

Dosimetric Improvements in Balloon Based Brachytherapy Using the Contura[®] Multi-Lumen Balloon (MLB) Catheter to Deliver Accelerated Partial Breast Irradiation

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Abstract

Purpose: Preliminary dosimetric findings in patients managed with the Contura[®] Multi-Lumen Balloon (MLB) breast brachytherapy catheter to deliver accelerated partial breast irradiation (APBI) on a multi-institutional phase IV registry trial were reviewed.

Material and methods: CT-based 3D planning with dose optimization was performed for all patients. For the study, new ideal dosimetric goals were developed: 1) $\geq 95\%$ of the prescribed dose (PD) covering $\geq 90\%$ of the target volume (TV), 2) a maximum skin dose $\leq 125\%$ of the PD, 3) maximum rib dose $\leq 145\%$ of the PD, and 4) the V150 ≤ 50 cc and V200 ≤ 10 cc. The frequency of concurrently achieving these dosimetric goals using the Contura[®] MLB was investigated.

Results: 194 cases were evaluable. Employing the MLB, all ideal dosimetric criteria were achieved in 76% of cases. Evaluating dosimetric criteria separately, 90% and 89% of cases met the new ideal skin and rib dose criteria, respectively. In 96%, ideal TV coverage goals were achieved and in 96%, dose homogeneity criteria (V150 and V200) were met. For skin spacing ≥ 5 -7 mm, the median skin dose was 121% of the PD and when < 5 mm, the median skin dose was 124.4%. For rib distances < 5 mm, the median rib dose was reduced to 136.4% of the PD. For skin spacing < 7 mm and distance to rib < 5 mm, the median skin and rib doses were concurrently limited to 121% and 142.8% of the PD, respectively.

Conclusions: The Contura[®] MLB catheter provides potential improvements in dosimetric capabilities (i.e., reduced skin and rib doses and improved TV coverage) in many clinical scenarios.

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Key words: breast conserving therapy, balloon brachytherapy, Contura[®].

Purpose

Accelerated partial breast irradiation (APBI) is being investigated as alternative option to deliver adjuvant radiation therapy (RT) after surgery in selected low-risk patients undergoing breast conserving therapy (BCT) [1]. Many phase I/II studies (and some recent phase III data) have demonstrated excellent 5 and 10-year rates of local control, cosmesis and minimal toxicity using this treatment approach [2-5]. Trials using catheter based interstitial brachytherapy (IB) as the APBI technique have provided the largest group of cases treated with the longest follow-up. One of the potential disadvantages of IB as a method to deliver APBI is the complexity and reproducibility of the procedure. In light of these concerns, the MammoSite[®] (MS) applicator (Hologic Inc, Bedford, Mas-

sachusetts) was developed and introduced in 2002 to provide a less complex implant with improved reproducibility of radiation delivery to the target volume when compared to IB.

The first phase I/II clinical trial of the MammoSite[®] balloon catheter included 43 patients who received RT as their primary treatment [6]. Patients experienced only mild-to-moderate side effects related to the RT treatment. The 5-year cosmetic results have been good to excellent in 83% of the cases treated and no local recurrences have been observed after a median follow-up of 66 months [7]. Numerous single-institution experiences have also produced acceptable early local control rates and cosmetic results (with only minimal toxicities) [8]. Data on the use of the MammoSite[®] to deliver APBI by the American Society of Breast Surgeons (ASBrS) demonstrates a 5-year

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Fig. 1. Contura® multi-lumen balloon (MLB) (SenoRx, Inc., Irvine, California)

ipsilateral breast tumor recurrence (IBTR) rate of only 3.8% in the first 400 patients treated on this registry trial (with a median follow-up 59 months) with 93% of these patients experiencing good/excellent cosmetic results [9-11].

