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Scientific Article

Robotic Stereotactic Body Radiation Therapy for the Adjuvant Treatment of Early-Stage Breast Cancer: Outcomes of a Large Single-Institution Study

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Abstract

Purpose: Advancements in breast radiation therapy offer innumerable benefits to patients and the health care system. Despite promising outcomes, clinicians remain hesitant about long-term side effects and disease control with accelerated partial breast radiation therapy (APBI). Herein, we review the long-term outcomes of patients with early-stage breast cancer treated with adjuvant stereotactic partial breast irradiation (SAPBI).

Methods and Materials: This retrospective study examined outcomes of patients who received diagnoses of early-stage breast cancer treated with adjuvant robotic SAPBI. All patients were eligible for standard ABPI and underwent lumpectomy, followed by fiducial placement in preparation for SAPBI. Using fiducial and respiratory tracking to maintain a precise dose distribution throughout the course of treatment, patients received 30 Gy in 5 fractions on consecutive days. Follow-up occurred at routine intervals to evaluate disease control, toxicity, and cosmesis. Toxicity and cosmesis were characterized using the Common Terminology Criteria for Adverse Events version 5.0 and Harvard Cosmesis Scale, respectively.

Results: Patients (N = 50) were a median age of 68.5 years at the time of treatment. The median tumor size was 7.2 mm, 60% had an invasive cell type, and 90% were estrogen receptor positive, progesterone receptor positive, or both. Patients (n = 49) were followed for a median of 4.68 years for disease control and 1.25 years for cosmesis and toxicity. One patient experienced local recurrence, 1 patient experienced grade 3+ late toxicity, and 44 patients demonstrated excellent cosmesis.

Conclusions: To our knowledge, this is the largest retrospective analysis with the longest follow-up time for disease control among patients with early breast cancer treated with robotic SAPBI. With follow-up time for cosmesis and toxicity comparable to that of previous studies, results of the present cohort advance our understanding of the excellent disease

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control, excellent cosmesis, and limited toxicity that can be achieved by treating select patients with early-stage breast cancer with robotic SAPBI.

Introduction

Breast cancer is the most common noncutaneous cancer diagnosed among women in the United States.[1] Though 96% of women with stage I or II breast cancer undergo some form of treatment, it remains the second leading cause of cancer death among women.[2] As screening typically identifies breast cancer early, these patients may be eligible for accelerated partial breast irradiation (APBI) using novel radiation platforms based on published criteria.

Until the 1970s, the Halsted radical mastectomy was performed on more than 90% of patients who received diagnoses of breast cancer in the United States.[3] Though the procedure touted impressive survival and local recurrence rates, the surgery was extremely morbid.[4] In response, breast-conserving therapy was developed and eventually became a standard of care with several seminal works published by Bernard Fisher.[5,6] With lumpectomy followed by irradiation, patients with early-stage breast cancer were able to avoid these postoperative complications while achieving similar or better survival outcomes.[7–13] Whole breast radiation therapy (WBRT) remained the standard of care for years, but in modern times with the development of improved imaging, advanced radiation machines, and image guided radiation therapy, more focal and targeted radiation techniques have been developed including APBI. The irradiation following lumpectomy can either be WBRT delivered over 3 to 4 weeks or APBI delivered over 1 to 2 weeks.[14–16] In well-selected patients, rates of locoregional tumor recurrence, distant metastases, breast cancer specific survival, and overall survival are similar between WBRT and APBI.[15] Moreover, acute and late adverse events may worsen with WBRT, while cosmesis better preserved with the APBI method intensity modulated radiation therapy as described by Meattini et al.[15]

It is critical to note several different APBI techniques exist. The oldest technique with the most follow-up is multicatheter interstitial brachytherapy (MIB), a technique that requires the insertion of 14 to 20 catheters through which high-dose brachytherapy is performed.[17] While MIB offers patients a shorter treatment time of 5 days, compared with 6 weeks with WBRT, a study of 71 MammoSite brachytherapy patients and 245 WBRT patients found palpable masses and telangiectasia occur at a significantly higher rate after MammoSite brachytherapy.[18,19] Moreover, a retrospective study of 92,735 women aged 67 years or older with invasive breast cancer found a significantly increased risk of subsequent mastectomy associated with breast brachytherapy compared with WBRT.[20] In contrast, a randomized controlled trial (RCT) of 1328 women aged 40 years or older with early stage breast cancer treated with either WBRT with a tumor bed boost of 10 Gy or APBI with interstitial brachytherapy found that cosmetic results were similar among both groups but that there were significantly fewer grade 2 to 3 late skin side effects after APBI with interstitial brachytherapy.[21]

