

Initial radiation experience evaluating early tolerance and toxicities in patients undergoing accelerated partial breast irradiation using the Contura Multi-Lumen Balloon breast brachytherapy catheter

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ABSTRACT

PURPOSE: We reviewed our institution's experience treating patients with the Contura Multi-Lumen Balloon (SenoRx, Inc., Irvine, CA) breast brachytherapy catheter to deliver accelerated partial breast irradiation.

METHODS AND MATERIALS: Forty-one patients treated with breast-conserving therapy received adjuvant radiation using the Contura catheter (34 Gy in 3.4 Gy fractions). Thirteen patients had Stage 0, 21 had Stage I, and 7 had Stage II breast cancer. Median followup was 8 months (range, 1–17).

RESULTS: Median, minimum skin spacing was 10 mm (range, 2–17). Median, maximum skin doses (% of prescribed dose [PD]) were 99.7 (range, 57.1–124.1). Eight patients were treated with a skin spacing \leq 5 mm and 2 had a spacing of 2 mm. Median, maximum rib doses were 102.6% of PD (10.0–187.7), and the median percentage of the planning target volume for evaluation (PTV_EVAL) receiving 95% of the PD was 98.8 (range, 79.4–107.4). The median volume receiving 200% of the PD was 5.7 cc (range, 1.3–9.9). The percentage of patients with excellent/good cosmetic results at 6 months ($n = 15$) and 12 months ($n = 12$) was 100%. Patient tolerance was assessed on a scale 0–10 (0 = no pain, 10 = requiring narcotic analgesics). In 37 out of 38 patients, pain was graded \leq 3 at the time of catheter insertion. Four breast infections (11%) and one transient symptomatic seroma (3%) developed.

CONCLUSION: Adjuvant accelerated partial breast irradiation using the Contura Multi-Lumen Balloon catheter exhibited similar toxicities to standard single lumen balloon brachytherapy with improvements in dosimetric capabilities (i.e., reduced skin and rib doses and improved PTV_EVAL coverage). © 2009 Published by Elsevier Inc on behalf of American Brachytherapy Society.

Keywords:

Balloon brachytherapy; Partial breast irradiation; Breast cancer; Contura MLB; MammoSite

Introduction

Accelerated partial breast irradiation (APBI) has been explored as a possible option to deliver adjuvant irradiation after lumpectomy in selected patients undergoing breast-conserving therapy (1). The primary advantage of APBI is the reduced treatment time and potentially reduced toxicities. Most Phase I/II studies (and more recently, Phase III

data) have demonstrated acceptable 5- and 10-year rates of local control and cosmesis using this treatment approach in low-risk patients (2, 3). Studies using catheter-based interstitial brachytherapy (IB) as the APBI technique have provided the largest group of patients with the longest followup to date (4, 5). However, one of the primary disadvantages of IB to deliver APBI is the complexity and reproducibility of the procedure. Even using the best imaging/placement methods available, the technique is complex and requires a great deal of experience and skill to position the needles or catheters to cover the required treatment volume (6). In addition, widespread patient acceptance of this method of APBI has not been demonstrated.

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The MammoSite applicator (Hologic Inc, Bedford, MA) was developed to address these issues (7). The MammoSite allows an easier implant to be performed as compared to IB. The inflation of the balloon displaces the cavity edge and adjacent target tissue into the necessary relationship with a single central source. This permits a symmetrical radiation dose distribution to be delivered from the inside of the cavity to the adjacent tissues surrounding the balloon.

In the first Phase I/II clinical trial with the MammoSite balloon catheter, 43 patients received radiation therapy as primary treatment (8). The study demonstrated that the device was safe and well tolerated, which resulted in Food and Drug Administration clearance on May 6, 2002. Five-year cosmetic results have been good to excellent in 83% of the women treated in this study and no local recurrences have been observed to date with a median followup of 66 months (9).