Many of the original dosimetric parameters used to assess the appropriateness for treatment with the MammoSite were based on the limited dosimetric capabilities of the initial single lumen device. The dosimetric performance of the device is dependent on 1) its location of placement within the breast, 2) the symmetry of the balloon implanted and 3) its fit (inflated) within the lumpectomy cavity relative to the skin surface and the chest wall/rib cage [12]. In addition, the dosimetry of the device is also limited (to a large extent) by the physics of dose deposition with an Ir-192 source coupled with the symmetrical nature of a single-lumen applicator. For the target volume to receive a dose gradient between 100% and 200% of the prescription dose (PD), the treatment margin must be generally limited to only 1 cm¹ or less. Due to the device's fixed geometry, the dose to the skin is uniquely tied to the skin distance: in other words, for a given distance the maximum dose to skin is precisely defined. As a result, the only technique to reduce skin dose is to potentially reduce the overall target dose coverage, down to the currently minimum accepted D90 of approximately 90%. In order to minimize the number of aborted cases, physicians are often forced to accept compromises on dosimetric endpoints and therefore to reduce the target volume coverage and/or to risk acute or chronic toxicity. Instead of setting dosimetric goals at a level for optimal utilization of APBI to treat patients, dosimetric parameters should be set to optimize target volume coverage and to reduce toxicity with the understanding that these goals should be achieved or the case (e.g., the application of balloon brachytherapy to deliver APBI) aborted.

In order to develop improved dosimetric goals associated with balloon based APBI (and for the purpose of the registry study detailed below), a new set of ideal dosimet-

ric parameters were derived based upon treatment outcome experiences using the MammoSite as well as with the appropriate application of basic brachytherapy principles [13]. These improved dosimetric goals are based upon achieving the following endpoints: 1) providing dosimetric coverage of 95% of the target volume with at least 95% of the prescribed dose (PD), 2) restricting the volume of breast tissue that receives 150% of the PD to ≤ 50 cc and 3) that which receives 200% of the PD to ≤ 10 cc, 4) insuring that the skin receives $\leq 125\%$ (42.5 Gy) of the PD and 5) that the chest wall/ribs receive $\leq 145\%$ (50 Gy) of the PD. For the purposes of comparison (in order to determine the percentage of cases in which these ideal dosimetric goals could be met with current single lumen balloon brachytherapy), dosimetric information from 82 patients treated at the Virginia Commonwealth University (VCU) between 2005 and 2008 with MammoSite® APBI were reviewed (Verbal communication, Arthur: 2008). In the majority of these cases, multiple dwell positions within the single central lumen were used to individually optimize dose delivery. Allowing for a 5% relaxation of dosimetric goal #1 listed above (e.g., dosimetric coverage of 95% of the target volume with 90% of the PD), evaluation of these data revealed that only 60% of the cases treated at VCU with the single-lumen MammoSite® device met all of the above listed new, ideal dosimetric criteria. All 82 cases were initially evaluated with CT scans of the implanted breast and 3D treatment planning was used to optimize dosimetry through multiple dwell positions (e.g., each case was fully optimized using contemporary brachytherapy tools and techniques).

The Contura® multi-lumen balloon (MLB) (SenoRx, Inc., Irvine, California) was developed to potentially improve the critical dosimetric shortcomings of current balloon brachytherapy and to provide physicians with additional methods to better conform the radiation dose to the target tissue (and to help reduce toxicities and improve cosmetics) [14]. With the addition of four lumens, each off-set 5 mm from a central catheter lumen (Fig. 1), clinically meaningful dose shaping becomes possible. This design helps to decouple the skin/rib dose from the distance of these structures to the balloon surface. As a result, the skin/rib dose can be minimized without necessarily compromising the target coverage. This provides the potential to overcome the restrictions of 1) limited skin distance, 2) close chest wall/rib proximity and 3) balloon asymmetry while consistently achieving dosimetric planning goals [14]. The unique design of the Contura® MLB catheter offers the potential for improved dose delivery in patients presently managed with balloon based brachytherapy as well as the ability to potentially treat cases that previously would have been excluded. These improvements are made possible due to the anticipated ability of the MLB to improve dose coverage of the breast target volume while concurrently minimizing dose to nearby structures such as the chest wall, pectoralis muscle and skin.

In January of 2008, a registry study using the Contura® MLB was designed and initiated to investigate and objec-

¹Slightly less than 1 cm and slightly more than 1 cm, for a small (2-2.5 cm radius) balloon and a large one (radius > 2.5 cm), respectively

tively define the dosimetric capabilities of the new device. More specifically, information was sought to help clarify the frequency and extent of dosimetric improvement using the device and to identify any clinical scenarios where the use of the Contura® MLB was clearly superior to single lumen balloon brachytherapy. Patient eligibility criteria were designed not to overlap with potential candidates for the NSABP 39/RTOG 0413 Phase III study [15]. Participating sites were required to complete and pass physics training prior to enrolling cases to assure optimal use of the more complicated, multi-lumen device. Dosimetric guidelines were provided to both improve the optimal target volume coverage while reducing doses to non-target tissues. Each participating site was required to provide (submit) comprehensive data from a dosimetric exercise comparing the ability to meet the new, ideal dosimetric goals between central lumen/single dwell, central lumen/multi-dwell and multi-lumen/multi-dwell treatment plans.