An alternative to MIB or balloon brachytherapy is a form of external beam radiation therapy called stereotactic body radiation therapy (SBRT), which delivers precise radiation doses using advanced radiation machines, image guided radiation therapy, and robust radiation planning, allowing higher doses to be delivered to precise volumes over fewer fractions.[22] SBRT delivered with a robotic radiosurgery system takes advantage of real-time tracking and respiratory motion monitoring to reduce radiation delivery uncertainty, while maximizing target coverage, which can spare and reduce dose to criticalnearby organs.[23–25] Thus far, the few studies examining toxicity and cosmetic outcomes among patients with early-stage breast cancer treated with stereotactic accelerated partial breast irradiation (SAPBI) delivered with a robotic radiosurgery system have reported no local recurrence, mild/minimal acute toxicity, and excellent or good cosmesis results.[23,25–28]

These results are promising, though our understanding of the clinical utility of robotic SAPBI is bound by the limited number of studies reporting on the clinical, toxicity, and cosmetic outcomes. Therefore, we aim to further investigate the long-term oncologic outcomes, Common Terminology Criteria for Adverse Events (CTCAE)–defined toxicity, and cosmesis of a large cohort of patients with early-stage breast cancer who underwent breast-conserving therapy with robotic SAPBI.

Methods and Materials

Patient evaluation and eligibility

The local institutional review board approved this single-institutional review (IRB# s18-01721) of patients treated for early-stage breast cancer. All patients were evaluated before treatment by a multidisciplinary breast oncology team and underwent diagnostic tests including mammogram of both breasts, postexcision ipsilateral mammogram, and surgical pathology analysis, which included analysis of tumor dimensions, confirmation of negative margins, and estrogen receptor (ER)/progesterone receptor (PR) analysis of the primary tumor. Patients were staged using the American Joint Committee on Cancer seventh edition staging system.

Patient selection criteria closely followed the American Society for Radiation Oncology consensus statement for "suitable" or "cautionary" candidates for APBI.[29] Eligibility criteria included the following: female patients of age ≥45 years, pathologically confirmed invasive carcinoma or ductal carcinoma in situ, tumor size ≤3 cm, lymph nodes negative for malignancy (if assessed), negative surgical margins (≥2 mm), volumetric ratio of lumpectomy cavity to ipsilateral breast ≤30%, and both enrollment and initiation of stereotactic radiosurgery within 42 days of last breast cancer surgery or last chemotherapy treatment.

Additional patient demographic data pertinent to this study such as age when treated, age of first menses, menopausal status at time of treatment, race/ethnicity, and Eastern Cooperative Oncology Group performance status was gathered from patient records, if available. In the case where menopausal status at the time of treatment was not available, age of menopause was assumed 50 years.[30]

Sentinel node biopsy and surgical removal

Patients underwent standard lumpectomy, and negative surgical margins of at least 2 mm were required before radiation therapy. In cases of positive or close surgical margins, re-excision was permitted. In keeping with guidelines, a sentinel lymph node biopsy was performed intraoperatively for invasive disease or high-risk ductal carcinoma in situ (DCIS).[31] The laterality, quadrant, size, and cell type of the tumor were noted. The size was reported as the tumor's largest dimension. In the case where a tumor comprised invasive and in situ components, cell type was classified as invasive. Additionally, per standard guidelines, ER, PR, and HER2 receptor status was analyzed for all invasive cancers. In certain situations, Ki-67 was also reviewed, if available.

Fiducial placement, simulation, contouring, planning, and treatment

Fiducial implantation was performed by the attending radiation oncologist and localized to the periphery of the lumpectomy cavity using image guidance on a computed tomography simulator with coordinate placement determined by the physics staff for optimal localization. Patients were immobilized using either a thermoplastic cast with a hole removed around the nipple or with an alpha cradle to allow the breast to remain in its natural position.

