volumes from all weekly CTs did not change; that is, replanning was not necessary for tumours to account for the volumetric changes. The actual delivered parotid gland dose was 10% higher than in the initial plan, so replanning would provide some sparing. However, other OARs such as brain stem, spinal cord and mandible would not benefit from replanning because doses to them were remarkably stable. Our results are consistent with the report by Wu et al [12] in terms of dose variability to the target volumes, whereas there is some dose variability to the OARs. This might be partly due to the bias in selecting cases. We had 11 stage III–IV NPC patients, while in Wu et al's study 11 locally advanced head and neck patients were involved.

Two questions arise from this study. First, unlike other studies, repeated CT scans in our series were acquired weekly only until the fifth week, rather than for the whole treatment. The strategy in obtaining repeated CT scans was initially designed to analyse changes of parotid volumes during NPC IMRT [13, 14], but it also contributed to the current study. In addition, our previous study has shown that the reduction of parotid volumes reaches a plateau at weeks 4–5 during NPC IMRT [13, 14]. As such, we conducted five consecutive weekly CT scans. However, this is different from the findings of Barker et al [3] and Bhide et al [15], who noticed that the plateau was at week 3–4. Anatomical disparity between patient populations, as well as parotid delineation variability between institutions (we routinely delineate the parotid to include both the superficial lobe and the deep lobe), were

Figure 6. Maximum dose (Dmean) changes of brainstem during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

Figure 7. Dose to 1% (D1) volumes of brain stem changes during nasopharyngeal carcinoma intensity-modulated radiotherapy (95% confidence intervals).

the probable causes of the different results. The other question is why we replanned at the fifth week. This is probably related to the following three reasons. (1) Based on the finding in our previous study mentioned above [13, 14] that reduction of parotid volumes reached a plateau at week 4–5, we therefore presume that doses to the parotids would not change significantly if their volumes remain stable. (2) Repeated CT imaging and replanning is laborious because of the increased workload for both physicists and dosimetrists, and the increased time spent for recontouring. (3) In a recent study by Wu et al [16], different IMRT replanning strategies for head and neck cancer were evaluated. There was no need for replanning more than once a week, and the improvement in parotid sparing saturated quickly beyond two replannings.

It should be noted that the initial planning CT scan and the repeated images obtained during the treatment course are merely snapshots of the whole course. As a result, this study offers a series of doses at the time of scanning, so it could not be completely accurate in terms of the actual delivered doses to the target volumes and OARs. However, this pilot study shows results of dosimetric discrepancy that offer some justification for replanning. In addition, larger sample sizes will be needed to further validate the conclusions acquired in this study.

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