This report presents an early analysis of the first 194 patients enrolled and treated on the Contura registry trial. The report is limited only to an analysis of the improved dosimetric capabilities of the MLB device and its ability to meet the previously discussed improved dosimetric goals and will not report on the primary or secondary endpoints of the trial (see below).

Material and methods

Details of the Contura® Registry study have been previously reported [16]. Briefly, the study is a multi-institutional, prospective, non-randomized phase IV protocol with a total accrual goal of 342 patients needed to address the primary endpoint: To compare the dosimetric success rate of the Contura® MLB with a single, central lumen balloon device to deliver APBI. "Success" in the trial was defined as the ability to meet all the dosimetric criteria (concurrently) as outlined in the protocol (see below). Secondary endpoints include disease control, cosmetic results at defined intervals and acute and chronic toxicity rates during a follow up period of 5 years. In addition, the trial was designed to identify clinical scenarios where only the Contura® MLB could be safely used to deliver adjuvant APBI using balloon brachytherapy.

The Registry protocol was approved by the Massey Cancer Center Protocol Review and Monitoring System Committee at the VCU. Institutional Review Board approval was obtained by each participating institution and the study registered with the National Institutes of Health (www.clinicaltrials.gov, No NCT00699101). As previously mentioned, this report focuses only on the dosimetric experience of multi-lumen use in the first 194 patients treated with complete data submitted and available for review. A similar study looking at the same endpoints in the first 144 patients has been previously reported [16].

Eligibility criteria

Patient eligibility for the trial required that all cases met the following conditions: age \geq 50 years old at diagnosis,

life expectancy greater than 10 years, surgical treatment of the breast (e.g., lumpectomy) with negative surgical margins per NSABP criteria, histologic examination confirming DCIS and/or invasive breast carcinoma, the tumor must be estrogen receptor positive, the T stage must be Tis, T1, or T2 (the tumor must be \leq 3.0 cm in maximum diameter) and for patients with invasive breast cancer, an axillary staging procedure must be performed (either SNB alone or axillary dissection with a minimum of six axillary nodes removed), and the axillary node(s) must be pathologically negative.

Exclusion criteria included: age $<$ 50 at diagnosis, pregnant or breast-feeding, active collagen-vascular disease, Paget's disease of the breast, prior history of DCIS or invasive breast cancer, prior breast or thoracic RT for any condition, multicentric carcinoma (DCIS or invasive), synchronous bilateral invasive or non-invasive breast cancer, surgical margins that cannot be microscopically assessed or that are positive, positive axillary node(s), T stage of T2 with the tumor $>$ 3 cm in maximum diameter or a T stage $>$ 3, or estrogen receptor negative tumor.

Brachytherapy procedure

After lumpectomy to remove the tumor with negative surgical margins was completed, the Contura® MLB was placed into the surgical cavity and inflated in a separate procedure using ultrasound guidance. The balloon remained inflated throughout the course of radiation treatment. Standard treatment planning guidelines for APBI were employed and CT imaging was mandatory (for treatment planning purposes). CT-based 3-D brachytherapy treatment planning was conducted using commercially available software and equipment specific to each participating site.

The total prescribed dose (PD) was 34 Gy delivered to the PTV_EVAL divided in 10 fractions over 5 consecutive working days. Treatment fractions were delivered twice daily with at least six hours separating each fraction. Prior to each fraction, the patient's position, balloon inflation and rotational alignment status was verified to be identical to that at the time of the initial planning CT. All treatments were completed using a commercially available HDR remote afterloader and 192-Ir radioactive source. After completion of treatment delivery, the balloon was deflated and applicator removed using site specific techniques.

Quality assurance criteria and dosimetric guidelines

As previously mentioned, all participating sites were required to complete and pass physics training. Dosimetric guidelines were provided to ensure maximum dose coverage of the target volume and the lowest possible risk of acute and chronic toxicity. At the time of CT planning, appropriateness of balloon placement was evaluated by the treating physician. Adjustments were made (balloon volume adjustment, removal of trapped air/fluid with the suction port, improved orientation through catheter rotation) as needed. Patient position and balloon rotational orientation were documented (via image/picture of catheter and orientation line) for comparison during treatment.

