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Prospective Comparison of Toxicity and Cosmetic Outcome After Accelerated Partial Breast Irradiation with Conformal External Beam Radiotherapy or Single-Entry Multilumen Intracavitary Brachytherapy

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Abstract

Objective: To prospectively characterize toxicity and cosmesis after accelerated partial breast irradiation (APBI) with 3D conformal radiotherapy (3D-CRT) or single-entry multilumen intracavitary brachytherapy.

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Conflicts of Interest Notification

All authors declare that they have no conflicts of interest.

Patients and Methods: Two hundred eighty-one patients with pTis, pT1N0, or pT2N0 (< 3.0 cm) breast cancer treated with segmental mastectomy were prospectively enrolled from December 2008 through August 2014. APBI was delivered using 3D-CRT ($N=29$) or with a SAVI® ($N=176$), Contura® ($N=56$), or MammoSite® ($N=20$) brachytherapy catheter. Patients were evaluated at protocol-specified intervals, at which time the radiation oncologist scored cosmetic outcome, toxicities, and recurrence status using a standardized template.

Results: Median follow-up is 41 months. Grade 1 seroma and fibrosis were more common with brachytherapy than with 3D-CRT (50.4% vs. 3.4% for seroma, $P<0.0001$; 66.3% vs. 44.8% for fibrosis, $P=0.02$), while grade 1 edema was more common with 3D-CRT than with brachytherapy (17.2% vs. 5.6%, $P=0.04$). Grade 2–3 pain was more common with 3D-CRT (17.2% vs. 5.2%, $P=0.03$). Actuarial five-year rates of “fair” or “poor” radiation oncologist-reported cosmetic outcome were 9% for 3D-CRT and 24% for brachytherapy ($P=0.13$). Brachytherapy was significantly associated with inferior cosmesis on mixed model analysis ($P=0.003$). Significant predictors of reduced risk of adverse cosmetic outcome after brachytherapy were D0.1cc (skin) 102%, minimum skin distance > 5.1 mm, dose homogeneity index > 0.54, and volume of non-conformance 0.89 cc. Five-year ipsilateral breast recurrence was 4.3% for brachytherapy and 4.2% for 3D-CRT APBI patients ($P=0.95$).

Conclusions: Brachytherapy APBI is associated with higher rates of grade 1 fibrosis and seroma than 3D-CRT but lower rates of grade 1 edema and grade 2–3 pain than 3D-CRT. Rates of radiation oncologist-reported “fair” or “poor” cosmetic outcome are higher with brachytherapy. We identified dosimetric parameters that predict reduced risk of adverse cosmetic outcome after brachytherapy-based APBI. Ipsilateral breast recurrence was equivalent for brachytherapy and 3D-CRT.

Introduction

Accelerated partial breast irradiation (APBI) is a convenient treatment option for some women with early-stage breast cancer who undergo breast-conserving surgery.^{1, 2} In appropriately selected patients, APBI results in local control and cosmetic outcome similar to those observed after external beam whole-breast radiotherapy. Numerous APBI techniques are available, including catheter-based interstitial brachytherapy, single-entry balloon and single-entry multilumen intracavitary brachytherapy applicators, and external beam radiotherapy. Most brachytherapy APBI today is done using single-entry multilumen applicators that allow improved tumor bed coverage while limiting dose to the skin, chest wall, and ribs. In this study, we prospectively compared toxicity and cosmetic outcome after APBI with single-entry multilumen brachytherapy and 3D conformal external beam radiotherapy (3D-CRT) and attempted to identify dosimetric parameters in brachytherapy patients that correlated with the development of discrete toxicities and adverse cosmesis.

Methods

Patient Eligibility

Patients electing APBI at a tertiary cancer center and its regional and national affiliates were eligible to participate in this prospective observational protocol provided they met all of the following criteria: age ≥ 50 years; pathologic diagnosis of invasive ductal or lobular

carcinoma, and/or DCIS measuring ≤ 3.0 cm; clinically unifocal disease; margins ≤ 2.0 mm; pN0 (for patients with invasive disease); and willingness to sign a study-specific consent form. Patients were excluded if they had LVSI, history of systemic lupus or scleroderma, prior breast or thoracic radiotherapy, prior ipsilateral breast cancer, clinically multifocal disease, or microscopic multifocality >3.0 cm. This study was reviewed and approved by the institutional review board.