Some of the major limitations of the use of the MammoSite to deliver APBI stem from the fixed relationship between the geometry of the balloon placement and the dose delivered. There is little ability to manipulate the dose distribution when using a single lumen, single dwell position, and limited ability when multiple dwell positions within a single lumen are used. Therefore, the dose delivered to the target and normal structures is directly related to the balloon geometry and fit within the cavity. Consistently providing an acceptable skin spacing and conformance of the lumpectomy cavity to the surface of the balloon have been the dominant challenges. Because the radiation dose is prescribed to 1.0 cm from the surface of the balloon, a separation of at least 7 mm (balloon surface-to-skin distance) is generally recommended to avoid excessive skin dose (and the potential for subsequent suboptimal cosmesis). In addition, if conformance around the balloon is poor, breast tissue surrounding the lumpectomy cavity may be suboptimally treated. As a result, there are limitations on the applicability of the use of the device in some patients.

The Contura Multi-Lumen Balloon (MLB) (Senorx, Inc., Irvine, CA) was developed to provide additional brachytherapy options needed to achieve more optimized dosimetric goals. Through the use of four additional lumens that are offset 5 mm from the single central catheter lumen design (see Fig. 1), dose shaping is theoretically possible. This should result in the ability to reduce the skin dose and some treatment restrictions (as a result of insufficient skin spacing). It is believed that these modifications in the design of the balloon may have the potential for greater utilization of balloon brachytherapy to deliver APBI. Preliminary dosimetric data on 10 clinical cases planned using the Contura MLB have shown that there are geometric scenarios where loading of only a central lumen presents dosimetric limitations and that these limitations can be overcome with the multilumen design (10). The MLB approach can lead to significant improvements in

dose coverage of the partial breast target with simultaneous dose reductions to adjacent structures such as skin and chest wall.

To examine the potential for improved use of balloon brachytherapy to deliver APBI, we reviewed our institution's preliminary experience treating patients with the Contura MLB breast brachytherapy catheter and determined short-term treatment efficacy, cosmesis, and toxicity and evaluated some of its dosimetric capabilities for dose delivery improvements.

Methods and materials

This retrospective analysis was given an exempt determination granted under 45 Code of Federal Regulations (CFR) 46 101(b) (4) by the Western Institutional Review Board. Patients were treated from June 25, 2007 through May 23, 2008.

Patient selection and eligibility criteria

Patients included in this analysis were selected for APBI at the discretion of the treating physician (radiation oncologist and/or surgeon) and preference (if eligible) of the patient. Generally, the American Society of Breast Surgeons and/or the American Brachytherapy Society guidelines for the treatment of patients with APBI off-protocol were followed (11). Patients were not enrolled on an Institutional Review Board-approved protocol.

Treatment planning

Once a patient was referred for possible APBI, a computed tomography (CT) scan with the patient in an easily reproducible position with the Contura MLB in place was performed for assessing appropriateness for treatment and treatment planning. The CT scan included at least 3 cm both cephalad and caudal to the Contura MLB. The following structures were contoured: (1) balloon surface, (2) planning target volume (PTV) for evaluation (PTV_EVAL—see below), (3) trapped air and/or fluid, (4) skin surface, and (5) aspect of the closest rib that was adjacent to the balloon. The target volumes and normal tissue structures were outlined on all CT cuts when appropriate. After placement, the vacuum lumen of the Contura was often used to remove fluid and/or air and further establish good tissue to balloon conformance. Adequate tissue to balloon conformance was confirmed under ultrasound and additional fluid added to the balloon if necessary and the final fill volume was recorded. Additionally under ultrasound guidance, minimum balloon to skin spacing was measured and recorded. However, final determination as to adequate conformance was made by CT scan examination before treatment planning. At the time of the planning CT, the rotational orientation of the Contura catheter was documented so that before each treatment the proper