The clinical target volume (CTV) was defined by uniformly expanding the excision cavity volume by 10 mm. However, the CTV was limited to 5 mm from the skin surface and by the posterior breast tissue extent, as defined by the chest wall. The planning target volume (PTV) was defined as the CTV plus a 5-mm margin, while ensuring again a 5-mm margin from the skin and respecting the chest wall. As delineated in Table 1, dose constraints were based upon the National Surgical Adjuvant Breast and Bowel Project/Radiation Therapy Oncology Group (NSABP B-39/RTOG) protocol.[32] For medial inner quadrant or lower inner quadrant lesions, acceptance of a higher point dose, not volume, was allowed for the contralateral breast, heart, and lungs. All patients received 30 Gy in 5 fractions over 5 consecutive days using a fixed collimator stereotactic radiosurgical device that used fiducial and respiration tracking. This technique of optimized image guided radiation therapy enabled us to maintain a high-fidelity dose distribution throughout treatment fractions.

Table 1 Organ at Risk Dose Constraints

Organ at Risk (OAR)	Constraint
Ipsilateral breast	V>50% < 60% V100% < 35%
Contralateral breast	D100 < 3%
Ipsilateral lung	V30% < 15%
Contralateral lung	V5% < 15%
Heart (right-sided lesions)	V5% < 5%
Heart (left-sided lesions)	V5% < 40%
Thyroid	Dmax < 3%
Skin	Dmax < 100%

Follow-up

Patients were followed by the treating radiation oncologist at 4 to 6 weeks posttreatment, 6 months posttreatment, 12 months posttreatment, and annually thereafter. Acute and late toxicity, disease control, and physician-determined cosmesis judged using the Harvard cosmesis scale were recorded at these time points.[33,34] Those who were lost to follow-up were excluded from toxicity analysis.

Acute toxicity was defined as occurring within 90 days of a patient's last treatment, and late toxicity was defined as occurring after 90 days. These were graded using CTCAE version 5.0. Per the Harvard cosmesis scale, an excellent outcome was defined as "minimal or no difference" in appearance and good cosmesis was defined as "a slight difference." Fair and poor cosmesis were defined as "obvious differences involving a quarter or less of the breast" and "as marked change involving more than a quarter of the breast tissue," respectively. If the patient's status was noted to be unremarkable at follow-up or no notes on cosmesis were provided, excellent cosmesis was assumed.

Length of follow-up for toxicity (acute and late) as well as cosmesis were calculated as the time from a patient's last radiation treatment to their most recent appointment with a radiation oncologist. Length of follow-up for

disease recurrence was calculated as the time from a patient's last radiation treatment to their most recent mammogram or radiation oncologist appointment.

Statistical analysis

Statistical analysis was performed using Microsoft Excel. Numerical variables were summarized using median, interquartile range (IQR), and range as appropriate. Categorical variables were summarized using proportions.

Results

Patient and tumor characteristics

This single-institution retrospective review analyzed 50 patients with early-stage breast cancer treated with robotic SBRT from February 2011 to December 2017. Patients were a median age of 68.5 years (IQR, 16.75; range, 46-91) with excellent performance status at the time of treatment initiation (median Eastern Cooperative Oncology Group score of 0). Patients were predominantly of Caucasian demographic (80%). Of note, the majority of patients received diagnoses of right-sided breast cancer (66%) and the most common quadrant location was upper outer (38%), as would be expected. Additional patient and tumor characteristics are reported in Table 2.

The median time from screening mammogram to surgery was 6.9 weeks (IQR, 4.1; range, 2.7-63.1). Following surgical resection, tumors measured a median of 7.2 mm (IQR, 2.65; range, 0.7-12) and the closest surgical margin was a median of 4 mm (IQR, 5; range, 1-14). Of the patients with positive margins, 1 underwent re-excision, and 2 were positive for DCIS at the margins despite having invasive disease. The majority (60%) of patients were clinical stage T1. The most common surgical pathology was found to be invasive cell type (60%). The majority were ER+ and/or PR+ (90%) and HER2− (60%). Only 1 patient was triple negative. Additional surgical and pathologic characteristics are capitulated in Table 3.

Table 2 Patient and Tumor Characteristics

	Median(Range)
Age (years) n=50	68.5 (46-91)
Age of First Menses (years) n=48	13 (9-16)
Menopausal Status at Treatment n=50	
Postmenopausal	94% (n=47)
Premenopausal	6% (n=3)
Race/Ethnicity n=50	
White	90% (n=45)
Black	4% (n=2)
Asian	4% (n=2)
Other	2% (n=1)
ECOG n=50	
0	84% (n=42)
1	4% (n=2)
Side n=50	
Right	66% (n=33)
Left	34% (n=17)
Quadrant n=50	
Upper Outer	38% (n=19)
Lower Outer	14% (n=7)
Lower Central	12% (n=6)
Upper Central	10% (n=5)
Upper Inner	6% (n=3)
Lower Inner	4% (n=2)
Other	4% (n=2)
AJCC 7th edition stage n=50	
Tis	38% (n=19)
T1	60% (n=30)
T1a	12% (n=6)
T1b	20% (n=10)
T1c	14% (n=7)
T2	2% (n=1)

Abbreviation: AJCC = American Joint Committee on Cancer; ECOG = eastern cooperative oncology group.

