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Clinical investigation

Parotid gland-sparing 3-dimensional conformal radiotherapy results in less severe dry mouth in nasopharyngeal cancer patients: A dosimetric and clinical comparison with conventional radiotherapy

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Abstract

***Background and purpose*: This study examined the efficacy of parotid gland sparing of three-dimensional conformal radiotherapy (3DCRT) compared with conventional radiotherapy for NPC patients. Both the dose given to the parotids and clinical assessment of dry mouth were conducted.**

***Materials and methods*: Dry mouth was assessed for 108 patients treated with conventional technique and 72 treated with 3DCRT. Dose analysis was performed in 48 patients of the 3DCRT group. A dose of 70 Gy was given to the midplane in conventional radiotherapy and to 90% isodose volume in 3DCRT. Prognostic factors affecting the severity of dry mouth were analyzed using Generalized Estimating Equation (GEE).**

***Results*: In the 3DCRT group about 50% of the patients' parotid glands received less than 25 Gy. Parallel analysis of dry mouth shows a significant decrease in the incidence of severe xerostomia after 3DCRT. The proportion of patients without dry mouth was also significantly higher in the 3DCRT group than the conventional group at 1–3 years after completion of radiotherapy. Although 3DCRT delivered a higher dose to the tumor, it spared the parotid gland significantly better than the conventional treatment. Late toxicities were mostly similar between the 2 groups while local control in T4 patients and survival were improved for 3DCRT.**

***Conclusion*: Dosimetrically and clinically 3DCRT is better than conventional technique regarding parotid gland protection.**

Keywords: Nasopharyngeal neoplasms; Three-dimensional conformal radiotherapy; Parotid gland; Xerostomia

Salivary gland damage with the subsequent xerostomia has been an unavoidable fate in nearly all nasopharyngeal carcinoma (NPC) patients using conventional radiotherapy portal arrangement [5,9]. This results from two facts: firstly, parotid gland receives direct impact of irradiation during conventional radiotherapy; and secondly, evidence from primates suggests that salivary gland may be one of the most radiosensitive organs in the body [20].

In order to reduce or prevent xerostomia in NPC patients for whom radiotherapy is mandatory, investigators have used various approaches, including salivary gland protecting drugs [1,16,25] and a 3-field conventional radiotherapy technique to decrease radiation dose to the parotids [15]. However, it is extremely difficult to spare the spinal cord and parotid glands as well as other critical organs without compromising tumor control using conventional radiotherapy for NPC that is surrounded by a complex anatomy. This makes three-dimensional conformal radiotherapy (3DCRT), which features a precise targeting and a three-dimensional (3D) display of the target in relation to its surrounding normal tissues, particularly attractive in theory for NPC.

Interestingly, although 3D technique has been widely used and frequently published in patients such as prostate cancer [2,6,19], lung cancer [18,23], and head and neck cancers other than NPC [3,4,21], very few publications are available reporting clinical experience of 3DCRT for NPC.

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Three-dimensional conformal radiotherapy has been assessed and used for NPC patients as early as 1991 [11,14], yet only preliminary results are available in the world literature reporting on 3D conformal boost on NPC patients. No particular intention to protect the parotid gland was mentioned in these studies [10,22]. Although dosimetric comparisons of conventional and 3D radiotherapy treatment plans have been reported, no attempt was made to spare the parotid glands [8], and the issue concerning the efficacy of parotid gland sparing using 3DCRT in NPC patients remains unaddressed.

Since 1998 we started replacing our conventional radiotherapy scheme with 3DCRT for NPC patients using a careful and gradual transition strategy. Subsequently we have treated 82 NPC patients using partly 3DCRT for 19 patients in the first year and then full 3DCRT for the rest of patients after gaining confidence of the technique. Our intentions were to reduce parotid gland damage and improve the quality of life of our NPC patients and at the same time achieve a more precise delivery of treatment. In this study, the efficacy of parotid gland sparing of 3DCRT compared to conventional radiotherapy was evaluated. This was done by both analyzing the dose to the parotid glands and assessing dry mouth data acquired clinically.