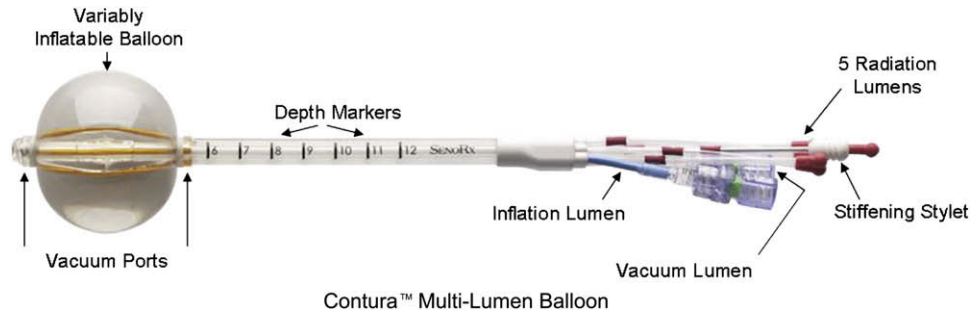


Fig. 1. Contura Multi-Lumen Balloon.

orientation could be reproduced. Generally, the shaft orientation line position was noted and a skin mark or the skin incision was used for consistent rotational positioning. Additionally, a single dummy marker wire was placed into lumen #1 to document orientation of the device for proper CT planning.

Target volumes

As per the guidelines of the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39/Radiation Therapy Oncology Group (RTOG) 0413 protocol, the PTV_EVAL = clinical target volume (CTV) = PTV. The PTV_EVAL was delineated as the breast tissue volume bounded by the uniform expansion of the balloon radius in all dimensions by 10 mm less the balloon volume and was limited to 5 mm from the skin surface and by the posterior breast tissue extent (chest wall and pectoralis muscles were not to be included).

When determining dose coverage of the PTV_EVAL, the volume of trapped air/fluid was accounted for as it displaces a percentage of the target beyond 1 cm from the balloon surface. The area of trapped air/fluid was contoured at each level, a total volume obtained and the percentage of the PTV_EVAL that it displaced was calculated. When determining the PTV_EVAL dose coverage, this displaced percentage was subtracted.

Contura MLB placement and treatment planning

The Contura MLB was placed with a closed-cavity placement technique in 41 patients (100%). A description of the subtle differences in surgical placement of the device is the subject of a separate publication. Radioactive source location, number of lumens, number of positions, and dwell times were at the discretion of the treating physician and were determined by the high-dose-rate CT-based 3D treatment planning BrachyVision (Varian Brachytherapy, Charlottesville, VA) to produce the optimal conformal plan in accordance with volume definition and dose requirements. The treatment plan used for each patient was based on an analysis of the volumetric dose including dose–volume histogram analyses of the PTV_EVAL and critical normal tissues.

Determination of appropriateness for treatment

Appropriateness for treatment was based on the ability to achieve the dosimetric goals. As stated, with the use of a single lumen–single dwell position device the ability to achieve dosimetric goals is directly related to the basic geometric parameters that include tissue–balloon conformance, balloon symmetry, and the balloon surface–skin distance. Maximal coverage of the target volume with full prescription dose was strived for but within this experience it was required that 90% of the target receive >90% of the prescription dose. Frequently, air and/or fluid were identified between the lumpectomy cavity and balloon surface. Either as a result of an irregular cavity shape or because the air/fluid was trapped, a less than ideal conformance resulted and displaced a corresponding percentage of the PTV_EVAL beyond the prescription isodose line coverage. To determine the significance of the trapped air/fluid, these volumes were contoured and used in calculating the PTV_EVAL dose coverage. Typically, when the volume of trapped air/fluid was <10% of the PTV_EVAL, acceptable dose coverage was achieved. Any detected balloon asymmetry was corrected with the dose shaping capabilities of the Contura MLB. The success and degree of correction was dependent upon the degree of asymmetry. Ideally, the minimal balloon surface–skin distance should be ≥ 7 mm. However, because the maximum acceptable skin dose for treatment was <145% of the prescribed dose (PD), then the use of the offset lumens reduced the skin dose if a balloon–skin thickness between 2 and 7 mm was encountered. Once the dosimetric goals were achieved, treatment was typically initiated within 1–5 days from the acquisition of the planning CT. The balloon remained inflated throughout the treatment course and patient positioning, balloon inflation, and proper balloon rotation were confirmed before each treatment delivery.