Radiation treatment characteristics

The median time from surgery to radiation treatment initiation was 2.5 months. An example of a robotic SBRT treatment plan is illustrated in Fig. 1. Radiation therapy was typically delivered on a consecutive day schedule with the average duration of treatment measured at 5 days (IQR, 0; range, 5-6). The median number of beams was 116 with a median PTV isodose prescription of 78% (IQR, 8%; range, 68%-86%). As such, despite a prescription dose of 30 Gy, mean doses to the lumpectomy cavity were noted to be higher given the low prescription isodose line. The median GTV and PTV were 19.06 cm^3 (IQR, 16; range, 4.78-86.86) and 111.98 cm^3 (IQR, 81; range, 24.20-280.26), respectively. Because we prescribed to a lower isodose line, the average mean GTV, CTV, and PTV doses were higher—34.1, 34.1, and 33.7 Gy, respectively. The median maximum GTV and PTV were 38.0 Gy (IQR, 4.9; range, 33.7-44.1) and 38.2 Gy (IQR, 4.2; range, 34.3-44.1), respectively.

The average median and maximum doses delivered to organs at risk are reported in Table 4. Regarding left-sided

Table 3 Surgical and Pathological Information

	Median (IQR); Range
Tumor Size (largest dimension in mm) n=46	7.2 (2.65); 0.7-12
Smallest Margin (mm) n=35	4 (5); 1-14
Surgical Margin Status n=50	
Negative	84% (n=42)
Positive (initially)	8% (n=4)
Sentinel Node Biopsy Performed n=50	
Yes	78% (n=39)
No	18% (n=9)
Cell Type n=50	
Invasive (IDC, Microinvasive Carcinoma)	60% (n=30)
In Situ (DCIS)	40% (n=20)
ER n=50	
Positive	90% (n=45)
Negative	6% (n=3)
PR n=50	
Positive	76% (n=38)
Negative	20% (n=10)
HER2 n=50	
Negative	60% (n=30)
Positive	8% (n=4)

lesions, the average mean and maximum doses delivered to the heart were 1.3 Gy (IQR, 0.7; range, 0.6-2) and 5.2 Gy (IQR, 5.3; range, 1.2-20.9), respectively. Right-sided lesions were notably lower at 1.1 Gy (IQR, 0.5; range, 0.5-1.5) and 2.1 Gy (IQR, 1.3; range, 0.9-5.1), respectively. Of note, 22% of patients received a maximum dose to the skin that was greater than 100% of the prescription dose. With respect to the contralateral breast, 21 patients received a maximum dose that was greater than 3% of the prescription dose. To the thyroid, 16 patients received a maximum dose that was greater than 3% of the prescription dose, with 3 patients having dosimetry reported for each lobe.

Follow-up

After receiving treatment, 1 patient was lost to follow-up. She was 83 years of age at the time she received a diagnosis of DCIS in 2012. The other 49 patients were followed for disease control for a median of 4.68 years (IQR, 4.65; range, 0.05-9.83). During this time, only 1 patient was found to have a local recurrence, which was discovered 8.67 years postradiation treatment. The patient identifies as Black and was 62 years of age when treated. Surgical margins were negative. Both her original tumor and recurrence were invasive ductal carcinoma of the left breast. Of note, the recurrence was found to be ER−/PR+ while her original tumor was ER+/PR+. Given the distance between initial treatment and recurrence as well as the variation in ER positivity, it is difficult to conclusively say if this represented a local recurrence or second primary malignancy. At the time of resection, there was no evidence of regional recurrence or metastatic disease.