Treatment

The PTV_EVAL volume was defined by method of APBI. For 3D-CRT, PTV_EVAL was defined as the lumpectomy cavity (LC) + 25 mm, limited to 5 mm from the skin and to the posterior extent of breast tissue. For the SAVI® catheter, PTV_EVAL was defined as (SAVI® device + 10 mm) – LC, limited to 2 mm from the skin (or periphery of the SAVI® device if closer than 2 mm from the skin) and to the posterior extent of breast tissue. For both the Contura® and MammoSite® catheters, PTV_EVAL was defined as (balloon + 10 mm) – balloon volume, limited to 5 mm from the skin and to the posterior extent of breast tissue. All brachytherapy patients were prescribed 34 Gy in twice-daily (BID) 3.4 Gy fractions. 3D-CRT patients were prescribed 34 Gy in BID 3.4 Gy fractions or 38.5 Gy in BID 3.85 Gy fractions. A minimum six-hour interfraction interval was required. 3D-CRT plans were optimized to have 90% of the PTV_EVAL volume covered by 90% (D90 = 90%) of the prescription dose, while brachytherapy APBI plans the goal was D95% = 95%, though D90% = 90% was considered acceptable. For all brachytherapy treatment plans, the normal breast V150 was required to be <50 cc. Normal breast V200 was required to be <20 cc for SAVI® and <10 cc for Contura® and MammoSite®. A 2 mm skin rind structure was used for volumetric skin dose calculations. Minimum skin distance and minimum rib distance were defined as the shortest 3D distance from the lumpectomy cavity (for 3D-CRT) or the brachytherapy applicator to the skin or rib surface, respectively.

Follow-up

Patients were assessed at six weeks after the date of completion of APBI, every six months until two years after completion of APBI, and then yearly. At each follow-up appointment, toxicity was scored according to CTCAE version 3.0 and cosmesis was scored according to the Harvard Breast Cosmesis Scale.³

Methods of Analysis

The actuarial cumulative incidence of each toxicity was calculated from the date of surgery to the date of the follow-up appointment at which the toxicity was first noted. To analyze the duration of each toxicity in patients who experienced an adverse event, the time to resolution was calculated from the date of the clinical evaluation at which the toxicity was first noted to the date of the clinical evaluation at which the toxicity was no longer present and did not recur. For both incidence and duration patients were censored at the date of last follow-up.

Results

Patient and Treatment Characteristics

A total of 281 patients were enrolled in this study from December 2008 to August 2014. The median age at diagnosis was 61 years (50–86 years). The median follow-up time at analysis was 41 months (1–94 months). Patient and treatment characteristics are summarized in Table 1. Brachytherapy patients had the device placed a median of 11 days (0–69 days) after segmental mastectomy or re-excision for close or positive margins. Median time to initiation of APBI from surgery was 14 days for brachytherapy and 29 days for 3D-CRT patients ($P<0.0001$). APBI was administered with 3D-CRT ($N=29$, 10.3%) or with a SAVI® ($N=176$, 62.6%), Contura® ($N=56$, 19.9%), or MammoSite® ($N=20$, 7.1%) brachytherapy applicator. Dosimetric parameters for 3D-CRT APBI and brachytherapy APBI patients are shown in Table 2.

Toxicity from Brachytherapy APBI and 3D-CRT APBI

The cumulative actuarial incidence and duration of each toxicity by APBI modality are shown in Supplemental Figure 1. Crude rates of seroma, infection, fat necrosis, pain, telangiectasia, rash, hyper- and hypopigmentation, fibrosis, and edema are shown in Supplemental Table 1. Intertoxicity associations are shown in Supplemental Figure 2.

Seroma—Seroma assessed by physical examination or diagnostic imaging was reported in 149 patients (59.1%) treated with brachytherapy and three patients (10.3%) treated with 3D-CRT ($P<0.0001$). Analyzed by CTCAE v3.0 grade, brachytherapy was associated with a significantly higher rate of grade 1 (G1; asymptomatic) seroma than 3D-CRT (brachytherapy, 50.4%; 3D-CRT, 3.4%; $P<0.0001$), but the rate of grade 2–3 (G2–3; symptomatic) seroma was equivalent (brachytherapy 8.7%; 3D-CRT, 6.9%; $P=1.00$).

Breast Infection—Breast infection was reported in 26 (10.4%) brachytherapy patients and no 3D-CRT patients ($P=0.09$).

