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CLINICAL INVESTIGATION **Head and Neck**

A COMPARISON OF INTENSITY-MODULATED RADIATION THERAPY AND CONCOMITANT BOOST RADIOTHERAPY IN THE SETTING OF CONCURRENT CHEMOTHERAPY FOR LOCALLY ADVANCED OROPHARYNGEAL CARCINOMA

Nancy Y. Lee, M.D.,* Fernando F. de Arruda, M.D.,* Dev R. Puri, M.D.,* Suzanne L. Wolden, M.D.,* Ashwatha Narayana, M.D.,* James Mechalakos, Ph.D.,† Ennapadam S. Venkatraman, M.D.,‡ Dennis Kraus, M.D.,§ Ashok Shaha, M.D.,§ Jatin P. Shah, M.D.,§ David G. Pfister, M.D.,¶ and Michael J. Zelefsky, M.D.*

Departments of *Radiation Oncology, †Medical Physics, ‡Biostatics, §Department of Surgery, Division of Head and Neck Surgery; and ¶Department of Medicine, Division of Head and Neck Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose: The aim of this study was to compare toxicity/efficacy of conventional radiotherapy using delayed accelerated concomitant boost radiotherapy (CBRT) vs. intensity-modulated radiotherapy (IMRT) in the setting of concurrent chemotherapy (CT) for locally advanced oropharyngeal carcinoma.

Methods and Materials: Between September 1998 and June 2004, a total of 293 consecutive patients were treated at our institution for cancer of the oropharynx. Of these, 112 had Stage III/IV disease and squamous cell histology. In all, 41 were treated with IMRT/CT and 71 were treated with CBRT/CT, both to a median dose of 70 Gy. Most common CT was a planned two cycles given every 3 to 4 weeks of cisplatin, 100 mg/m^2 i.v., but an additional cycle was given to IMRT patients when possible. Both groups were well-matched for all prognostic factors.

Results: Median follow-up was 46 months (range, 3–93 months) for the CBRT patients and 31 months (range, 20–64 months) for the IMRT group. Three-year actuarial local-progression–free, regional-progression-free, locoregional progression-free, distant-metastases–free, disease-free, and overall survival rates were 85% vs. 95% ($p = 0.17$), 95% vs. 94% ($p = 0.90$), 82% vs. 92% ($p = 0.18$), 85% vs. 86% ($p = 0.78$), 76% vs. 82% ($p = 0.57$), and 81% vs. 91% ($p = 0.10$) for CBRT and IMRT patients, respectively. Three patients died of treatment-related toxicity in the CBRT group vs. none undergoing IMRT. At 2 years, 4% IMRT patients vs. 21% CBRT patients were dependent on percutaneous endoscopic gastrostomy ($p = 0.02$). Among those who had ≥20 months follow-up, there was a significant difference in Grade ≥2 xerostomia as defined by the criteria of the Radiation Therapy and Oncology Group, 67% vs. 12% ($p = 0.02$), in the CBRT vs. IMRT arm.

Conclusion: In the setting of CT for locally advanced oropharyngeal carcinoma, IMRT results in lower toxicity and similar treatment outcomes when compared with CBRT. © 2006 Elsevier Inc.

IMRT, Oropharyngeal carcinoma, Concomitant boost, Intensity-modulated, Head-and-neck cancer.

INTRODUCTION

Cancer of the oropharynx, because of its anatomic location and rich lymphatic supply, is often locally advanced at presentation (1). Although surgery and postoperative radiotherapy (RT) with or without chemotherapy (CT) is one treatment approach, definitive chemoradiotherapy is often preferable (2–4). In addition, advanced oropharyngeal carcinomas can be unresectable, making the use of nonsurgical interventions necessary (5). The recently published trial of the French Head and Neck Oncology and Radiotherapy Group (GORTEC) favors the use of chemoradiotherapy vs. RT alone for advanced-stage cancer of the oropharynx (6). An update of the Pignon meta-analysis continues to show an absolute overall survival benefit of 8% at 5 years with combined modality therapy vs. RT alone for head-and-neck cancer (7).

Although the addition of CT has improved outcomes, toxicity associated with chemoradiotherapy should not be underestimated (8–10). Conventional two-dimensional (2D) RT encompasses the primary tumor and surrounding lymphatics. Such treatment will often have an impact on the salivary glands, causing xerostomia and consequent decrease in patient quality of life (QOL) (11). In contrast,

Reprint requests to: Nancy Y. Lee, M.D., Memorial Sloan-Kettering Cancer Center, Department of Radiation Oncology, 1275 York Avenue, Box 22, New York, NY 10021. Tel: (212) 639-3341; Fax: (212) 717-3104; E-mail: leen2@mskcc.org

Dr. de Arruda is currently affiliated with Sirio Libanes Hospital in Sao Paulo, Brazil.

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intensity-modulated radiation therapy (IMRT) (12) uses a computer-optimized treatment planning system to deliver a high dose of RT to the tumor while limiting dose to nearby normal tissues, e.g., the parotid glands (13–16). Studies have shown the advantage of IMRT in head-and-neck cancer with respect to salivary preservation, and a recent randomized trial has confirmed these findings (17–19). Furthermore, several centers have shown that IMRT reduces xerostomia without compromising tumor control (17, 18). Given considerations of toxicity as well as tumor geometry and anatomy, we now routinely use IMRT with concurrent CT to treat oropharyngeal carcinoma. The purpose of this article is to compare retrospectively the toxicity and efficacy of IMRT with conventional 2D RT using delayed accelerated concomitant boost (CBRT) in the setting of concurrent platinum-based CT for patients with locally advanced oropharyngeal carcinoma. To our knowledge, this is the first direct comparison of these two different treatment approaches in this disease site.

