Skin and chest wall dose with multi-catheter and MammoSite breast brachytherapy: Implications for late toxicity
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ABSTRACT

PURPOSE: Accelerated partial breast irradiation (APBI) continues to increase in popularity. Up to 14% of patients treated with the MammoSite (MS) report some degree of chronic pain, which may be related to chest wall toxicity. Reports from several institutions using the multicatheter (MC) technique have not shown associated elevated chest wall toxicity. Additionally, a recent investigation has suggested that increased toxicity may occur with the MS when the dose to the chest wall exceeds 125% of the prescribed dose. This investigation compares the skin and chest wall doses of a cohort of patients treated with the MC technique to a group treated with the MS.

METHODS AND MATERIALS: The dosimetric data for 43 patients treated with the MC technique and 83 patients treated with the MS at Virginia Commonwealth University were reviewed. This cohort represents consecutively treated patients from our most recent experience to minimize any learning curve effect on dosimetry. Plans were generated using 3D software (Brachyvision, Varian Medical Systems, Inc., Palo Alto, CA). Multiple dwell positions were used for all MS patients to optimize dose delivery. The minimum distances from the planning target volume to the skin and chest wall were calculated, as well as the maximum doses delivered to the skin and chest wall.

RESULTS: The mean skin distances for patients treated with the MC technique and the MS were 0.5 and 0.9 cm, respectively ($p < 0.002$). Despite the significantly smaller mean skin distance, the mean skin dose for the MC technique was only 2.3 Gy per fraction (67% of prescription dose). The mean skin dose for the MS was 3.2 Gy per fraction (94% of prescription dose, $p < 0.001$). The mean chest wall distance was 0.9 cm for the MC technique and 1.0 cm for the MS ($p = 0.55$). Again, the mean chest wall dose for the MC technique was only 2.3 Gy per fraction (67% of prescription dose). The mean skin dose for the MS was 3.6 Gy per fraction (105% of prescription dose, $p < 0.001$). The percentage of patients receiving skin doses in excess of 125% for the MC and MS were 0% and 9.6%, respectively. The percentage of patients receiving chest wall doses in excess of 125% for the MC and MS were 0% and 38.6%, respectively.

CONCLUSION: The MC technique results in more conformal dose delivery, with significantly lower mean skin and chest wall doses. Treatment with the MS was associated with significantly more patients receiving doses to the skin or chest wall in excess of 125% of the prescription. Given the limited followup available for the MS, and the significant dose delivered to the chest wall, the use of this device may be associated with a higher incidence of late chest wall toxicity than previously expected. © 2009 Published by Elsevier Inc on behalf of American Brachytherapy Society.

Keywords: MammoSite; Accelerated partial breast irradiation; Brachytherapy; Breast conservation therapy

Introduction

The equivalence of conservative surgery and radiation therapy to mastectomy in the treatment of women with early-stage breast cancer has been demonstrated in several Phase III trials (1, 2). With modern surgical, pathological, and radiotherapy techniques, good to excellent cosmetic results with local control rates exceeding 90% can be expected. Postoperative radiation for invasive breast cancer
has also been associated with improved local control and overall survival compared with breast-conserving surgery alone (3).

Despite significantly lower local control rates with surgery alone, the number of women treated with breast-conserving surgery but without radiation is approximately 15–20% (4–6). The protracted time course required to complete standard whole-breast radiotherapy is thought to play a significant role in the underutilization of postoperative treatment. Although treatment of the entire breast for presumed occult disease can be safely accomplished in as few as 16 treatments (7), further acceleration would probably result in unacceptable cosmetic outcomes. If the target for radiotherapy is limited only to the volume of tissue at greatest risk for local recurrence, a more dramatic reduction in overall treatment time becomes possible.