Fat Necrosis—Fat necrosis was uncommon with both brachytherapy ($N=7$, 2.8%) and 3D-CRT ($N=0$, 0.0%), and its frequency was not significantly different between the two treatment groups ($P=0.44$).

Pain—Breast pain was observed in 115 patients (45.7%) treated with brachytherapy and 17 patients (58.6%) treated with 3D-CRT ($P=0.24$). G1 breast pain was common in both brachytherapy and 3D-CRT patients (brachytherapy, 40.5%; 3D-CRT, 41.4%; $P=0.52$), but G2–3 breast pain was significantly more frequent in patients treated with 3D-CRT (3D-CRT, 17.2%; brachytherapy, 5.2%; $P=0.03$).

Radiation Dermatitis, Telangiectasia, and Late Pigmentation Changes—Acute radiation dermatitis was common in both the brachytherapy ($N=142$, 56.4%) and 3D-CRT ($N=16$, 55.1%) groups, and cumulative incidence and grade did not differ between the groups. Telangiectasia developed in 50 patients (19.9%) treated with brachytherapy and seven patients (24.1%) treated with 3DCRT ($P=0.33$). G2–3 radiation dermatitis and G2–3

telangiectasia were interrelated in both brachytherapy patients ($P=0.003$) and 3D-CRT patients ($P=0.02$). Cumulative incidence of G2–3 telangiectasia did not differ by treatment group. Treatment-related hyper- and hypopigmentation were seen in 162 and 32 brachytherapy patients (64.2% and 12.7%), respectively and 19 and one 3D-CRT patients (65.5% and 3.4%), respectively. Cumulative incidence of hyper- or hypopigmentation or pigment changes by grade did not differ between treatment groups.

Fibrosis—Subcutaneous fibrosis was reported in 183 brachytherapy patients (72.7%) and 14 3D-CRT patients (48.2%) ($P=0.01$). The majority of fibrosis in both treatment groups was G1, and cumulative rates of G1 fibrosis were 66.3% in the brachytherapy group and 44.8% in the 3D-CRT group ($P=0.02$). Rates of G2–3 fibrosis did not differ between the treatment groups (brachytherapy, 6.4%; 3D-CRT, 3.4%; $P=1.00$).

Edema—Breast edema was more common in patients treated with 3D-CRT (3D-CRT, 17.2%; brachytherapy, 6.0%; $P=0.03$). Nearly all cases of breast edema were G1 (100% for 3D-CRT and 93.3% for brachytherapy).

Cosmetic Outcome with Brachytherapy APBI and 3D-CRT APBI

Crude rates of worst cosmetic score during follow-up are shown in Table 3. At 3 and 5 years, actuarial incidence of “fair” or “poor” cosmetic outcome (adverse cosmesis) were 9.0% and 9.0%, respectively, for 3D-CRT and 16% and 24%, respectively, for brachytherapy ($P=0.13$, Figure 1A). In a mixed model, cosmetic scores gradually increased in 3D-CRT patients and decreased in brachytherapy patients ($P<0.003$, Figure 1B). The effect of time was also a significant modifier of cosmesis ($P=0.002$). Historically, many women with small breasts were felt to be unsuitable for brachytherapy APBI due to concerns for severe adverse cosmesis. While we did observe a trend towards lower risk of adverse cosmesis with larger bra cup size, “poor” cosmesis was infrequent across bra cup sizes and was in fact more common in women with larger breasts (Figure 1C). While brachytherapy patients initiated treatment significantly sooner than did 3D-CRT patients, receiver operating characteristic analysis within the brachytherapy APBI group did not show a significant relationship between time to catheter placement (AUC=0.47) or time to treatment initiation (AUC=0.47) and risk of adverse cosmesis.

Dosimetric Correlates of Toxicity and Adverse Cosmesis in Brachytherapy APBI Patients

