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Incidence and prognostic factors for seroma development after MammoSite breast brachytherapy

John M. Watkins[1], Jennifer L. Harper[1], Anthony E. Dragun[1], Michael S. Ashenafi[1], Debajyoti Sinha[2], Jun Li[1], David J. Cole[3], Joseph M. Jenrette[1,*]

[1]*Department of Radiation Oncology, Medical University of South Carolina, Charleston, SC*
[2]*Department of Biostatistics and Biometrics, Medical University of South Carolina, Charleston, SC*
[3]*Department of Surgery, Medical University of South Carolina, Charleston, SC*

ABSTRACT

PURPOSE: Describe the incidence and identify risk factors for seroma development after MammoSite breast brachytherapy (MBT).

METHODS AND MATERIALS: MBT patient data were prospectively recorded into a quality assurance database. Departmental and electronic records were reviewed to extract patient-, treatment-, and outcome-specific data. Stepwise logistic regression analysis was performed to identify factors associated with development of any seroma including the subset of clinically significant seroma (CSS). CSS was defined as a symptomatic seroma requiring multiple aspirations, biopsy, and/or excision. Variables analyzed included age, weight, number of excisions, time from resection to catheter placement, placement technique, balloon volume, dosimetric factors, and postbrachytherapy infection.

RESULTS: MBT was performed in 109 patients, of whom 97 had minimum 6 months (median, 36) post-MBT follow-up or earlier development of seroma. All patients received 34 Gy to 1 cm depth from balloon surface, delivered twice daily in 10 fractions. Seroma developed in 41% of patients at a median of 3 months (range, 0.1–25) post-MBT. One-third of seromas (13% of all patients) were CSS. The only factor identified as statistically significant for development of any seroma was catheter placement on day of resection vs. $\geq$1 day later (59% vs. 33%; $p = 0.0066$). Post-MBT infection was highly statistically significant for development of CSS (64% vs. 7%; $p < 0.0001$). Prophylactic antibiotics reduced the risk of post-MBT infection from 37.5% to 6% ($p = 0.011$).

CONCLUSIONS: The incidence of CSS after MBT is low. Post-MBT infection is statistically significantly associated with CSS development, the incidence of which is reduced with prophylactic antibiotics.

Keywords: Breast neoplasms; Intracavitary brachytherapy; MammoSite; Seroma; Breast conservation therapy

Introduction

MammoSite breast brachytherapy (MBT) is a form of accelerated partial breast irradiation, which is presently being evaluated as an alternative to whole breast radiotherapy in resected early-stage breast cancer. Although a formal multi-institutional randomized trial is underway to compare efficacy and tolerability of partial breast irradiation with whole breast radiotherapy, previously published multi-institutional reports of MBT have been promising (1–3). As the collective experience with MBT grows, identification of factors predictive for MBT-specific toxicity remains to be described (4). Seroma development, in particular, has been described as occurring in as few as 9% and up to 76% of patients after MBT, with varying levels of severity (4, 5). The present report describes a large cohort of patients treated with uniform dose of MBT at a single institution.

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* Corresponding author. Department of Radiation Oncology, Medical University of South Carolina, 169 Ashley Avenue, Charleston, SC 29425. Tel.: +1-843-792-3271; fax: +1-843-792-5498.

E-mail address: jenretbm@musc.edu (J.M. Jenrette).

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Specifically, patient- and treatment-specific variables are assessed to determine factors predictive for development of MBT-associated seroma.

Methods and materials

Between May 2002 and August 2006, 109 patients underwent lumpectomy followed by intracavitary MammoSite catheter breast brachytherapy (MBT) at the Medical University of South Carolina. Of the 109 patients, 12 were excluded from the present analysis due to insufficient follow-up (minimum 6 months unless earlier development of seroma). All patients who initiated MBT are included in this analysis, and all patients but one completed prescribed therapy (did not receive final fraction). After initiation of MBT, only 1 patient experienced balloon rupture requiring replacement. MBT was used as the sole radiotherapy modality in the entire population; no patient received external beam therapy to the whole breast.