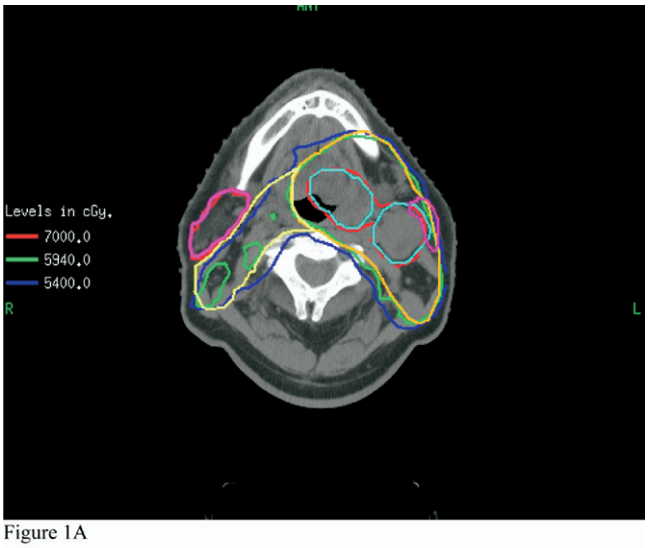

Figure 1A

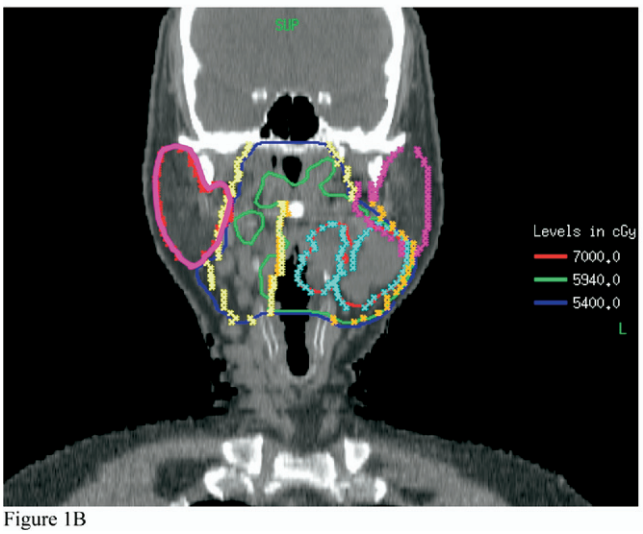

Figure 1B

Fig. 1. An example showing the effects of intensity-modulated radiotherapy (IMRT) in parotid sparing for oropharyngeal carcinoma. (a) Axial view; (b) coronal view. Notice the ability of IMRT to conform the 70-Gy isodose curve around the planning target volume for the gross tumor and 59.4 Gy to the ipsilateral neck while giving 54 Gy to the contralateral neck planning target volume simultaneously.

METHODS AND MATERIALS

Patient evaluation

From September 1998 to June 2004, a total of 293 consecutive patients with oropharyngeal cancer underwent RT at Memorial Sloan-Kettering Cancer Center. To maximize homogeneity between the two groups, 181 were excluded from this analysis: non-SCC, early Stage, Stage IVC, prior RT with or without CT, synchronous primary, performance status <60 resulting in palliative treatment, patients with upfront surgery, IMRT as boost, and those who received chemoradiotherapy + cetuximab.

This analysis included 112 patients who underwent RT concurrent with platinum-based CT. Of these, 71 were treated with conventional 2D RT using CBRT and 41 underwent IMRT. Pretreatment evaluations were history and physical, indirect, and/or direct fiberoptic endoscopic examination, CBC, chemistries, urinalysis, creatinine clearance, ECG, audiogram, CXR, computed tomography (CAT), and/or magnetic resonance imaging (MRI) of head/neck, and dental evaluation. Positron emission tomography (PET) was performed whenever possible. CAT scan of the chest/abdomen, bone scan was obtained when indicated. Disease was staged per the 1997 American Joint Committee on Cancer classification. All had histologic confirmation of SCC.

Radiation treatment

Patients were immobilized with a thermoplastic head-and-neck mask encompassing the shoulders to ensure reproducibility of RT. CAT simulation was performed in some treated with CBRT and in all IMRT patients. Patients were planned using the MSKCC treatment planning system with 6-MV photons (20). Electrons were used when indicated. No patients had brachytherapy.

Of the patients, 71 underwent CBRT to a dose of 70 to 72 Gy. Large RT portals using parallel-opposed fields encompassing the primary, draining sites, and bilateral necks were treated to 54 Gy/1.8 Gy per fraction for 6 weeks. During the last 2 to 2.5 weeks, smaller portals either using parallel-opposed fields or simple 3D boost to all gross disease were treated to 16 Gy/1.6 Gy or 18 Gy/1.5 Gy per fraction (11, 21). These boost fields were treated 6 h apart from the larger RT fields. All patients received a low anterior neck field (LAN) matched to upper neck RT fields.

A total of 41 patients underwent IMRT. Of these, 32 had dose-painting (DP) IMRT (a.k.a., simultaneous integrated boost), which is our current practice (Fig. 1), whereas 9 underwent concomitant boost IMRT. Details of these IMRT techniques as used at our institution have been previously published (22). All but 1 received IMRT to the primary/upper neck above vocal cords, whereas the low neck/supraclavicular fossae received a LAN field using conventional RT. One patient was treated with extended-field IMRT from skull base to low neck. It is our preference to only treat patients with extended-field IMRT when there is gross primary disease or involved nodes in the low neck. Of those who underwent concomitant boost IMRT, the large field and boost field treatments were 6 h apart. These fields were planned using IMRT.

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