Patients (n = 49) were rigorously followed for cosmesis and toxicity assessment for a median of 1.25 years (IQR, 3.14; range, 0.04-9.31). At follow-up visits, cosmesis was assessed by the radiation oncologist using the Harvard cosmesis scale. Toxicity was assessed and graded using CTCAE version 5.0. Over the course of the follow-up period, 45 patients achieved excellent cosmesis and 2 patients achieved good cosmesis. No patients were determined to have fair or poor cosmesis. An example of a patient's cosmetic outcome at 4- and 24-month follow-up is provided in Fig. 2. Regarding toxicity, 4 acute and 5 late toxicities were observed. Only 1 patient experienced a grade 3+ toxicity, which was defined as late grade 3 breast pain. This patient's maximum point dose was 4167 cGy, which was 10% higher than the average for our cohort. Overall, 3 patients experienced acute toxicity, 3 patients experienced late toxicity, and 1 patient experienced both acute and late toxicity. The most frequent toxicity was acute grade 1 breast pain. Finally, 1 patient experienced acute grade 1 deep connective tissue fibrosis, and 1 patient experienced late grade 1 decreased joint range of motion. Though the shoulder was not routinely contorted, it was well out of the field of radiation. Moreover, no patients experienced symptomatic rib fracture. While there was no constraint on ribs explicitly, there was little high-dose radiation to the chest wall given the exclusion of 5 mm of the chest wall.

Discussion

This study highlights the safety and efficacy of robotic SAPBI in the treatment of early-stage breast cancer in carefully selected patients. Out of 50 patients treated, only 1 was lost to follow-up, 1 was found to have a local recurrence, 1 experienced a grade 3 late toxicity, and the vast majority achieved excellent cosmesis.

As 67% of breast cancer recurrence is local, either in the same location as the original tumor or nearby the original tumor, robotic SAPBI can be an effective means of achieving disease control in select patients with breast cancer.[35] Moreover, breast recurrences distant from the primary site tend to occur later, as opposed to those near the lumpectomy bed, and may represent second primaries rather than true recurrences, which would not be expected to be prevented by WBRT.[36] However, to date, RCTs