Associations between the dosimetric parameters listed in Table 2 and adverse cosmesis are shown in Table 4. The distributions of D0.1cc (skin) ($P<0.0001$), minimum skin distance ($P<0.0001$), dose homogeneity index (DHI) ($P=0.04$), and volume of non-conformance ($P=0.02$) were significantly different in patients who did and did not develop adverse cosmesis. Receiver operating characteristic analysis (Euclidean Distance) identified D0.1cc (skin) 102%, minimum skin distance >5.1 mm, DHI >0.54, and volume of non-conformance 0.89 cc to be associated with reduced risk of adverse cosmesis (Inlays in Figure 2A). Actuarial occurrence of adverse cosmesis using these thresholds is shown in Figure 2A. We performed a multi-variable logistic regression with these four parameters and found that minimum skin distance >5.1 mm (OR=0.26, 95%CI=0.13–0.55, $P=0.0004$) and volume of non-conformance 0.89 cc (OR=0.53, 95%CI=0.28–0.99, $P=0.048$) remained

independently associated with reduced risk of adverse cosmesis, while D0.1cc (skin) 102% (OR=0.64, 95%CI=0.32–1.28, $P=0.21$) and DHI >0.54 (OR=0.99, 95%CI=0.50–1.94, $P=0.97$) did not. We then examined the number of brachytherapy APBI patients who violated one or more of these dosimetric parameters. Eighty-five percent violated one or more of these parameters; D0.1cc 102% was violated in 49%, minimum skin distance >5.1 mm was violated in 47%, DHI >0.54 was violated in 54%, and volume of non-conformance 0.89 was violated in 39% (Figure 2B). We then examined the risk of “fair” or “poor” cosmetic outcome based on the number of dosimetric parameters and found that the risk of adverse cosmesis was clearly associated with the number of dosimetric parameter violations (Figure 2C).

Ipsilateral Breast Recurrence

At five years, seven brachytherapy patients (4.3%) and one 3D-CRT patient (4.2%) had experienced ipsilateral breast recurrence ($P=0.95$, log-rank). Five of seven (71.4%) ipsilateral breast recurrences in brachytherapy patients were scored as in-field, and the remaining two (28.6%) were consistent with second primary breast cancers. The single 3D-CRT ipsilateral breast recurrence was out-of-field.

Discussion

In the current study, we analyzed toxicity and cosmetic outcome in a prospective observational study of patients who were treated with APBI with either 3D-CRT or single-entry multilumen intracavitary brachytherapy. We also analyzed the association of various brachytherapy dosimetric parameters with the development of discrete toxic effects and cosmetic outcome to refine treatment planning for brachytherapy APBI.

The prospective randomized NSABP B-39/RTOG 0431 trial ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00103181) Identifier NCT00103181), which should be reported in the near future, will provide data on toxicity, cosmetic outcome, and ipsilateral breast recurrence with both intracavitary brachytherapy and 3D-CRT APBI. To date, there are no prospective comparisons of these two treatment modalities, and comparison of toxicity, disease control, and cosmesis across studies is complicated by heterogeneity in patient populations and reporting methods. The RAPID trial randomized women with ductal carcinoma *in situ* or invasive ductal carcinoma 3.0 cm after breast-conserving surgery to whole-breast irradiation or 3D-CRT APBI.⁴ At 3 years, an interim analysis showed significantly higher rates of patient-, nurse-, and physician-reported adverse cosmetic outcome (according to the EORTC Cosmetic Rating System for Breast Cancer)⁵ in the APBI arm (physician-reported, 35% vs. 17%; $P<0.001$). The 3-year rate of physician-reported adverse cosmesis in our 3D-CRT APBI cohort was significantly better (12%), though use of different cosmetic scoring systems precludes direct comparison. Notably, the PTV_EVAL in the RAPID trial was optimized such that the volume was to receive 95% to 107% of the prescription dose, while we optimized the PTV_EVAL for our 3D-CRT APBI plans such that 90% of the volume was to receive 90% of the nominal prescription dose. This optimization parameter was chosen because of the high rates of adverse cosmesis that had previously been reported with 3D-CRT APBI to 38.5 Gy in 10 BID fractions⁶, and is in concordance with the ongoing NSABP B-39/RTOG 0431 trial.

Accordingly, our median 3D-CRT PTV_EVAL coverage by the 95% isodose line was only 71.1% (range 25.2%–100.0%); the relatively lower doses delivered in our cohort may explain part of the observed difference in cosmetic outcome. The more recent UK IMPORT LOW trial (ISRCTN Identifier ISRCTN12852634) randomized patients with early-stage breast cancer to whole breast radiotherapy (40 Gy in 15 daily fractions), reduced-dose whole breast radiotherapy (36 Gy whole breast and 40 Gy partial breast in 15 daily fractions), and partial breast radiotherapy (40 Gy partial breast in 15 daily fractions). This study showed non-inferiority of both reduced-dose and partial breast treatment in terms of disease control, late normal tissue effects, and appearance of the treated breast.⁷ Preliminary toxicity data from the NSABP B-39/RTOG 0431 trial also suggest that APBI can be delivered with acceptably low rates of late normal tissue effects.⁸

