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CLINICAL INVESTIGATION **Head and Neck**

SPATIAL AND DOSIMETRIC VARIABILITY OF ORGANS AT RISK IN HEAD-AND-NECK INTENSITY-MODULATED RADIOTHERAPY

James L. Robar, Ph.D.,*†‡ Allan Day, B.Sc.,‡ James Clancey, B.Sc.,‡ Robin Kelly, Ph.D.,*‡ Mammo Yewondwossen, Ph.D.,*‡ Helmut Hollenhorst, M.D.,*‡ Murali Rajaraman, M.D.,*‡ and Derek Wilke, M.D.*‡

Departments of *Radiation Oncology, and †Physics and Atmospheric Science, Dalhousie University, Halifax, NS, Canada; ‡Nova Scotia Cancer Centre, Halifax, NS, Canada

Purpose: The accuracy of intensity-modulated radiotherapy (IMRT) delivery may be compromised by random spatial error and systematic anatomic changes during the treatment course. We present quantitative measurements of the spatial variability of head-and-neck organs-at-risk and demonstrate the resultant dosimetric effects.
Methods and Materials: Fifteen consecutive patients were imaged weekly using computed tomography during the treatment course. Three-dimensional displacements were calculated for the superior and inferior brainstem; C1, C6, and T2 spinal cord; as well as the lateral and medial aspects of the parotid glands. The data were analyzed to show distributions of spatial error and to track temporal changes. The treatment plan was recalculated on all computed tomography sets, and the dosimetric error was quantified in terms of the maximal dose difference (brainstem and spinal cord) or the mean dose difference and the volume receiving 26 Gy (parotid glands).
Results: The mean three-dimensional displacement was 2.9 mm for the superior brainstem, 3.4 mm for the inferior brainstem, 3.5 mm for the C1 spine, 5.6 mm for the C6 spine and 6.0 mm for the T2 spine. The lateral aspects of both parotid glands showed a medial translation of 0.85 mm/wk, and glands shrank by 4.9%/wk. The variability of the maximal dose difference was described by standard deviations ranging from 5.6% (upper cord) to 8.0% (lower cord.) The translation of the left parotid resulted in an increase of the mean dose and the volume receiving 26 Gy.
Conclusion: Random spatial and dosimetric variability is predominant for the brainstem and spinal cord and increases at more inferior locations. In contrast, the parotid glands demonstrated a systematic medial translation during the treatment course and thus sparing may be compromised. © 2007 Elsevier Inc.

Intensity-modulated radiotherapy, IMRT, Head and neck, Spinal cord, Brainstem, Parotid.

INTRODUCTION

Treatment of head-and-neck cancer represents one of the most frequent applications of intensity-modulated radiotherapy (IMRT) (1). IMRT is a promising technique for this site because of its capacity to provide high-dose conformity to irregularly shaped, concave tumor volumes and, with the use of inverse-planning, to spare multiple, proximal organs at risk, including the brainstem, spinal cord, and parotid glands (2–4). The dosimetric goals are described using constraints during inverse treatment planning—a method that depends critically on the delineation of target volumes and organs at risk as determined from the imaging findings (*e.g.,* computed tomography [CT], magnetic resonance imaging, or positron emission tomography). Most commonly, treatment planning is performed using an image set acquired at a single point in time before treatment begins; however, this approach is inconsistent with observations (5–10) that the patient anatomy, as well as the setup of the patient anatomy relative to fixed reference points, are variable between sessions during a 5- to 7-week treatment course.

Spatial variability may arise from either random or systematic error. Sources of random error include limited repositioning of the patient within a thermoplastic mask or inaccuracy in aligning a predetermined anatomic point to the treatment room coordinate system (*e.g.,* the linear accelerator isocenter) (11–13). Random error produces blurring of the edge of the dose distribution, which moves higher isodose lines toward the target and lower isodose lines toward the organ at risk (14). Systematic errors produce a shift of the isodose distribution as a whole relative to the anatomy. Systematic errors that are constant for a patient throughout the treatment course include those arising during

Reprint requests to: James L. Robar, Ph.D., Nova Scotia Cancer Centre, 5820 University Ave., Rm. 3000A, Halifax, NS B3L 1S5, Canada. Tel: (902) 473-3546; Fax: (902) 473-6120; E-mail: James.robar@cdha.nshealth.ca