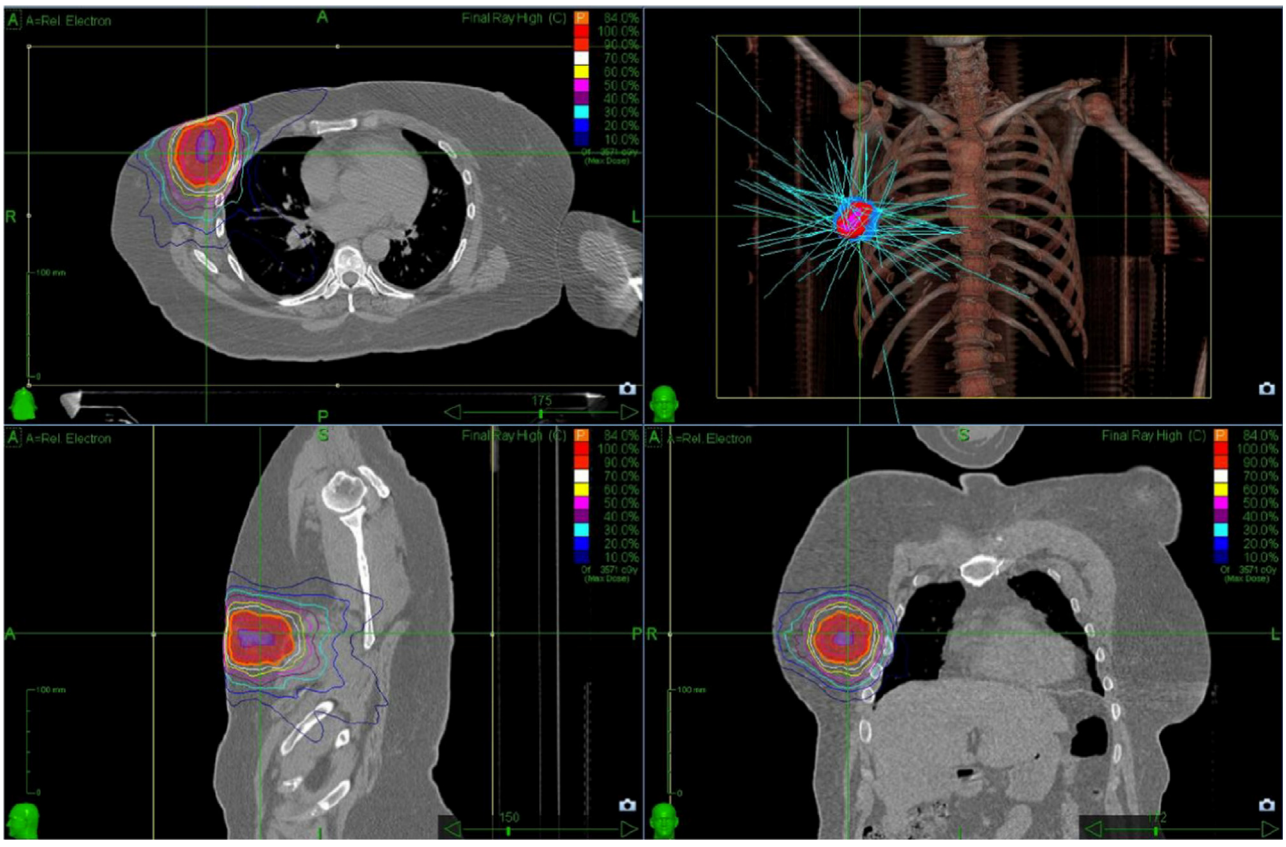

Figure 1 Treatment plan of a 44-month follow-up for a 63-year old female presenting with Tia, well-differentiated invasive carcinoma of the left breast.

comparing APBI to WBRT have demonstrated conflicting results.[15,32,37] While Vicini et al[32] found that APBI did not meet the criteria for equivalence to WBRT in preventing ipsilateral breast tumor recurrence, Whelan et al[37] determined external beam APBI to be noninferior to WBRT. A key difference between the studies is that Whelan et al excluded patients <40 years of age and patients with lobular or multifocal breast cancer where Vicini et al did not. Regarding late radiation toxicity, Whelan et al[37] found that it was more common in patients treated with APBI than WBRT, where Meattini et al[15] (2020) observed the opposite. Importantly, Whelan et al treated patients with 38.5 Gy in 10 fractions delivered twice per day, whereas Meattini et al treated patients with 30 Gy in 5 fractions delivered once per day. Unsurprisingly, as patient selection criteria narrowed and the treatment dose delivered daily decreased across these RCTs, associated findings increasingly demonstrated external beam APBI to be safe and effective, which is inline the results of our study.[15,37]

While patient selection is instrumental to the safety and efficacy of APBI, so too are advancements in radiation therapy technology. When Vaidya et al[38] compared WBRT to intraoperative radiation therapy (IORT), a nominally higher risk of local recurrence was found to be associated with IORT, suggesting the possibility of an excessively narrow dose distribution with this technology. However, with advancements in radiation therapy technology, such as robotic SAPBI that allows for more robust treatment, improved long-term local control may be realized with limited toxicity.[15,39] Furthermore, with treatment modalities that reduce potential inaccuracy during treatment delivery such as patient positioning and tumor shift during respiration, less normal tissue may be irradiated.[40,41] To eliminate much of the uncertainty of target positioning, surgically placed fiducial markers, which have been shown to be a strong radiographic surrogate for the breast lumpectomy cavity, can be used.[42] These internal surrogate markers become particularly advantageous when irradiating breast tissue as the positioning of mobile tissue can be challenging if a patient's body habitus is larger. To account for patient respiration, a 3-dimensional model of chest wall movement and target motion during respiration can be built and continuously updated during treatment with live x-rays.[40] This technique of leveraging both fiducials and respiration tracking serves to optimize image guided radiation therapy to maintain a high-fidelity dose distribution throughout treatment fractions. As evidence of the feasibility of using robotic SAPBI for the treatment of early-stage breast cancer, our study demonstrated high-fidelity placement of fiducials by radiation oncologists themselves.