In our study, G1 fibrosis and seroma were more common with brachytherapy than with 3D-CRT. Rehman et al.⁹ retrospectively studied 132 patients treated exclusively with the SAVI® device and reported a cumulative incidence of seroma of 9% and no cases of G2–3 seroma. The Rehman et al. study also showed a cumulative rate of fibrosis of 12%. Plans in that study were optimized to have 90% of the PTV_EVAL covered by 100% of the prescription dose. The observed 50.4% rate of grade 1 seroma, 8.7% rate of grade 2–3 seroma, and 72.7% rate of any fibrosis observed in our prospective cohort of brachytherapy APBI patients, 70% of whom were treated with a SAVI® applicator with less dose-intense coverage requirements, suggest more rigorous documentation of seroma and fibrosis in our study. The cumulative incidence of symptomatic (G2–3) seroma in our trial was 8.7%, which is similar to the rate of symptomatic seroma reported in other brachytherapy APBI series.^{10–12} We also reported significant associations between seroma, infection, pain, hyperpigmentation, and fibrosis. These data suggest that early treatment-related symptomatic seroma may predispose to infection, and that this robust inflammatory response may ultimately contribute to late tissue responses like hyperpigmentation and fibrosis that adversely affect cosmesis. Though not a trial of brachytherapy APBI, both seroma and infection arose as significant predictors of adverse cosmesis in an analysis of the RAPID trial.¹³ Analysis of cosmetic outcomes in our study revealed that compared to 3D-CRT, brachytherapy was associated with higher rates of radiation oncologist-reported adverse cosmesis, and that these trends persisted and perhaps became more prominent over time. Of particular interest were our findings relating breast size to cosmetic outcome after brachytherapy APBI. Women with smaller breasts are often deemed inappropriate candidates for brachytherapy APBI due to a perceived high risk of adverse cosmesis. We show here that most women with small breasts achieved “good” or “excellent” cosmetic outcome, and while “fair” cosmetic outcome was not uncommon, truly “poor” cosmesis was exceedingly rare. For historical comparison, the rates of mild and marked cosmetic change after hypofractionated whole breast radiotherapy in the START-B trial were 31% and 3%, respectively, and in the Canadian hypofractionated whole breast radiotherapy trial approximately 70% of patients achieved long-term “good” or “excellent” cosmesis.^{14, 15} Furthermore, although radiation oncologist-reported cosmetic outcome declined over time in brachytherapy APBI patients, this is not necessarily reflective of patient satisfaction with treatment or cosmetic outcome. A recent study found that among older early-stage breast cancer patients who received adjuvant radiotherapy, brachytherapy APBI patients had the

most favorable CanSORT, BREAST-Q, and physical well-being scores, despite having statistically significantly increased risks of adverse radiation effects, ipsilateral breast recurrence, and subsequent mastectomy compared to patients who underwent whole-breast irradiation.¹⁶

We also show that brachytherapy APBI patients started treatment significantly sooner than did 3D-CRT APBI patients. Brachytherapy patients necessarily had the intracavitary catheter placed soon after surgery, as obliteration of the lumpectomy cavity would preclude device placement. Our analysis did not reveal an association between early device placement or early treatment initiation and higher risk of adverse cosmesis. Likely the most important implication of the early and rapid treatment with brachytherapy APBI is on patient convenience.¹⁷

A major strength of our study is the rigorously collected dosimetric data for both 3D-CRT and brachytherapy APBI. Our analyses identified values of D0.1cc (skin), minimum skin distance, DHI, and volume of non-conformance that predict development of adverse cosmesis. Adherence to these dosimetric values, while maintaining the thresholds set forth by the brachytherapy device manufacturers, should further mitigate the risk of adverse cosmetic outcome with brachytherapy APBI. Limitations of our study include the relatively small number of patients treated with 3D-CRT, the lack of patient-reported outcomes or cosmetic satisfaction data, and the fact that patients had to be ≥ 50 years of age. Despite these limitations, our study is valuable as it is among the largest prospective studies comparing toxicity and cosmetic outcome with 3D-CRT and brachytherapy APBI published to date.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(A) Actuarial incidence of “fair” or “poor” cosmetic outcome at any point during observation period for brachytherapy APBI and 3D-CRT APBI patients. Statistic is log-rank. Numbers below indicate number remaining at risk at each time point. (B) Trends in cosmetic outcome over time. All patients and all observations are displayed; each dot denotes a separate observation. P is the effect of treatment (3DCRT vs. brachytherapy), and P' is the effect of time. (C) Effect of bra cup size on worst cosmetic score in brachytherapy APBI patients.

