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INTRAOPERATIVE RADIOTHERAPY FOR PAROTID CANCER: A SINGLE-INSTITUTION EXPERIENCE

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Purpose: Our practice policy has been to provide intraoperative radiotherapy (IORT) at resection to patients with head-and-neck malignancies considered to be at high risk of recurrence. The purpose of the present study was to review our experience with the use of IORT for primary or recurrent cancer of the parotid gland.

Methods and Materials: Between 1982 and 2007, 96 patients were treated with gross total resection and IORT for primary or recurrent cancer of the parotid gland. The median age was 62.9 years (range, 14.3–88.1). Of the 96 patients, 33 had previously undergone external beam radiotherapy as a component of definitive therapy. Also, 34 patients had positive margins after surgery, and 40 had perineural invasion. IORT was administered as a single fraction of 15 or 20 Gy with 4–6-MeV electrons. The median follow-up period was 5.6 years.

Results: Only 1 patient experienced local recurrence, 19 developed regional recurrence, and 12 distant recurrence. The recurrence-free survival rate at 1, 3, and 5 years was 82.0%, 68.5%, and 65.2%, respectively. The 1-, 3-, and 5-year overall survival rate after surgery and IORT was 88.4%, 66.1%, and 56.2%, respectively. No perioperative fatalities occurred. Complications developed in 26 patients and included vascular complications in 7, trismus in 6, fistulas in 4, radiation osteonecrosis in 4, flap necrosis in 2, wound dehiscence in 2, and neuropathy in 1. Of these 26 patients, 12 had recurrent disease, and 8 had undergone external beam radiotherapy before IORT.

Conclusions: IORT results in effective local disease control at acceptable levels of toxicity and should be considered for patients with primary or recurrent cancer of the parotid gland. © 2012 Elsevier Inc.

Intraoperative radiotherapy, Head and neck, Cancer, Parotid, IORT.

INTRODUCTION

Tumors of the salivary glands are relatively rare, representing 3–6% of all head-and-neck neoplasms and 0.3% of all malignancies (1). Parotid gland tumors account for 50–85% of salivary gland tumors, with 50–80% of parotid tumors benign and 20–30% malignant. Definitive treatment of these tumors primarily involves surgical resection and adjuvant radiotherapy (RT) for lesions at high risk of recurrence. The 5-year risk of local recurrence after surgical resection alone is 25–30%. The addition of adjuvant RT further decreases this risk to 9–10% (2–4). Disease recurrence carries a poor prognoses owing to invasion of vital structures within the head and neck.

Radiotherapy is commonly used as adjuvant treatment or, rarely, as definitive treatment when surgical resection is not possible. Delivering RT at resection of parotid cancers is particularly helpful in cases in which gross or microscopic residual disease is present or for recurrent disease (5). The safety and effectiveness of intraoperative RT (IORT) for head-and-neck cancer (HNC) have been established in several studies from our institution and others (6–8). Two forms of IORT have been studied for HNC: high-dose-rate brachytherapy (9) and external electron beam RT (6, 7).

Historically, IORT was first introduced in the United States in the 1970s after advances in anesthesia settings. One of the first applications of IORT was for abdominal and gynecologic malignancies (10). IORT is applied directly to the tumor bed, with customized shielding of adjacent healthy tissues and critical structures (11–13). When combined with external beam RT (EBRT), IORT has the advantages of reducing the

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volume of the radiation boost field, limiting the dose to radiosensitive structures, and increasing the effective dose. The disadvantages include the need for extra manpower and utilities and the addition of approximately 45 minutes to the total operative time.

Intraoperative RT for HNC was implemented at Methodist Hospital, Indianapolis, beginning in 1982 in hopes of improving patient outcomes and local disease control. Previously, our group reported on the outcomes of this approach in cervical metastases (14) and skull base tumors (15) . However, little is known about the effectiveness of IORT in parotid cancer. The purpose of the present retrospective study was to review a single-practice experience over 26 years with the use of IORT in patients with primary or recurrent cancer of the parotid gland.