Structures contoured and/or created as a part of the treatment planning process included: a) the balloon surface, b) the planning target volume for evaluation (PTV_EVAL), c) trapped air and/or fluid, d) the skin surface, and e) the aspect of the closest rib. Target volumes and normal tissue structures were outlined on all CT cuts when appropriate and possible. The PTV_EVAL was defined and delineated in each case as the breast tissue volume bounded by a uniform expansion of the balloon radius in all dimensions by 10 mm (less the balloon volume) and limited to 5 mm from the skin surface and by the posterior breast tissue extent (chest wall and pectoralis muscles were not included). When calculating dose coverage of the PTV_EVAL to assure compliance with dose requirements, 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 CT level, a total volume obtained and the percentage of the PTV_EVAL that it displaced was calculated. When defining the PTV_EVAL dose coverage, this displaced percentage was subtracted. If the percentage of PTV_EVAL displaced by trapped air/fluid was greater than 10%, then it is not possible to achieve acceptable dose coverage. The final treatment plan used for each patient was based on an evaluation of the volumetric dose including dose-volume histogram (DVH) analyses of the PTV_EVAL and critical normal tissues.

The final decision for treatment was based on the ability to meet dosimetric goals anticipating that the multi-lumen design of the Contura would provide the opportunity to overcome some degree of geometric variance. General geometric rules included: 1) optimal tissue-balloon conformance 2) optimal balloon symmetry and 3) a balloon surface to-skin distance ≥ 3 mm (ideally ≥ 7 mm).

Quality assurance of dose distribution "ideal" dosimetric goals

The "ideal" dosimetric goals in the trial were defined as follows: Dose volume histogram analysis of target coverage needed to confirm that $\geq 95\%$ of the PD covered $\geq 95\%$ of the PTV_EVAL (accounting for the volume of trapped air/fluid and allowing a 5% relaxation). The maximum skin dose needed to be reduced to as low as achievable and could not exceed 125% of the PD. The maximum rib dose was reduced to as low as achievable and could not exceed 145% of the PD. The volume of breast tissue receiving 150% (V150) of the PD had to be reduced to as low as achievable and could not exceed 50 cc. The volume of breast tissue receiving 200% (V200) of the PD had to be reduced to as low as achievable and could not exceed 10 cc.

"Acceptable" doses

"Acceptable" dosimetric goals were defined as follows: Dose volume histogram analysis of target coverage confirmed that $\geq 90\%$ of the PD covered $\geq 90\%$ of the PTV_EVAL (again, accounting for the volume of trapped air/fluid). The maximum skin dose was to be reduced to as low as achievable while satisfying all dose parameters but could not exceed 145% of the PD. The maximum rib

dose was unrestricted. The volume of breast tissue receiving 150% (V150) of the PD should be reduced to as low as achievable while satisfying all dose parameters but could not exceed 50 cc. The volume of breast tissue receiving 200% (V200) of the PD should be reduced to as low as achievable while satisfying all dose parameters but could not exceed 10 cc.

"Unacceptable" doses

"Unacceptable" criteria for treatment included any of the following: dose volume analyses of the target volume confirming $< 90\%$ of the prescribed dose and/or $< 90\%$ coverage of the PTV_EVAL, a maximum skin dose exceeding 145% of the PD, the volume of breast tissue receiving 150% (V150) of the PD exceeded 50 cc or the volume of breast tissue receiving 200% (V200) of the PD exceeded 10 cc.

Data collection

Data that were collected during the study included baseline patient demographics, tumor characteristics related to the time of implant, radiation therapy details, and removal of the device as well as recurrence data, cosmetic outcomes and toxicities. Patient follow-up data were collected during standard follow-up visits. The study was designed to accrue 342 patients and follow them for 5 years. All data were submitted to SenoRx by participating institutions and all data are verified for accuracy and stored by an independent company: BioStat, Int. Interim analysis was performed by Biostat and final statistical evaluation (overall endpoints of the trial) will be performed by the involved VCU statistician.

Results

Study population

As of January 2010, 194 cases had complete data sets available for review at the time of this analysis (see Table 1). The median age is 64.1 years and 20.1% had stage Tis, 72.2% with T1N0 and 7.7% with T2N0 (< 3 cm). The median tumor size was 1.2 cm.