Accelerated partial breast irradiation (APBI) has been investigated in selected patients with early-stage breast cancer (8). APBI limits the radiation target to the volume of tissue immediately surrounding the lumpectomy cavity and reduces the overall treatment time from approximately six weeks to five days. If proven equivalent to standard whole-breast radiotherapy, such an approach may improve the utilization of breast-conserving treatment, decrease treatment-related toxicity, and improve the quality of life for breast cancer patients (9).

By reducing the target to only a portion of the breast, acceleration of the dose delivery and completion of treatment in five days becomes feasible. APBI can be delivered with several techniques. The best studied APBI technique is multicatheter (MC) interstitial brachytherapy. This technique uses multiple catheters which are inserted into the breast tissue around the lumpectomy cavity. During treatment, an Iridium-192 source is temporarily placed into each catheter lumen in a series of dwell positions using a remote after-loader. This technique offers significant dosimetric flexibility and typically results in excellent target coverage with minimal dose to normal tissues.

Multiple mature experiences with the MC technique have shown 3- to >5-year actuarial local recurrence rates of less than 5% in carefully selected patients (10–19). The MC technique is extremely well tolerated and most of the patients treated experience either an excellent or a good cosmetic outcome. Late toxicity is uncommon with >5 years of followup (14, 20, 21). Significant (Grade 2–3) fibrosis/subcutaneous toxicity and fat necrosis have been reported in 5–8% and about 15% of patients, respectively. Significant chronic pain or telangiectasia occurs in only about 1% of patients. Chest wall pain or rib fractures have not been reported. Although overall cosmesis appears to improve over time, the severity of telangiectasias and the incidence of fat necrosis continue to increase with longer followup.

The MammoSite (MS) Radiation Therapy System (RTS) (Hologic, Inc., Marlborough, MA) is a balloon catheter treatment device designed to simplify breast brachytherapy and approximate the dose delivery of MC implants. The device uses a single treatment lumen. Although multiple dwells positions can be used to optimize treatment delivery, significant alterations in the shape of the dose distribution are not possible. The MS was originally investigated in a multi-institutional trial that led to clinical approval by the United States Food and Drug Administration (FDA) for its use in May of 2002 (22). Multiple series have now reported acceptable local control and toxicity using the MS (23–35), but most have less than two years of followup data available. Although most patients experience either an excellent or good cosmetic result, late toxicities have been reported. In contrast with the MC technique, up to 40% of patients experience significant (Grade 2–3) subcutaneous toxicity at two years. Intermittent or persistent pain has been reported in 5–14% of patients, and around 15% experience significant telangiectasias (23, 26, 36, 37).

Unacceptable toxicity with the MS is associated with skin distances ≤ 6 mm (24, 36, 37). Additionally, a recent investigation used the linear quadratic formula to estimate the tolerance dose which would result in a 50% risk of rib/chest wall late effects at five years (TD50/5). This report suggested that increased toxicity may occur with the MS when the dose to the chest wall exceeds 125% of the prescribed dose (36). This investigation compares the skin and chest wall doses of a cohort of patients treated with the MC technique to a group treated with the MS in an attempt to better characterize the late effects that may be associated with the MS technique.

Methods and materials

The dosimetric data for 43 patients treated with the MC technique and 83 patients treated with the MS at Virginia Commonwealth University were reviewed. This cohort represents consecutively treated patients from our most recent experience to minimize any learning curve effect on dosimetry. Plans were generated using 3D software (Brachyvision, Varian Medical Systems, Inc., Palo Alto, CA). Multiple dwell positions were used for all MS patients to optimize dose delivery. The minimum distances from the planning target volume to the skin and chest wall were calculated, as well as the maximum doses delivered to the skin and chest wall. The percentage of patients in whom the dose to either the skin or chest wall exceeded the proposed tolerance dose was tabulated.