A total of 34 Gy was prescribed to the PTV_EVAL such that the dosimetric requirements of target coverage, dose homogeneity, and reduced skin dose were satisfied. Two fractions per day, each of 3.4 Gy, separated by at least 6 h, were given in 5 consecutive working days. For each patient, the dosimetric plan was customized using the five high-dose-rate brachytherapy channels of the Contura catheter by selecting from 40 different dwell positions (8 per

catheter). Before each treatment, the following steps were taken: (1) The continued integrity of the balloon throughout treatment, as determined by ultrasound or X-ray performed before each delivered fraction was evaluated for any change in balloon diameter. These were compared to a similar study performed at the time of treatment planning. If a change in balloon geometry was noted, this was addressed before additional treatment (i.e., a repeat CT scan was performed to reverify conformance, skin distance, etc.). If necessary, the plan was recalculated to account for any significant changes noted. (2) The patient's position in which the planning CT was obtained was reproduced before each fraction. (3) To assure proper orientation of the device throughout treatment, the orientation line was identified and the proper alignment, as compared to the alignment at the time of planning was verified and easily corrected if any rotational deviation was seen before each fraction.

Quality assurance of dose distribution

Dose–volume histogram analyses of target coverage were performed in each case to confirm that a minimum of $\geq 90\%$ of the PD covered $\geq 90\%$ of the PTV_EVAL (per NSABP B-39/RTOG 0413 criteria). The maximum skin dose was reduced to as low as achievable while satisfying all dose parameters and not exceeding 145% of the PD. The maximum rib dose was reduced to as low as achievable while satisfying all dose parameters not to exceed 200% of the PD (if possible). The volume of breast tissue receiving 150% (V_{150}) of the PD was reduced to as low as achievable while satisfying all dose parameters, but was not to exceed 50 cc. The volume of breast tissue receiving 200% (V_{200}) of the PD was reduced to as low as achievable while satisfying all dose parameters, but was not to exceed 10 cc.

Toxicity evaluations

Patients were followed up (physical examination, cosmesis, and toxicity assessment) at 3-month intervals by their radiation oncologist and surgeon. Baseline mammography was performed 6–12 months after the completion of treatment. Followup was complete through November 11, 2008.

Infections

Any breast infection, mastitis, cellulitis, or abscess that was observed during followup was considered as an “infectious event.” Device-related infections were those believed to be secondary to the use of the Contura applicator. However, no stringent criteria were established.

Pain score

Pain was assessed at the time of catheter insertion using the following scale: 0, 1, 2, or 3 = minimal to no pain, only requiring (at most) temporary, occasional non-narcotic

analgesics; 4, 5, 6, or 7 = persistent (course of treatment only) pain/discomfort controlled with non-narcotic analgesics; 8, 9, or 10 = persistent (course of treatment only) pain/discomfort controlled with narcotic analgesics.

Seromas

The presence of a seroma was evaluated at each follow-up visit and diagnosed clinically or mammographically. Seromas were subcategorized into either symptomatic (associated with pain and/or requiring intervention by the physician) or asymptomatic.

Cosmesis

Cosmetic outcome was evaluated using the Harvard criteria. An excellent cosmetic result score was assigned when the treated breast looked essentially the same as the contralateral breast (as it relates to radiation effects). A good cosmetic score was assigned for minimal but identifiable radiation effects of the treated breast. A fair score meant radiation effects were readily observable and significant. A poor score was used for severe sequelae of breast tissue secondary to radiation effects.

Results

The median age at diagnosis was 59 years (range, 42–81). The median tumor size was 15 mm (range, 3–38) (33 evaluable patients—there was no measurable tumor remaining post-biopsy in the lumpectomy specimen [per path report] in 8 of the 41 patients), and 21 patients (51.2%) were clinical Stage T1. Table 1 provides a comprehensive summary of all other patients, tumor, and treatment-related characteristics. The median followup in surviving patients was 8 months (range, 1–17).