Eligibility for MBT included patients with unicentric invasive ductal or lobular carcinoma, or ductal carcinoma *in situ* (DCIS) tumors. Extent of disease was pathologic Stage 0 (pTisN0, or DCIS), I (pT1N0), IIA (pT2N0 or pT1N1), or select IIB (pT2N1). Surgical margins were cleared to $\geqslant$2 mm to invasive or *in situ* carcinoma, occasionally requiring postlumpectomy re-excision. All patients with invasive disease underwent sentinel lymph node biopsy, with subsequent axillary dissection if the sentinel node was positive for malignancy. Timing of MammoSite catheter placement varied from intraoperative (0 days) to up to 66 days postexcision. In general, most catheters were placed within 2 weeks after final excision and verification of margins. Placement approach varied with surgeon and experience, with both scar entry technique and lateral trocar approaches being used. The lateral trocar approach, used in most cases in the present population, involves advancing the MammoSite catheter through an approximate 1 cm incision in the lateral breast, toward the ultrasonographically identified resected tumor cavity. The catheter balloon is then filled to expand the cavity.

Patients next underwent a computed tomography scan using thin axial images (2.5–3 mm thickness) for treatment planning and implant quality verification. A minimum overlying skin thickness of 7 mm was required, though 5 mm thickness was permitted on single axial slice. Treatment planning was aborted if there was insufficient overlying skin thickness, excessive intracavitary air, or balloon rupture. Most patients underwent postexcision catheter placement; however, in those patients with intraoperative catheter placement, treatment planning was aborted if surgical margins were unsatisfactory or sentinel lymph node returned positive for disease (requiring axillary dissection). Beginning the first day of treatment and continuing through the final treatment day, patients underwent daily fluoroscopic simulation for balloon volume verification. All patients were prescribed to 34 Gy at 3.4 Gy per fraction to 1 cm depth beyond balloon surface. Treatments were administered twice daily during weekdays, with minimum 6 h between fractions.

Planning was performed using Nucletron Planning System version 3.5 (Nucletron, BV, Veenendaal, The Netherlands). Treatments were delivered using high-dose-rate brachytherapy with ^{192}Ir (activity 3.8–9.8 mCi). Dose–volume histograms were constructed for the contoured balloon and for the "target" (balloon + surrounding breast tissue). Plans were evaluated to ensure minimal air cavity artifact (<3 cc). Dosimetric variables were retrospectively calculated, and included the volume (in cubic centimeters; cc) of breast receiving 34 Gy ($V_{100\%}$), 51 Gy ($V_{150\%}$), and 68 Gy ($V_{200\%}$). Volumes were calculated by subtracting the balloon-specific volume (e.g., $V_{100\%}$) from the "target"-specific volume ($V_{100\%}$). Whenever the electronic plans were available, the Nucletron Planning System was used to calculate these parameters. When electronic records were not available, the calculations were performed manually using the hard-copy balloon and target dose–volume histograms. Five cases with electronic plans were randomly selected for manual calculation as a measure of quality assurance, and the mean difference between volumes was 0.9 cc (maximum 3 cc).

After the final fraction of MBT, the balloon is drained and catheter removed. Prophylactic antibiotics were not prescribed to the initial 14 MBT patients treated at our institution. Subsequently, patients have been prescribed cephalexin 500 mg, four times per day from catheter placement through catheter removal. Although the catheter remains in the breast, patients are advised to keep the breast dry and avoid submersion (swimming, tub bathing) until after the catheter has been removed. Immediately after catheter removal, the breast is gently massaged to evacuate fluid and blood, after which antibiotic ointment and gauze are applied with overlying transparent adhesive dressing. Patients are recommended not to remove dressing for 2–3 days after initial placement, then to change regularly until the cavity tract has sealed.

Data were collected on patient-, tumor-, treatment-, and outcome-related factors. Patient factors included age at diagnosis, race, history of diabetes, current cigarette smoking, and weight. Tumor-related factors included pathologic T- and N-stage, performance of axillary lymph node dissection, and number of lymph nodes excised and involved. Treatment-related factors included time from biopsy to first lumpectomy, requirement for re-excision, time from final excision to MammoSite catheter placement, MammoSite catheter placement technique and approach, time from lumpectomy to MBT initiation, number of days from MBT start to finish, number of days catheter remained in breast, overlying skin thickness (narrowest), number of MBT plan dwell positions, $V_{100\%}$, $V_{150\%}$, $V_{200\%}$, post-MBT chemotherapy, post-MBT anti-estrogen therapy, administration of prophylactic antibiotics, and development of post-MBT subcutaneous infection. Outcome measures