Table 4 Radiation Treatment Characteristics

	Median (IQR)	Range
Number of Beams n=41	121 (38)	(54-194)
GTV (cc) n=28	19 (16)	(4.8, 87)
CTV (cc) n=34	79 (52)	(3.4, 174)
PTV (cc) n=41	112 (81)	(24, 280)
GTV Mean Dose (Gy) n=29	34 (3.4)	(28, 39)
GTV Max Dose (Gy) n=29	38 (4.9)	(34, 44)
CTV Mean Dose (Gy) n=34	34 (2.2)	(32, 38)
CTV Max Dose (Gy) n=34	38 (4.9)	(35, 44)
PTV Mean Dose (Gy) n=38	34 (1.6)	(28, 37)
PTVMax Dose (Gy) n=38	38(4.2)	(34, 44)
Max Point Dose (Gy) n=41	38 (4.6)	(27, 44)
Isodose % n=41	78 (8.0)	(68, 86)
Ipsilateral Breast n=40		
Mean Dose (Gy)	12 (4.1)	(5.5, 21)
Max Dose (Gy)	38 (4.2)	(34, 44)
Contralateral Breast n=40		
Mean Dose (Gy)	0.6 (0.2)	(0.2, 1.1)
Max Dose (Gy)	0.9 (1.1)	(0.3, 3.4)
Heart (left sided lesion) n=14		
Mean Dose (Gy)	1.3 (0.7)	(0.6, 2.0)
Max Dose (Gy)	5.2 (5.3)	(1.2, 21)
Heart (right sided lesion) n=27		
Mean Dose (Gy)	1.1 (0.5)	(0.5, 1.5)
Max Dose (Gy)	2.1 (1.3)	(0.9, 5.1)
Ipsilateral Lung n=40		
Mean Dose (Gy)	3.3 (1.5)	(1.3, 6.7)
Max Dose (Gy)	21(12)	(6.7, 32)
Contralateral Lung n=41		
Mean Dose (Gy)	1.0 (0.4)	(0.6, 1.6)
Max Dose (Gy)	3.1 (2.0)	(1.5, 7.0)
Skin n=40		
Mean Dose (Gy)	1.7 (1.4)	(0.7, 15)
Max Dose (Gy)	29 (2.3)	(23, 39)
Thyroid n=44		
Mean Dose (Gy)	0.7 (0.4)	(0.3, 1.4)
Max Dose (Gy)	0.8 (0.4)	(0.3, 1.6)
Ipsilateral Chest Wall n=10		
Mean Dose (Gy)	15 (3.0)	(9.1, 22)
Max Dose (Gy)	33 (4.1)	(29, 34)

Though there has yet to be published results from a RCT demonstrating the safety and efficacy of robotic SAPBI, results from pilot and retrospective studies have been promising and in line with our findings. As part of a pilot study, Lozza et al[27] used robotic SAPBI to deliver 30 Gy in 5 fractions to 29 patients with early-stage breast cancer. At 1-, 3-, 6-, 9-, 12-, and 24-month follow-up, toxicity and cosmesis were evaluated and found to improve over time; at a median 27.7 months, no local recurrences or distant relapses were recorded.[27] While the radiation dose, fractionation schedule, and use of robotic SAPBI is in keeping with our protocol, their prescription isodose line was higher (86% vs 78%) and median PTV was smaller (88.1 cm^3 vs 111.98 cm^3). As a part of a prospective study, Mészáros et al[28] used robotic SAPBI to deliver 25 Gy in 4 daily fractions to 27 patients with early-stage breast cancer. At a median follow-up of 12 months, no locoregional recurrence, distance metastasis, or grade 2 or worse side effects were observed, and the cosmetic outcome was excellent in 62.9% of patients.[28] In a retrospective analysis, Obayomi-Davies et al[25] examined 10 patients with early-stage breast cancer treated with robotic SAPBI—30 Gy in 5 consecutive fractions—and found excellent/good cosmesis and no breast events at a median follow-up of 1.3 years. Taking it to its extreme, as part of a single-dose escalation trial, Rahimi et al[43] examined 30 patients aged 18 years or older with invasive or in situ disease treated with either 22.5, 26.5, or 30 Gy in 1 fraction. No patients experienced acute toxicity and 2 experienced grade 3 late toxicity. There was no detriment in cosmesis relative to baseline, and at median follow-ups 47.9, 25.1, and 16.2 months, no disease recurrence was reported.[43]

Of note, while fractionation schedules have largely evolved to treat smaller targets in fewer fractions, Murray Brunt et al[44] examined whether hypofractionated WBRT (either 27 Gy in 5 fractions or 26 Gy in 5 fractions) is noninferior to conventional WBRT fractionation (40 Gy in 15 fractions). At the 5-year follow-up, local control, breast appearance, and late toxicity were found to be noninferior in patients treated with 26 Gy in 5 fractions.[44] Though promising, whether or not excess late toxicity is ultimately observed in the hypofractionation arm with increased follow-up remains to be seen.