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treatment plan preparation and transfer (14) (*e.g.,* the effect of organ motion during imaging). Perhaps more complicated are the systematic errors that change during the treatment course such as tumor shrinkage and weight loss, causing a time–variant disparity between the planning and treatment anatomy. Barker *et al.* (6) reported on a series of 14 head-and-neck patients, who were treated mainly using non-IMRT techniques. This group observed a median rate of gross tumor volume (GTV) reduction of 0.2 cm^3/treatment day, accompanied by a median shift of the center-of-mass of the GTV of 3.3 mm by the end of treatment. Also observed were a median rate of the reduction of the parotid gland volume of 0.19 cm^3/d and a medial translation of the parotid glands (median, 3.1 mm by the end of treatment). This group did not observe the resultant dosimetric effects of these changes, and these effects are difficult to estimate intuitively, because they depend highly on the geometry of the dose distribution relative to the target volume and normal structures. Recently, Hansen *et al.* (5) presented an analysis of 13 patients for whom a second, midtreatment CT scan was prompted by observed weight loss or tumor shrinkage. Among this sample, recalculation of the treatment plan (without replanning) revealed an increase of the maximal dose to the spinal cord and brainstem for 100% and 85% of patients, respectively. In a recent study by Ballivy *et al.* (10), IMRT plans were generated for 8 patients who underwent CT imaging weekly, using a range of planning target volume (PTV) and planning risk volume (PRV) margins. The plans recalculated using the repeat CT scans showed a sensitivity of the dosimetric error to the margin selected.

The present work provides an analysis of a temporal series of CT imaging for 15 head-and-neck cancer patients, acquired during the treatment course. The data were analyzed using a two-part process. First, the spatial variability of the organs at risk was characterized. The specific goals of this analysis were as follows:

1. To determine the distributions of the three-dimensional spatial displacements, relative to the planning geometry, of selected points along the craniospinal axis, including the superior and inferior brainstem and the C1, C6, and T2 spinal cord.
2. To quantify the spatial displacements of the lateral and medial aspects of the parotid glands, particularly in the lateral dimension (in light of the data from Barker *et al.* [6]).
3. To determine the variation of the parotid gland volume over time.

Second, for each patient the IMRT dose distribution was recalculated on each CT image set in the series to determine the dosimetric effect of this spatial variability. For structures along the craniospinal axis, the dosimetric variability was quanitfied in terms of the maximum dose received. For the parotid glands, the variability of the mean dose and volume receiving $\geq$26 Gy was determined.

METHODS AND MATERIALS

Patient sample

All patients were treated with IMRT to provide either better target volume coverage or organ-at-risk sparing (or both) compared with standard conformal techniques. Consecutive patients were selected, and the sample was heterogeneous in terms of head-and-neck site (Table 1). The patients had Stage 3, 4, 4A, or 4B disease. All patients, except for two, received 2.0-Gy fractions. Only 1 patient had first undergone surgery (Patient 2, with RT beginning 55 days after surgery.) The mean and median magnitudes of the weight change during the treatment course were −7.5% and −7.3%, respectively.

Table 1. Patient sample

Pt. No.	Gender	Age at diagnosis (y)	Site	Stage	Dose (Gy)/ fractions	Concurrent chemotherapy	Weight change during treatment course (%)
1	F	74	Nasopharynx	4A	7,000/35	Yes	−4.9
2	M	45	Carcinoma of skin of scalp/neck (recurrent BCC)	3	6,600/33	No	−1.7
3	M	60	Nasopharynx	3	7,000/35	Yes	−9.5
4	M	57	Oropharynx (recurrent)	4B	7,000/35	Yes	−12.6
5	F	67	Sinonasal	4	6,000/30	Yes	−10.0
6	F	62	Hypopharynx	4A	7,000/35	Yes	−6.5
7	F	46	Right parapharyngeal space (recurrent meningioma)	NA	5,984/32	No	−7.3
8	F	66	Sinonasal rhabdomyosarcoma	4	5,000/25	No	−11.7
9	M	52	Nasopharynx	3	7,000/35	Yes	−0.7
10	M	59	Oropharynx	3	7,000/35	Yes	−13.4
11	M	74	Hypopharynx	4B	7,000/35	No	−7.8
12	M	46	Nasopharynx	4A	7,000/35	Yes	−15.2
13	M	70	Sinonasal	4	6,000/30	Yes	−2.0
14	F	62	Oropharynx	4B	7,000/35	Yes	−5.1
15	M	47	Oral cavity (recurrent)	4B	5,040/28	No	−3.5

Abbreviations: Pt. No. = patient number; F = female; M = male; BCC = basal cell carcinoma; NA = not available.