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CLINICAL INVESTIGATION **Breast**

MULTI-INSTITUTIONAL EXPERIENCE USING THE MAMMOSITE RADIATION THERAPY SYSTEM IN THE TREATMENT OF EARLY-STAGE BREAST CANCER: 2-YEAR RESULTS

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Purpose: To present a retrospective multi-institutional experience of patients treated with the MammoSite radiation therapy system (RTS).

Methods and Materials: Nine institutions participated in a pooled analysis of data evaluating the clinical experience of the MammoSite RTS for delivering accelerated partial breast irradiation. Between 2000 and 2004, 483 patients were treated with the MammoSite RTS to 34 Gy delivered in 10 fractions. Treatment parameters were analyzed to identify factors affecting outcome.

Results: Median follow-up was 24 months (minimum of 1 year). Overall, infection was documented in 9% of patients, but the rate was only 4.8% if the catheter was placed after lumpectomy. Six patients (1.2%) experienced an in-breast failure; four failures occurred remote from the lumpectomy site (elsewhere failure). Cosmetic results were good/excellent in 91% of patients. Treatment parameters identified as significant on univariate analysis were tested in multivariate regression analysis. The closed-cavity placement technique significantly reduced the risk of infection ($p = 0.0267$). A skin spacing of <6 mm increased the risk of severe acute skin reaction ($p = 0.0178$) and telangiectasia ($p = 0.0280$). The use of prophylactic antibiotics reduced the risk of severe acute skin reaction ($p < 0.0001$). The use of multiple dwell positions reduced the risk of severe hyperpigmentation ($p = 0.0278$). Infection was associated with an increased risk of fair or poor overall cosmesis ($p = 0.0009$).

Conclusions: In this series of patients, the MammoSite RTS seems to have acceptable toxicity rates and cosmetic outcomes, comparable to those with whole-breast radiotherapy. On the basis of these data, the closed-cavity placement technique, use of prophylactic antibiotics, use of multiple dwell positions, and a minimum skin spacing of 6 mm seem to improve patient outcome.

MammoSite, Accelerated partial breast irradiation, Brachytherapy, Breast conservation therapy.

INTRODUCTION

The accepted approach to breast-conserving treatment for early-stage breast cancer is the surgical removal of the primary breast lesion followed by whole-breast radiotherapy. Conventional whole-breast irradiation is delivered daily, 5 days per week for 5 to 6.5 weeks. With modern surgical, pathologic, and radiotherapy techniques, good to excellent cosmetic results with in-breast control rates exceeding 90% can be expected (1–4).

Despite significantly lower local control rates with the addition of whole-breast radiotherapy over surgery alone, the protracted course of radiotherapy can present a logistical problem for many patients. This is reflected in the continued high rate of women who either choose to have a mastectomy

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or complete their local treatment with lumpectomy alone, thus facing a potentially higher risk of in-breast failure (5). With this problem in mind, there has been an increasing interest in accelerated partial breast irradiation (APBI) among both patients and physicians.

Clinical and pathologic evidence suggests that the primary target requiring adjuvant treatment after lumpectomy (with negative surgical margins) is likely limited to within 1 to 2 cm from the edge of the lumpectomy cavity (5). By reducing the target to only a portion of the breast, acceleration of the dose delivery and completion of treatment in 5 days becomes feasible. Accelerated partial breast irradiation can be delivered with several techniques. The best-studied APBI technique is multi-catheter interstitial brachytherapy. Multiple mature institutional experiences with the multiple catheter technique have shown 3 to >5-year actuarial local recurrence rates of less than 5% (5, 6–16).

The MammoSite radiation therapy system (RTS) (Cytyc Corporation, Marlborough, MA) is a balloon catheter treatment device designed to simplify breast brachytherapy and approximate the dose delivery of multi-catheter implants. The device was originally investigated in a multi-institutional trial, which led to clinical approval by the U.S. Food and Drug Administration (FDA) for its use in May 2002 (17). With 39-month follow-up data now available, this original trial included 43 patients and resulted in excellent outcomes, with 100% in-breast control with acceptable toxicity (18). Because the patient number in the original trial was small, we constructed a larger experience to improve our understanding of the expected early outcome from the use of this device. In this report, we present a retrospective multi-institutional experience of patients treated with the MammoSite device.

METHODS AND MATERIALS

The MammoSite Users' Group was financially supported by the Massey Cancer Center at the Virginia Commonwealth University (VCU) and organized by the Department of Radiation Oncology. The earliest users, including two institutions that previously reported higher-than-expected incidences of toxicity, were invited to participate on the basis of clinical experience with the device. The meeting was held in September 2004 in Richmond, VA. Data were collected on treatment techniques, toxicity, and local control.

After the meeting the database was expanded and updated to include the most recent outcome data. Cases included were required to have at least 1-year follow-up. Data were collected exclusively by radiation oncologists then compiled, reviewed, and analyzed at VCU. Data collection, transfer, and review were approved by our institutional review board. There was no involvement of the device manufacturer except for a supplementary research grant funding travel expenses of VCU faculty necessary to complete the database.

Patient eligibility criteria

Each participating institution had individually determined patient selection criteria. Upon review, inclusion criteria varied only slightly between institutions and were relatively conservative. Each center required patients to have small tumors (<3 cm), negative surgical margins, and no evidence of multicentricity. Although most centers restricted treatment to infiltrating ductal carcinoma, one allowed *in situ* disease. The majority of institutions (six of nine) permitted treatment of patients with one to three positive lymph nodes without extracapsular extension. Most centers (seven of nine) required patients to be at least 45 years of age.

Data collection

Information on technique, technical variables, antibiotic use, systemic treatment, toxicity, and failure pattern were collected on data forms supplied to each participating institution. Because the focus of the original meeting was on technical and treatment-related data, specific information on tumor size, histology, and nodal status were not collected. The compilation of the data requested can be seen in Tables 1–3. All data forms were collected electronically and reviewed for inaccuracies, omissions, and conflicting information by a single radiation oncologist at VCU. Patients were not included in the analysis unless all information was provided.

Technical and treatment variables

Technical and treatment data are shown in Table 1. Placement of the device was performed either at the time of lumpectomy (referred to as open-cavity placement) or at a separate procedure after final pathology review after lumpectomy (referred to as closed-cavity placement). A lateral trocar approach was commonly used for both open- and closed-cavity placement. This technique utilizes a trocar, provided with the MammoSite RTS, to create a path from a remote location of the breast through the skin, traversing breast tissue and entering the lumpectomy cavity. Once the path is created the trocar is removed and the MammoSite catheter navigated through this path with the balloon placed in the cavity. The scar entry technique is an additional technique alternatively used in closed catheter placement. With this technique the lumpectomy incision is reopened just to allow placement of the balloon catheter into the cavity. Single sutures are placed adjacent to the catheter to

Table 1. Technical and treatment variables

Characteristic	Finding
Placement technique	
Open	232 (48)
Closed	251 (52)
Placement approach	
Lateral trocar	357 (74)
Scar entry	126 (26)
No. of days in place	9.8 (4–28)
Track length (cm)	4.3 (1–10.6)
Skin thickness (mm)	11.7 (1–54)
Fill volume (cm^3)	55 (27–125)
Dwell positions	
Single	382 (79)
Multiple	101 (21)
Prophylactic antibiotics	
None	343 (71)
Oral	135 (28)
Intravenous plus oral	5 (1)
Systemic chemotherapy	
None	420 (87)
Any	63 (13)
Hormonal therapy	
None	179 (37)
Tamoxifen or anastrozole	304 (63)

Values are number (percentage) or mean (range).