A

Dosimetric Parameters Affecting Cosmetic Outcome in Brachytherapy APBI Patients

B

C

Figure 2.

Actuarial incidence curves of “fair” or “poor” cosmesis in brachytherapy APBI patients using the identified threshold values (inlays). Statistic is log-rank.

Table 1.Patient, Tumor, and Treatment Characteristics ^a

Characteristic	All Patients (N=281)	Brachytherapy (N=252)	3D-CRT (N=29)	P Value
APBI method				NA
3D-CRT	29(10.3)	0 (0.0)	29(100.0)	
SAVI®	176(62.6)	176(69.8)	0 (0.0)	
Contura®	56(19.9)	56 (22.2)	0 (0.0)	
MammoSite®	20(7.1)	20 (7.9)	0 (0.0)	
Prescription dose/fractionation				
34.0 Gy at 3.40 Gy BID	254 (90.4)	252(100.0)	2 (6.9)	<0.0001
38.5 Gy at 3.85 Gy BID	27 (9.6)	0 (0.0)	27(93.1)	
Median age (range), years	61 (50–86)	61 (50–86)	62 (50–73)	0.88
Race/ethnicity				1.00
White	229 (81.5)	204 (81.0)	25 (86.2)	
Black	25 (8.9)	23(9.1)	2 (6.9)	
Hispanic	17(6.0)	15(6.0)	2 (6.9)	
Asian	4(1.4)	4(1.6)	0 (0.0)	
Other	6(2.1)	6 (2.4)	0 (0.0)	
pT category				0.38
pTis	78 (27.8)	71 (28.2)	7(24.1)	
pT1	194(69.0)	174(69.0)	20 (69.0)	
pT2 (≥ 3.0 cm)	9 (3.2)	7 (2.8)	2 (6.9)	
Bra cup size				0.78
A	13 (4.6)	12(4.8)	1 (3.4)	
B	56(19.9)	53(21.0)	3(10.3)	
C	84 (29.9)	77 (30.6)	7(24.1)	
D	56(19.9)	54(21.4)	2 (6.9)	
DD	36(12.8)	33(13.1)	3(10.3)	
>DD	13(4.6)	13(5.2)	0 (0.0)	
Unknown	23 (8.2)	10(4.0)	13(44.8)	
Subtype				
<i>In situ</i>				1.00
HR+	64(82.1)	58 (81.7)	6 (85.7)	
HR–	11 (14.1)	10(14.1)	1 (14.3)	
Unknown	3 (3.8)	3 (4.2)	0 (0.0)	
Invasive				0.56
HR+/HER2–	180(88.7)	161 (89.0)	19(86.4)	
HR+/HER2+	8 (3.9)	6 (3.3)	2(9.1)	
HR–/HER2+	2(1.0)	2(1.1)	0 (0.0)	

Characteristic	All Patients (N=281)	Brachytherapy (N=252)	3D-CRT (N=29)	P Value
HR-/HER2-	7 (3.4)	6 (3.3)	1 (4.5)	
HR+/HER2 unknown	2(1.0)	2(1.1)	0 (0.0)	
Unknown	4 (2.0)	4 (2.2)	0 (0.0)	
APBI suitability ^b				0.54
Suitable	225(80.1)	202 (80.2)	23 (79.3)	
Cautionary	56(19.9)	50(19.8)	6 (20.7)	
<i>In situ</i>				1.00
Grade 3	30 (88.2)	27(87.1)	3(100.0)	
Margin <3.0 mm	2 (5.9)	2 (6.5)	0 (0.0)	
Grade 3 and margin <3.0 mm	2 (5.9)	2 (6.5)	0 (0.0)	
Invasive				1.00
ER-	9 (40.9)	8(42.1)	1 (33.3)	
pT1 with <i>in situ</i> lesion >2.0 cm	3(13.6)	3(15.8)	0 (0.0)	
pT2 (3.0 cm)	10(45.5)	8(42.1)	2 (66.7)	
Adjuvant systemic therapy				
Hormone therapy	193(68.7)	175(69.4)	18(62.1)	0.41
Chemotherapy/biochemotherapy	16(5.7)	15(6.0)	1 (3.4)	1.00

BID, twice daily; ER, estrogen receptor; HR, hormone receptor.