The safety and efficacy of robotic SAPBI is particularly consequential because the adoption of ultrahypofractionation techniques offers numerous benefits to patients, providers, and society at large.[45] By reducing the number of days patients are on treatment, patients are required to come into the office less often.[46] In the setting of traditional transportation challenges that many patients and their families face, as well as pandemic concerns around disease transmission, the public health and patient accessibility implications are far reaching.[46–48] Moreover, ultrahypofractionated radiation therapy requires less utilization of resources, reducing financial toxicity to patients and the health care system as a whole.[49–51] However, despite the many advantages, many radiation oncologists are hesitant to embrace ultrahypofractionated radiation therapy. When

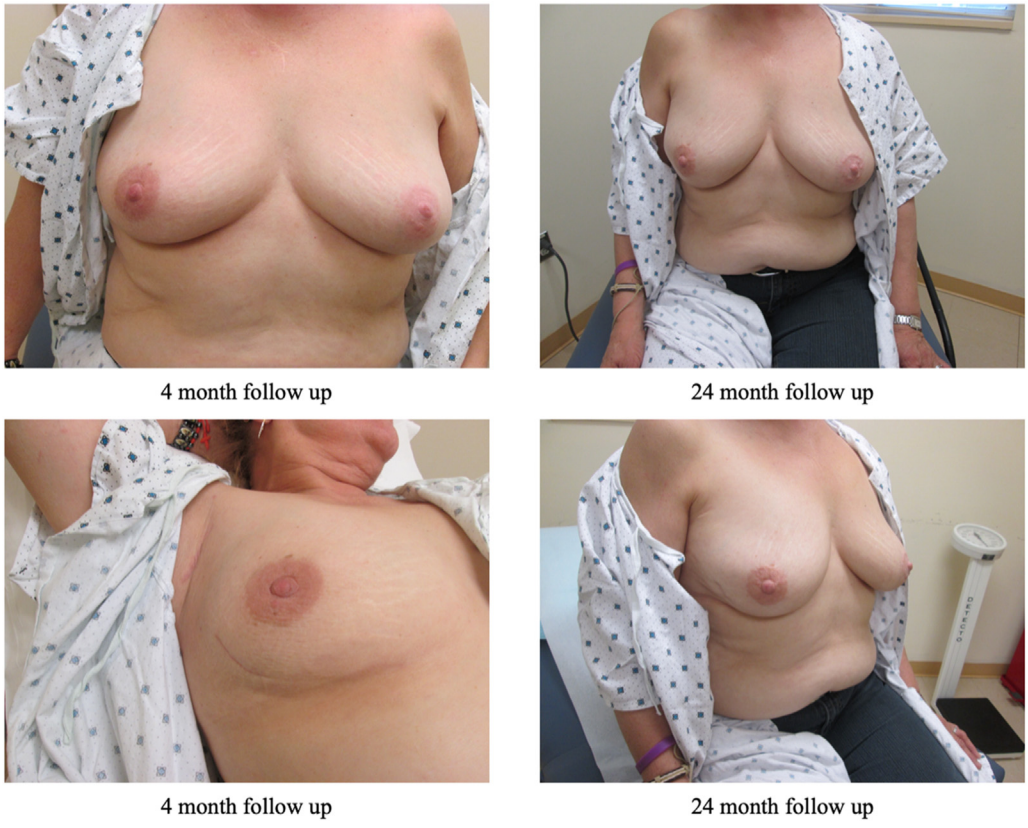

Figure 2 Comparison between Cosmesis at 4-month and 24-month follow-ups. Patient is a 77-year old, postmenopausal female with a high grade DCIS of the left breast.

asked about the barriers to adoption, concerns about local control and toxicity continue to be cited.[52]

Limitations of our study include its retrospective nature, small sample size, and relatively limited toxicity follow-up. Going forward, further descriptions of advanced treatment techniques and long-term outcomes of patients with early breast cancer treated with robotic SAPBI be explored. To our knowledge, this study is the largest retrospective analysis of patients with early breast cancer treated with robotic SAPBI to date. While our median follow-up time for cosmesis and toxicity was only 1.25 years, its length and outcomes are similar to that of Obayomi-Davies et al and Mészáros et al.[25,28] However, our median follow-up time of 4.68 years for disease recurrence is longer than that of previous studies and aids in advancing our understanding of the excellent disease control that can be achieved with robotic SAPBI.

Conclusion

Despite advancements in radiation treatment technology leading to SAPBI for patients with early-stage breast cancer, questions around its long-term efficacy limit its adoption. We reviewed the records of 50 patients with early-stage breast cancer treated with robotic SBRT at a single institution. Robotic SAPBI enables targeted, less invasive treatment in fewer fractions while still achieving outstanding disease control, excellent cosmesis, and limited toxicity. As such, robotic SAPBI appears to be a safe and effective treatment option for carefully selected patients with early breast cancer. Longer-term follow-up will be required, and future prospective trials should study the comparative effectiveness of this radiation technique.

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