Toxicity and cosmetic result evaluations

Transient breast infections were seen in 10.8% of patients (4/37 evaluable patients). No patient required surgical intervention (i.e., debridement). All infections resolved with oral antibiotics. Symptomatic seromas were noted in 2.8% of patients (1/36 evaluable patients). This resolved after needle aspiration. Symptomatic fat necrosis has not been observed and no rib fractures have been noted. One patient died from complications resulting from chemotherapy (she had no evidence of disease at the time of death).

Pain was assessed at the time of insertion using a scale of 0–10 (see previous section). Pain was graded ≤ 3 at the time of catheter insertion in 37 (97.4%) out of 38 of evaluable patients (no patient scored greater than 5).

Cosmetic results were rated as good/excellent in 100% of all evaluable patients ($n = 38$). At 6 months ($n = 15$) and 12 months ($n = 12$), good/excellent cosmesis was recorded in 100.0% of patients.

Table 1
Patient, tumor, and treatment-related characteristics

Characteristic	#	%
Total no. of patients	41	—
Median followup (mo)	8	—
Range	(1–17)	
Age (yr)		
Median	59	—
Range	(42–81)	
Postmenopausal	32	78.1
Tumor size (mm); <i>n</i> = 33		
Median	15	
Range	(3–38)	
<10	6	18.2
≥10 <20	18	54.6
≥20	9	27.3
T-stage		
TIS	13	31.7
T1	21	51.2
T2	7	17.1
Estrogen receptor positive (ER+)	30	73.2
Progesterone receptor positive (PR+)	19	46.3
Invasive cancer (<i>n</i> = 28)		
Node (–)	28	100.0
Node (+)	0	0.0
Chemotherapy (yes)	10	24.4
Tamoxifen (yes)	10	24.4
Arimidex (yes)	12	29.3
Femara (yes)	6	14.6
Final margin (–)	41	100.0

Dosimetric results

All critical dosimetric quality parameters are listed in Tables 2 and 3.

With respect to PTV_EVAL coverage, all patients met NSABP B-39/RTOG 0413 criteria (90% of PTV_EVAL covered by 90% of PD), regardless of skin spacing or proximity to chest wall. In fact, the median dose to 95% of the PTV_EVAL was 98.8%. Concurrently, the median and maximum doses to the skin were 99.7% and 124.1% of the PD. No excessive hot spots developed (median and maximum V_{200} = 5.7 and 9.9 cc, respectively) and no excessive rib doses were noted in these same groups of patients (median and maximum % of PD = 102.6 and 187.7, respectively).

Discussion

We reviewed our institution's experience treating patients with the Contura MLB breast brachytherapy catheter to deliver APBI to determine short-term treatment efficacy, cosmesis, toxicity, and possible improved dosimetric capabilities. Although followup is short, toxicity profiles appear similar to those observed with other forms of brachytherapy to deliver APBI with similar followup (12, 13). The percentage of patients with excellent/good

cosmetic results at 6 and 12 months was 100% and only four breast infections (11%) and one transient symptomatic seroma (3%) developed. In addition, improvements in several dosimetric parameters appear feasible suggesting the ability to expand the use of balloon brachytherapy to treat more patients with APBI and/or to potentially improve standard balloon-based brachytherapy with APBI.

Acute toxicity

One of the fundamental differences between the Contura and the MammoSite is the slightly larger shaft to accommodate the additional lumens (8 vs. 6 mm, respectively). In this series of patients, placement techniques (based on pain score, infection rates) appear similar. Only 10.8% of patients developed an infection. This rate is similar to what was observed in the American Society of Breast Surgeons MammoSite Registry trial (10%) (14). In addition, patient