Dosimetric characteristics and findings

Employing the multi-lumen capabilities of the Contura device, all the new 'ideal' dosimetric criteria were met concurrently in 76.3% of cases treated. Examining dosimetric criteria individually, it was found that 90.2% of all cases met the new ideal skin dose criteria and in 89.2%, the ideal rib dose criteria were met. In a total of 96.4% of the cases treated, the ideal target volume coverage goals were met and in 98.5% and 95.9%, ideal dose homogeneity criteria of V150 and V200 were achieved, respectively (see Tables 2 and 3).

Difficult clinical scenarios

In all scenarios where skin and/or rib distances were felt to be close and meeting dosimetric goals "difficult", the capability of the Contura multi-lumen balloon to improve dose conformance was examined (see Table 4).

When the skin distance was ≥ 5 mm but < 7 mm ($n = 39$), median skin doses were limited to 121.0% (range, 74.0–135.3) of the PD and when the distance to the skin was < 5 mm ($n = 22$), the median skin dose was calculated at 124.4% (range, 85.6–144.0) of the PD. When the distance of the balloon to the rib was < 5 mm ($n = 70$), the median rib dose was limited to 136.4% (range, 103.0–178.0) of the PD. In the most difficult and demanding clinical scenarios ($n = 27$) when both the distance to the skin was < 7 mm and the distance to the rib was < 5 mm, the median skin and rib dose were concurrently limited to 121.0% and 142.8% of the PD, respectively.

Discussion

In the current analysis, we analyzed the early clinical experience in patients treated with the new Contura® MLB breast brachytherapy catheter to deliver APBI in a registry trial developed to evaluate potential improvements in the dosimetric capabilities of balloon based brachytherapy. Employing the multi-lumen capabilities of the Contura device, all the new ideal (improved) dosimetric criteria were achieved (simultaneously) in a total of 76% of all cases treated. When evaluating dosimetric criteria individually, use of the device allowed 90.2% and 89.2% of cases to meet the new ideal skin and rib dose criteria (respectively), 96.4% of cases to meet the new/ideal target volume coverage goals and in 95.9%, the dose homogeneity criteria of V150 and V200 were achieved. In those difficult cases where both skin and/or rib distances to the balloon surface were felt to be too close, improved dosimetry was also consistently documented. These improvements in dosimetric findings suggest that the Contura® MLB can provide additional options to improve dose delivery over present, single lumen balloon treatment (for patients currently treated with balloon brachytherapy) and to possibly expand the use of balloon based brachytherapy to manage patients not previously considered acceptable (or borderline) for the application of APBI.

Establishing ideal dosimetric criteria with balloon based brachytherapy

Establishing ideal dosimetric guidelines for the use of balloon based brachytherapy to deliver APBI has remained challenging and continues to evolve. Initially, recommendations for the use of the single-lumen MammoSite® device were generated primarily from the experience utilizing IB to deliver APBI. These initial goals included 1) providing adequate coverage of the breast target volume (to deliver a therapeutic dose of radiation to the breast tissue at greatest risk for harboring residual disease after surgery), 2) reducing the skin dose as much as possible (in order to avoid significant chronic late effects that have been shown to affect cosmesis), and 3) mandating a limit on the inhomogeneity of the brachytherapy implant (again, in order to avoid late tissue effects related to hot-spots potentially causing such toxicities such as fat necrosis, fibrosis, retraction, induration, etc). For the most part, these initial treatment guidelines represented a practical compromise between the desire to provide acceptable target and nor-