^aValues in table are number of patients (percentage) unless otherwise indicated.

^bSuitability per updated ASTRO consensus guidelines.

Table 2.Dosimetric Parameters ^a

Parameter	Brachytherapy	3D-CRT	P
PTV_EVAL, cc	82.9 (30.3–161.5)	224 (83.1–454.3)	<0.001
Minimum skin distance, mm	6.0 (0.0–42.6)	5.1 (1.3–15.3)	0.54
Minimum rib distance, mm	11.0 (0.0–69.0)	8.4 (1.0–44.4)	0.71
DO.1cc (skin), % of nominal Rx dose	102.0 (35.0–141.0)	87.8 (77.5–99.4)	<0.001
DO.1cc (rib), % of nominal Rx dose	84.0 (11.0–142.0)	91.5 (51.9–106.5)	0.06
V100, cc	78.3 (28.1–155.0)	6.7 (0.0–264.3)	<0.001
V150, cc	33.7 (14.1–49.7)	0 (0.0–0.0)	<0.001
V200, cc	14.2 (0.0–20.0)	0 (0.0–0.0)	<0.001
Dose homogeneity index	0.54 (0.35–0.77)	NA	-
Volume of non-conformance, cc	0.60 (0.0–8.90)	NA	-
% Rx dose covering 100% of PTV_EVAL	78.3 (40.2–96.2)	74.5 (33.7–95.8)	0.01
% Rx dose covering 95% of PTV_EVAL	97.7 (81.9–106.9)	89.9(84.9–100.1)	<0.001
% Rx dose covering 90% of PTV_EVAL	103.3 (91.5–112.2)	91.7(90.2–101.1)	<0.001
% PTV_EVAL covered by 100% of Rx dose	93.3 (81.0–99.5)	3.1 (0.0–95.2)	<0.001
% PTV_EVAL covered by 95% of Rx dose	96.8 (86.5–99.9)	71.1(25.2–100.0)	<0.001
% PTV_EVAL covered by 90% of Rx dose	98.7 (90.5–100.0)	94.9 (90.5–100.0)	<0.001

Rx, nominal dose prescribed to PTV_Eval

^aValues in table are median (range).

Table 3.

Worst Cosmetic Score Reported During Observation Period

Brachytherapy				3D-CRT			
Poor	Fair	Good	Excellent	Poor	Fair	Good	Excellent
9 (3.6)	62 (24.6)	154 (61.1)	27 (10.7)	0 (0.0)	5 (17.2)	20 (69.0)	4 (13.8)

Table 4.

Association of Dosimetric Parameters with “Fair” or “Poor” Cosmetic Outcome after Brachytherapy APBI

Parameter	Odds Ratio (95% CI)	P Value
PTV_Eval (cc)	0.990 (0.979–1.002)	0.11
Minimum Skin Distance (mm)	0.867 (0.814–0.924)	<.0001
D0.1cc (Skin) (% of Nominal Rx Dose)	1.056 (1.029–1.084)	<.0001
D0.1cc (Rib) (% of Nominal Rx Dose)	1.005 (0.995–1.015)	0.30
V100 (cc)	0.989 (0.977–1.002)	0.10
V150 (cc)	0.988 (0.953–1.025)	0.52
V200 (cc)	1.052 (0.994–1.113)	0.08
Dose Homogeneity Index	0.018 (0.000–0.805)	0.04
Volume of Non-Conformance	1.317 (1.043–1.663)	0.02
%Rx Dose Covering 100% of PTV_Eval	0.980 (0.951–1.010)	0.18
%Rx Dose Covering 95% of PTV_Eval	1.012 (0.935–1.097)	0.76
%Rx Dose Covering 90% of PTV_Eval	0.968 (0.896–1.046)	0.42
%PTV_Eval Receiving 100% of Rx Dose	0.948 (0.864–1.040)	0.26
%PTV_Eval Receiving 95% of Rx Dose	0.921 (0.808–1.050)	0.22
%PTV_Eval Receiving 90% of Rx Dose	0.930 (0.780–1.110)	0.42