Table 2
Radiation and treatment-related characteristics

Characteristic	#
Total no. of patients	41
Minimum skin spacing (mm)	
Median	10.0
Mean	9.2
Range	(2–17)
Skin spacing	
>7 mm	27
>5 ≤ 7 mm	6
≥2 ≤ 5 mm	8
Balloon volume (cc)	
Median	40
Mean	43.9
Range	(33–58)
Balloon diameter (cm)	
Median	4.3
Mean	4.4
Range	(3.8–5.0)
Skin dose (cGy)	
Median	339
Range	(194–422)
Skin dose (% of PD)	
Median	99.7
Range	(57.1–124.1)
Rib dose (% of PD)	
Median	102.6
Range	(10.0–187.7)
V_{150} (cc)	
Median	29.0
Mean	29.5
Range	(21.0–37.9)
V_{200} (cc)	
Median	5.7
Mean	5.7
Range	(1.3–9.9)

PD = prescribed dose; V_{150} = volume of breast tissue receiving 150% of the PD; V_{200} = volume of breast tissue receiving 200% of the PD.

Table 3
Radiation quality indices

Characteristic	#
Total no. of evaluable patients	41
% of PD to 95% of PTV_EVAL	
Median	98.8
Mean	97.6
Range	(79.4–107.4)
% of PD to 90% of PTV_EVAL	
Median	102.8
Mean	102.8
Range	(96.2–111.2)
Volume of PTV_EVAL (cc)	
Median	87.1
Mean	89.7
Range	(71.9–108.9)
V_{100} (cc)	
Median	80.3
Mean	83.8
Range	(60.7–105.0)

PD = Prescribed dose, PTV = planning target volume; PTV_EVAL = planning target volume for evaluation; V_{100} = volume of breast tissue receiving 100% of the PD.

tolerance based on the pain scale used showed no perceptible differences in patient acceptance.

Improved dosimetric capabilities

Although this study was not designed to directly compare dosimetric capabilities of the Contura MLB to single lumen balloon brachytherapy, some interesting observations can be made. First, a total of 14 patients had a balloon surface-to-skin spacing of ≤ 7 mm (range, 2–7). In all cases, the use of the multiple lumens resulted in acceptable skin doses as per NSABP B-39/RTOG 0413 criteria (i.e., $<145\%$ of the PD). Several of these patients would not have been considered acceptable candidates for APBI (<5 mm skin spacing) without the ability to tailor the dose away from the skin. In all cases, this contouring of the dose distribution through the use of multiple lumens (to maintain an acceptable skin dose) just as importantly did not increase the V_{150} or V_{200} or the dose to the ribs.

Second, the preliminary use of this device suggests that higher dosimetric goals can be set and achieved. For example, the NSABP B-39/RTOG 0413 Phase III trial mandates that 90% of the PTV_EVAL is covered by 90% of the PD. With the Contura, 99% of the PTV_EVAL was able to be covered at minimum by 95% of the PD without excessively increasing hot spots (V_{150} or V_{200}), skin dose, or rib dose.

Although not addressed in this analysis, it is theoretically possible to increase the radiation margin (through the use of multiple lumens) to expand the CTV margin (i.e., prescribing the dose beyond 1.0 cm) to treat possible areas of disease beyond this distance (15–17). The possible, safe increase in the CTV achievable with the

Contura MLB catheter (while maintaining acceptable V_{150} and V_{200} volumes) is unknown and awaits further additional analyses. Nonetheless, the use of multiple lumens in our limited study warrants investigation if the CTV for APBI with balloon brachytherapy could potentially be expanded to improve treatment efficacy in certain subsets of patients.

Conclusions

For balloon-based brachytherapy to continue to grow in use and represent a prominent method of APBI delivery, technologic improvements beyond the single lumen–single dwell design are necessary. The Contura MLB represents one method of improvement by providing the radiation oncologist with additional options to better customize the radiation dose profile generated from an intracavitary device to the specific case needs to be treated. In this experience, adjuvant APBI using the Contura MLB catheter exhibited similar early toxicities to standard single lumen, single dwell balloon brachytherapy with potential improvements in dosimetric capabilities (i.e., reduced skin dose, improved PTV_EVAL coverage, and normal tissue avoidance). However, additional studies are needed to confirm these encouraging early findings.

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