Table 1. Patient, tumor and treatment related characteristics – study population

Characteristic	Treated subjects
Number of subjects	194
Follow-up (months)	
Median (range)	6.0 (0.3-18.1)
Patient age	
Median (range) (years)	64.1 (50.3-89.8)
≥ 60 years <i>N</i> (%)	134 (69.1)
50-60 years <i>N</i> (%)	60 (30.9)
Menopausal status <i>N</i> (%)	
Pre/Peri	14 (7.2)
Post	179 (92.3)
Breast Cup Size <i>N</i> (%)	
A	8 (4.1)
B	22 (11.3)
C	17 (8.8)
D+	21 (10.8)
Not measured	126 (64.9)
Lesion location <i>N</i> (%)	
UIQ	37 (19.1)
LIQ	6 (3.1)
Central	23 (11.9)
UOQ	95 (49.0)
LOQ	33 (17.0)
Histology <i>N</i> (%)	
DCIS	39 (20.1)
Invasive ductal	145 (74.7)
Invasive lobular	5 (2.6)
Maximum tumor size (mm)	
Median (range)	12.0 (0.5-30.0)
< 5	24 (12.4)
$\geq 5 - < 10$	57 (29.4)
$\geq 10 - \leq 20$	95 (49.0)
> 20	15 (7.7)
Unknown	3 (1.5)
Primary tumor grade <i>N</i> (%)	
I	71 (36.6)
II	86 (44.3)
III	35 (18.0)
AJC tumor status <i>N</i> (%)	
Tis	39 (20.1)
T1	140 (72.2)
T2, ≤ 3 cm	15 (7.7)
Overall AJC stage <i>N</i> (%)	
0	39 (20.1)
I	141 (72.7)
II	13 (6.7)
Final surgical margins <i>N</i> (%)	
Negative	153 (78.9)
Close	40 (20.6)
Positive	1 (0.5)
Estrogen receptor status <i>N</i> (%)	
Positive	194 (100.0)
Negative	0 (0.0)

Table 2. Radiation and treatment related findings

Characteristic	#
Number of subjects	194
Skin spacing	
Median (range) (mm)	9.7 (1.0-46.0)
< 5 mm <i>N</i> (%)	22 (11.3)
5-7 mm <i>N</i> (%)	39 (20.1)
> 7 mm <i>N</i> (%)	133 (68.6)
Balloon volume (cc)	
Mean	48.2
Median	42
Range	26.0-116
Skin dose (% of PD)	
Median	94.1
Range	33.2-144.0
Rib dose (% of PD)	
Median	110.9
Range	5.8-178.0
V150 (cc)	
Median	27.1
Mean	28.4
Range	11.6-82.2
V200 (cc)	
Median	5.7
Mean	6.2
Range	0.0-54.9

PD – Prescribed dose

V150 – Volume receiving 150% of the PD

V200 – Volume receiving 200% of the PD

mal tissues doses and the inherent physical design limitations of a single-lumen device (as well as its orientation in the breast).

Accumulated clinical outcome data obtained from the actual application of the MammoSite® now clearly indicate that improving many of these initial dosimetric guidelines could prove beneficial. For example, it is well established that optimal cosmetic results are directly related with increased skin-spacing (balloon surface-to-skin distance) [10, 14]. (The greater the distance of the balloon to the skin surface, the more optimal the short and long-term cosmetic result). With the single central lumen design of the MammoSite, increased distances directly translate into lower maximum doses to the skin. Due to the limitations of a single-lumen balloon design (even when employing multiple dwell positions with full optimization), clinicians are forced (in many scenarios) to either unnecessarily accept unwanted/excessive skin doses (secondary to insufficient skin spacing) or to remove the device and abort the APBI procedure. By making available an additional mechanism (e.g., multiple, off-set lumens) to minimize the skin dose (*after* the balloon has been placed and independent to the fixed balloon-to-skin distance), it is possible (in many cases) to both improve cosmetic results in many patients and/or to allow treatment with balloon brachytherapy in previously borderline or unacceptable cases (e.g., < 5-7 mm skin spacing). In addition, there is no reason to believe that

Table 3. Radiation quality indices

Characteristic	#
# of evaluable patients	194
% of PD to 95% of PTV_Eval	
Mean (Std)	96.5 (3.5)
Median (range)	96.2 (84.8-108.5)
% of PD to 90% of PTV_Eval	
Mean (Std)	100.4 (3.5)
Median (range)	99.7 (90.4-117.0)
Volume of PTV Eval (cc)	
Mean (Std)	84.7 (19.8)
Median (range)	81.7 (40.2-152.3)
V100 (cc)	
Mean (Std)	81.1 (21.2)
Median (range)	77.2 (34.5-156.9)

PD – Prescribed dose, *PTV* – Planning target volume

V150 – Volume receiving 150% of the PD

V200 – Volume receiving 200% of the PD

lowering (even further) the skin dose will not prove beneficial for all patients (e.g., even those with acceptable balloon-to-skin distances).