Materials and methods

Patients

This study analyzes data of 180 NPC patients including 108 treated with conventional radiotherapy and another 72 with 3DCRT during the period from Aug. 1998 to Jun. 2003. Only patients who completed full radiotherapy course were included. However, some patients with full radiotherapy during this period were not assessed for their dry mouth and were not included for analysis. They were histologically proved and had no previous cancer treatment. Patient characteristics are listed in Table 1. The criteria of the American Joint Committee on Cancer, 1997 were used for staging.

Table 1
Patient characteristics

Characteristics	Conventional	Three-dimensional conformal	*P* value
Number of patients	108	72	
Sex: male	89 (82.4%)	61 (84.7%)	0.439
female	19 (17.6%)	11 (15.3%)	
Age: median	43.5 years	43 years	0.437
range	18–84 years	19–80 years	
T 1[a]	44 (40.7%)	26 (36.1%)	0.610
2	28 (25.9%)	22 (30.6%)	
3	14 (13.0%)	6 (8.3%)	
4	22 (20.4%)	18 (25.0%)	
N 0[a]	19 (17.6%)	16 (22.2%)	0.888
1	53 (49.1%)	33 (45.8%)	
2	29 (26.9%)	19 (26.4%)	
3	7 (6.5%)	4 (5.6%)	
Stage 1[a]	3 (2.8%)	2 (2.8%)	0.919
2	42 (38.9%)	27 (37.5%)	
3	35 (32.4%)	21 (29.2%)	
4	28 (25.9%)	22 (30.6%)	

Figures indicate patient number except in the 'age' row.
[a] American Joint Committee on Cancer, 1997.

Radiotherapy technique

Conventional

The detailed portal arrangement and dosing have been previously described [9]. Briefly, conventional radiotherapy was given in 3 different phases. A total dose of 70 Gy was given to the midplane. Two large bilateral opposed fields were used to treat the nasopharynx and the upper neck, and an anterior port was applied to the rest of the neck and the supraclavicular fossa (SCF), with 1.8 Gy per fraction per day. When the dose reached 36 Gy, the second phase started with a pair of bilateral opposed reduced NP portals using spinal cord blocks. Another 24 Gy was delivered using 2 Gy per fraction per day and a field size of 7×8–8×10 cm. The entire neck and SCF were treated using a pair of anterior–posterior portals. In the third phase, right and left anterior oblique infraorbital portals 5×7–6×8 cm in size were applied using 2 Gy per fraction for another 10 Gy. The neck was treated as in phase 2 but usually with the SCF and lower neck shielded.

3D conformal

In 3DCRT, 70 Gy was given to the 90% isodose volume with 1.8 Gy per fraction throughout the entire course. Portal arrangement and size for the primary tumor were individualized according to the tumor size and location. Most 3DCRT used coplanar beams with 5–6 angles. A vertex, non-coplanar portal occasionally was used in some T4 patients. The lower neck and SCF were treated with a separate anterior port. Before simulation, all patients were immobilized with a facial mask. For 3DCRT patients, the mouth was held open with a mouth bite. A temporary isocenter was located and marked using an X-ray simulator. The patient was then brought to the Diagnostic Radiology unit for a scanning. CT images were obtained from the vertex down to the clavicles with a Siemens CT unit. Slices of 3 mm were obtained for the nasopharyngeal area. For the rest of the scanning, 0.5–1 cm intervals were used. The image data were run with a 3D computer planning system. Beam data of our 6MV photons from an Elekta Precise linear accelerator were used for planning.

Target contouring in 3D conformal radiotherapy

Nasopharynx

For 3D conformal planning, the clinical target volume (CTV) included the gross target volume (GTV) and the following: the medial pterygoid muscles, the parapharyngeal spaces, carotid space, the sphenoid sinus, posterior 1/3–1/4 nasal cavity, and the anterior 1/4–1/3 of the clivus and vertebral body. The lower margin was set at C2 in the absence of oropharyngeal extension. In patients with cavernous sinus or intracranial invasion, the cavernous sinus and the whole sella and suprasellar region were also included. We added an 8 mm margin to the CTV for setup errors except at the brainstem and spinal cord where the