Results

Results are shown in Table 1. The mean skin distances for patients treated with the MC technique and MS were 0.5 and 0.9 cm, respectively (p < 0.002). Despite the significantly smaller mean skin distance, the mean skin dose for the MC technique was only 2.3 Gy per fraction
Table 1
Skin and chest wall doses with MC and MS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MC (Gy)</th>
<th>MammoSite (Gy)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean skin distance (cm)</td>
<td>0.5</td>
<td>0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean skin dose (Gy)</td>
<td>2.3</td>
<td>3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean chest wall distance (cm)</td>
<td>0.9</td>
<td>1.0</td>
<td>0.55</td>
</tr>
<tr>
<td>Mean chest wall dose (Gy)</td>
<td>2.3</td>
<td>3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patients with skin dose &gt;125%</td>
<td>0</td>
<td>9.6</td>
<td>n/a</td>
</tr>
<tr>
<td>Patients with chest dose &gt;125%</td>
<td>0</td>
<td>38.6</td>
<td>n/a</td>
</tr>
</tbody>
</table>

MC = multicatheter; MS = MammoSite.

(67% of prescription dose). The mean skin dose for the MS was 3.2 Gy per fraction (94% of prescription dose, \( p < 0.001 \)).

The mean chest wall distance was 0.9 cm for the MC technique and 1.0 cm for the MS (\( p = 0.55 \)). Again, the mean chest wall dose for the MC technique was only 2.3 Gy per fraction (67% of prescription dose). The mean skin dose for the MS was 3.6 Gy per fraction (105% of prescription dose, \( p < 0.001 \)).

The percentage of patients receiving skin doses in excess of 125% for the MC and MS were 0% and 9.6%, respectively. The percentage of patients receiving chest wall doses in excess of 125% for the MC and MS were 0% and 38.6%, respectively.

Discussion

Since the introduction of the MS, several experiences have been published documenting its use. Many of these publications have been limited by small patient numbers and lack of meaningful followup. Despite the relative paucity of mature outcome data, published series have already reported significant late effects. Fortunately, some of the toxicities associated with this device can be reduced or even eliminated when proper placement and treatment guidelines are followed.

In contrast, with 10-year followup data from some institutions as well as results from a European randomized trial now available, the MC technique has not been associated with significant late toxicity. Interstitial brachytherapy results in a more conformal and homogeneous dose distribution than even the most optimal MS application.

This report is a dosimetric comparison of MC and MS brachytherapy and does not include patient outcome data. The results clearly demonstrate that treatment with the MC technique is associated with lower doses to the skin and chest wall. Because it is a single-lumen balloon, the MS has some important dosimetric limitations. Even if multiple dwell positions are used, a single-lumen catheter has limited dosimetric flexibility in patients with balloons placed near the skin or chest wall. For this reason, several new applicators using multiple lumens have recently been introduced. Although not having the degree of flexibility inherent in the MC technique, these new balloons offer significantly more complex source arrangements than the single-lumen balloon with the potential to address the dosimetric limitations experienced with a single-lumen device.

Although many patients in this study treated with the MS received doses in excess of the proposed tolerance dose, all plans met the dosimetric requirements of the currently accruing Phase III trial (NSABP B-39/RTOG 0413), which limits the skin dose to \( \leq 145\% \) of the prescription dose but does not limit the chest wall dose. Although the proposed tolerance dose has not yet been widely incorporated into clinical practice, most series using the MS report acceptable overall cosmesis and toxicity. In addition, the MC technique is highly user-dependent and requires considerable skill and physics support. The MS makes AP-BI available to many patients in areas where MC is not offered. This report is not intended to be a condemnation of balloon brachytherapy. Rather, this study emphasizes the significant differences in the doses delivered with each technique. Outcome data for the MS continues to evolve, and physicians should be aware that some toxicities associated with this device may continue to increase.

Conclusion

The MC technique results in more conformal dose delivery, with significantly lower mean skin and chest wall doses. Treatment with the MS was associated with significantly more patients receiving doses to the skin or chest wall in excess of 125% of the prescription. Given the limited followup available for the MS, and the significant dose delivered to the chest wall, the use of this device may be associated with a higher incidence of late chest wall toxicity than previously expected.

References