Likewise, improving balloon based brachytherapy (through the use of multiple-lumens) could also address other important dosimetric limitations previously reported with the MammoSite. 1) These include improving the coverage of the target volume (clinical and planning) beyond what is currently considered acceptable, 2) reducing the dose to the chest wall/ribs (to avoid late effects to these structures) and 3) limiting the volume of excessive hot-spots (V150 and V200). Similar to how skin dose guidelines were derived, initial recommendations for these other dosimetric endpoints also represented a less than optimal compromise between what was believed to be minimally required for optimal clinical outcome and what was possible within the limitations of a single-lumen balloon design. Very recent data are now indicating that excessive chest wall/rib doses can potentially cause rib fractures and/or chest wall discomfort in some patients. In addition, older MammoSite® data have also demonstrated the potential toxicity of excessive hot spots (V150 and V200) causing fat necrosis, fibrosis, or retraction [17, 18]. Although most clinical outcome data on the use of the MammoSite® to deliver APBI appear acceptable (even with its single-lumen limitations), there clearly is significant room for improvement in all these critical dosimetric areas [11, 19]. It should be emphasized again that the minimization of dose to adjacent normal tissue structures (skin and chest wall) while maximizing the target coverage is currently only achievable in a multi-lumen paradigm when applying balloon brachytherapy. In order to achieve these apparently contradictory dosimetric goals, both the geometry of the device and the optimization of the treatment plan play significant roles.

Improving dosimetric capabilities

As previously discussed, this interim analysis does not directly compare the dosimetric capabilities of the Contu-

Table 4. Dosimetric findings versus clinical scenario

Clinical Scenario	N	Skin dose (% of PD)	Rib dose (% of PD)	% of PD to % of PTV_EVAL		
				90	95	100
Skin spacing						
≥ 7 mm	133	87.5 (33.2-128.0)	108.0 (13.0-164.0)	99.8 (90.4-113.4)	96.4 (84.8-107.7)	85.2 (56.3-97.9)
≥ 5-7 mm	39	121.0 (74.0-135.3)	125.0 (30.8-178.0)	99.5 (94.7-117.0)	95.6 (91.3-108.5)	84.0 (56.3-97.9)
< 5 mm	22	124.4 (85.6-144.0)	119.0 (5.8-165.0)	99.9 (91.7-110.6)	96.9 (86.0-105.6)	85.1 (74.6-96.4)
TOTAL Median (range)	194	94.1 (33.2-144.0)	110.9 (5.8-178.0)	99.7 (90.4-117.0)	96.2 (84.8-108.5)	84.9 (56.3-97.9)
Rib distance						
≥ 7 mm	103	95.0 (35.0-136.8)	75.0 (5.8-141.4)	99.7 (91.7-112.0)	97.0 (86.0-105.0)	87.8 (56.3-97.9)
≥ 5-7 mm	21	89.0 (38.0-130.0)	118.7 (65.0-170.0)	99.7 (96.1-111.0)	96.4 (92.5-106.0)	86.1 (69.1-97.3)
< 5 mm	70	94.4 (33.2-144.0)	136.4 (103.0-178.0)	99.9 (90.4-117.0)	95.6 (84.8-108.5)	82.8 (56.3-97.9)
TOTAL Mean (Std)	194	93.7 (25.7)	101.6 (40.7)	100.4 (3.5)	96.5 (3.5)	84.3 (8.7)
Skin < 7 mm and Ribs < 7 mm	31	121.0 (74.0-144.0)	140.2 (104.0-178.0)	100.0 (94.7-117.0)	95.9 (89.3-108.5)	85.0 (56.3-97.9)
Skin < 7 mm and Ribs < 5 mm	27	121.0 (82.0-144.0)	142.8 (105.6-178.0)	100.2 (94.7-117.0)	95.9 (89.3-108.5)	84.0 (56.3-97.9)
Clinical Scenario		V100 (cc)	V150 (cc)	V200 (cc)	PTV_EVAL	
Skin Spacing						
≥ 7 mm		81.1 (34.5-151.9)	27.8 (11.6-82.2)	5.6 (0.0-54.9)	84.1 (40.2-144.7)	
≥ 5-7 mm		64.3 (41.7-108.0)	25.4 (17.6-73.4)	5.6 (1.3-50.4)	70.5 (47.1-103.0)	
< 5 mm		81.1 (45.3-156.9)	27.0 (17.4-41.3)	6.5 (0.1-12.5)	80.8 (52.3-152.3)	
TOTAL Median (range)		77.2 (34.5-156.9)	27.1 (11.6-82.2)	5.7 (0.0-54.9)	81.7 (40.2-152.3)	
Rib distance						
≥ 7 mm		78.4 (43.3-156.9)	27.9 (19.0-73.0)	5.4 (0.0-10.6)	82.7 (40.2-152.3)	
≥ 5-7 mm		76.3 (57.9-151.9)	27.1 (18.5-39.8)	5.2 (0.0-17.3)	82.5 (63.4-143.7)	
< 5 mm		75.8 (34.5-149.9)	26.1 (11.6-82.2)	6.3 (0.0-54.9)	77.7 (42.7-144.7)	
TOTAL Mean (Std)		81.1 (21.2)	28.4 (8.1)	6.2 (5.6)	84.7 (19.8)	
Skin < 7 mm and Ribs < 7 mm		64.3 (41.7-140.5)	25.8 (17.4-73.4)	5.6 (0.5-50.4)	70.5 (47.1-140.3)	
Skin < 7 mm and Ribs < 5 mm		64.3 (41.7-140.5)	25.8 (17.4-73.4)	6.4 (0.5-50.4)	70.5 (47.1-140.3)	