METHODS AND MATERIALS

Study population

The present retrospective study was approved by the institutional review boards at Methodist Hospital and St. Vincent Hospital (Indianapolis, IN). All patients were treated by members of a single practice. Between August 1982 and July 2007, 96 patients were treated at Methodist Hospital for primary or recurrent cancer of the parotid gland (Table 1). The median age of the study population at primary or salvage surgery with IORT was 62.9 years (range, 14.3–88.1). The general indications for treatment included *(1)* tumor that could not be dissected with obviously clean margins from vital nerves, muscles, the carotid artery, or bony structures; *(2)* disease that was thought to be more aggressive than usual; *(3)* suspected close or positive margins or cases of suspected residual microscopic disease; and *(4)* previous EBRT. A total of 33 patients had undergone previous RT, with a median dose of 60 Gy (range, 17.50–70.0), and a median interval from completion of previous RT to IORT of 8.7 months (range, 0.8–71.6). All patients provided informed consent at consultation in the radiation oncology department before surgery.

Treatment

In the present study, 46 patients were treated with salvage surgery and 50 with primary surgery. Surgical removal of all resectable disease was attempted before the application of IORT to the tumor bed. All patients received IORT at surgery. Between 1982 and 2003, the patients were transported between the operation suite and the linear accelerator under general anesthesia for IORT. Starting in 2003, a mobile electron unit (Mobetron, Intraop, Santa Clara, CA) was used in the operating suite. The area at greatest risk of recurrence was delineated, with input from the surgeon. The appropriate cone was chosen by the radiation oncologist, and manually positioned over the target area. Critical structures inside the cone were covered with pliable 1–2-mm-thick lead shields. A thin layer of petrolatum-soaked gauze was used as bolus if desired by the radiation oncologist. Blood or other accumulated fluids in the operative bed were suctioned before treatment. When using the Mobetron, the cone was fixed to the operating table using a special clamp, and the applicator was docked to the linear accelerator using the guidance of a laser docking system.

Table 1. Patient characteristics

Characteristic	Patients (%)
Gender	
Male	60 (62)
Female	36 (38)
Treatment	
Primary	50 (52)
Salvage	46 (48)

Data in parentheses are percentages.

The dose, cone size, electron energy, and the use of a bolus were set at the discretion of the treating physician. The treatment cones ranged from 3.0 to 10.2 cm in diameter. The electron energies were 4 MeV in 30 patients, 5 MeV in 57 patients, and 6 MeV in 9 patients, all dosed to the maximal dose. Of the 96 patients, 57 received 15 Gy and 39 received 20 Gy. Postoperative EBRT was prescribed to 55 patients at the discretion of the attending radiation oncologist. The median dose was 45 Gy (range, 20–66). Overall, 18 patients received some type of chemotherapy (*e.g.*, adjuvant, palliative, neoadjuvant). Follow-up consisted of clinical examinations with radiographic follow-up as clinically indicated.

Statistical analysis

The endpoints analyzed were local control, recurrence-free survival (RFS), and overall survival (OS). All events were measured from the date of primary or salvage surgery with IORT. Local failure was defined as tumor recurrence anywhere within the IORT field. Failures outside the IORT field but within or adjacent to the parotid bed were considered regional. The 1-, 3-, and 5-year estimates of RFS and OS were derived using the Kaplan-Meier method, with comparisons among groups performed using 2-sided log–rank tests. A Cox proportional hazards model was used to identify characteristics predictive of survival and disease recurrence. Univariate and multivariate analysis were used. All tests were two-tailed comparisons, and the acceptable probability of a type I error was set as $< .05$ for statistical significance.

Not all patients had complete charts with respect to the variables analyzed. As such, the statistical analyses performed considered only those patients with the relevant information, with patients having no record of, or no data on, a specific variable excluded from that particular analysis. All patients had complete records with respect to the endpoints studied.

RESULTS

Disease characteristics

In the present study, the patient population consisted of 96 patients who underwent IORT for primary or recurrent parotid tumors. The most common histologic subtypes were mucoepidermoid carcinoma in 20, followed by squamous cell carcinoma in 15 patients. The other subtypes encountered included adenoid cystic carcinoma in 11, adenocarcinoma in 10, and others. The pathologic specimens revealed that 40 patients had perineural invasion, 33 had positive margins, 5 had lymphovascular (LVI) or angiolymphatic (ALI) invasion, 3 had extracapsular extension, 3 had vascular invasion, 18 had dermal invasion, and 3 had carotid involvement. Also, 40 patients had clinical cranial nerve VII paresis. The median tumor size was 2.5 cm (range, 0.7–9.5). The disease characteristics are summarized in Table 2.

Local control, recurrence, and recurrence-free survival

A total of 32 patients (33%) experienced recurrent disease (local, regional, or distant) within a median follow-up of 5.6