ra® MLB to single lumen balloon brachytherapy. That is the primary endpoint of the Registry trial and will be addressed in a separate manuscript when the trial completes accrual. Nonetheless, this analysis provides several interesting observations that can be useful and applied today. For example, 61 patients in this analysis had a balloon surface-to-skin spacing that was < 7 mm (range, 1.0-6.1). In each case, use of the Contura’s multiple lumens resulted in acceptable skin doses (as per NSABP B39/RTOG 0413 criteria [e.g., < 145% of the PD]). Certainly, several of these patients would not have been considered acceptable candidates for APBI (< 5 mm skin spacing) without the ability to ‘push’ the dose away from the skin surface. In all cases, this ‘adjustment’ of the dose distribution through (the use of multiple lumens to maintain an acceptable skin dose) just as critically did not increase the V150 or V200 or reduce coverage of the PTV. Improving one dosimetric

endpoint at the expense of several others would not necessarily represent an improvement in the delivery of balloon based APBI. All endpoints need to be analyzed and optimized concurrently.

Second, this interim analysis clearly suggests that higher dosimetric goals can be sought and achieved in most cases. As previously discussed, the NSABP B-39/RTOG 0413 phase III trial requires that 90% of the PTV_EVAL is covered by 90% of the PD. This dosimetric target translates (in many cases) into geometric coverage that is less than the initially intended 1 cm (the typical margin required to cover subclinical disease remaining in the breast). This is particularly true for asymmetric PTV_EVAL volumes due to proximity of the balloon surface to the skin and/or chest wall. In the vast majority of cases included in this analysis (96%), use of the Contura® enabled 95% of the PTV_EVAL to be covered at minimum by 95% of the PD without exces-

sively increasing hot spots (V150 or V200), skin dose, or rib dose. Again, this was achieved simultaneously only because of the added capabilities from the use of multiple lumens.

Although the available clinical outcome data at 5 years using the MammoSite® to deliver APBI are quite good, long-term toxicities (suboptimal cosmesis, chest wall and/or rib discomfort and fat necrosis/fibrosis) could potentially increase with further follow-up [17, 18] and should be addressed with any new APBI technique or modification of current APBI devices. Having the ability to potentially eliminate these concerns by reducing unnecessary doses to these normal tissues, non-target structures or by decreasing excessive hot spots seems warranted. Data from this early analysis demonstrate that multi-lumen balloon based brachytherapy is one technique that offers the potential to address these critical concerns.

Conclusions

Balloon based brachytherapy requires technological improvements (beyond a single lumen – single dwell design) for its continued growth and representation as a prominent method for the application of APBI. The Contura® MLB represents a unique method of improvement by providing the radiation oncologist with multiple offset lumens and multiple dwell positions to better conform and modify the radiation dose profile to the specific target volume to be treated after balloon placement. This modification in the balloon's design can translate into better PTV_EVAL coverage while simultaneously limiting dose to the skin, rib and normal breast tissue. Using the Contura® MLB catheter in the current registry trial, resulted in the achievement of a higher standard of dosimetric goals in the majority of cases despite frequent encounters with geometric restrictions and limitations.

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