



Retrospective review of three-fractioned accelerated partial breast irradiation

Laura Elizabeth Simon^{1,*}, Daniel Scanderbeg², John Einck², Jyoti Mayadev², Derek Brown², Anne Wallace², Sarah Blair², Catheryn Yashar², Minh-Phuong Huynh-Le³

¹University of California San Diego School of Medicine, La Jolla, CA

²Department of Radiation Medicine and Applied Sciences, University of California San Diego Health Moores Cancer Center, La Jolla, CA

³Division of Radiation Oncology, The Brooklyn Cancer Center, Brooklyn, NY

ABSTRACT

METHODS: This retrospective study evaluated patients who received three-fraction accelerated partial breast irradiation (APBI) via brachytherapy for breast cancer between January 2016 and April 2020. Inclusion criteria included age ≥ 18 years and early-stage unilateral breast cancer with negative lymph nodes. We evaluated acute toxicity (< 6 weeks), late toxicity (≥ 6 weeks), and cosmetic outcomes. Frequencies of each variable were calculated. Cancer-specific outcomes were determined via the Kaplan-Meier method.

RESULTS: Thirty consecutive patients received three-fraction APBI of 2,250 cGy over 2 d. All cancers were stage T2 or less. Median time to last follow-up was 22 months. Local recurrence-free survival was 95.8% at 22 months. Seventeen (56.7%) patients reported an acute toxicity event. All were grade 1 except one patient with grade 2 (fatigue). No patient experienced \geq grade 3 acute toxicity. One (3.3%) patient reported grade 3 late toxicity (tissue fibrosis). No patients had breast edema, fat necrosis, or non-healing wounds. There were no \geq grade 3 cosmetic events.

DISCUSSION: Three-fraction APBI via brachytherapy was successful in preventing disease recurrence and death in this study, with still limited follow-up. Although acute and late toxicities or adverse cosmetic outcomes were seen, very few were grade 2 or higher and compare favorably to those reported in prior 10-fraction APBI studies.

CONCLUSIONS: This study provides early single institutional evidence that three-fraction APBI may become a feasible treatment alternative. © 2022 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords:

Breast cancer; Brachytherapy; Accelerated partial breast irradiation

Introduction

Breast conserving therapy is a standard option for women with early-stage breast cancer who decline mastectomy (1–3). Adjuvant radiation has been shown to improve the locoregional control and survival for patients receiving breast conserving surgery (4). Accelerated partial breast irradiation (APBI) is an effective option to minimize toxicity to normal tissues while preserving excellent oncologic outcomes (5,6). Recently updated guidelines include both whole breast irradiation (WBI) and APBI as options for select patients (5–9).

APBI, delivered with both external beam radiotherapy and brachytherapy, has non-inferior local recurrence, disease free survival, and grade 2–3 toxicity events compared to WBI in select early stage breast cancer patients (1,6,7,10). NSABP B-39 enrolled a broader selection of patients than prior studies and did not demonstrate equivalence between WBI and APBI with an absolute difference of $< 1\%$ at 10 years between the two arms (11). Published APBI cosmetic outcomes delivered via brachytherapy have consistently been rated as good or excellent (1,12–14). The typical APBI brachytherapy fractionation remains 10 fractions of radiation therapy delivered twice daily, over 5 d. Select studies have researched an abbreviated schedule of APBI brachytherapy that delivers the full course of radiation in three to four fractions over 1–2 d (1,10,15). For example, Khan *et al.* recently published a study evaluating APBI delivery in three brachytherapy fractions demonstrating safety and effectiveness, with recurrence and tox-

Received 12 December 2021; received in revised form 17 February 2022; accepted 17 February 2022

* Corresponding author. University of California San Diego School of Medicine, 9500 Gillman Dr., La Jolla, CA 92093. Phone: 858-822-6785; Fax: 858-822-5568.

E-mail address: lsimon@health.ucsd.edu (L.E. Simon).

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<https://doi.org/10.1016/j.brachy.2022.02.002>

icity rates similar to published data for 10-fraction radiation therapy, although with short follow-up (1). With a median follow-up of 12 months, the short-term local control rate was 99% and cosmetic outcomes were promising. Ninety-seven percent of patients were rated as having good or excellent cosmesis using the Harvard Criteria (1). Similar success has been reported by Wallace *et al.* in a study of four-fraction APBI brachytherapy (10). Some studies have also commented on the potential utility and positive safety profile of postoperative single fraction brachytherapy, though this too has not become standard practice (16,17).

The abbreviated three-fraction APBI brachytherapy has multiple potential benefits over external beam WBI and 10-fraction APBI brachytherapy including convenience, accessibility, and decreased cost (1). However, there remains limited data regarding the effectiveness, safety, and cosmetic outcomes of these abbreviated brachytherapy schedules. This manuscript reports on a single-institutional retrospective review of patients with breast cancer who received three-fraction APBI via brachytherapy to determine (1) toxicity outcomes, (2) cosmetic outcomes, and (3) cancer-specific outcomes.

Methods and materials

Setting and participant selection

Since 2016, the University of California San Diego (UCSD) Moores Cancer Center has been performing three-fraction APBI via brachytherapy for eligible patients with early-stage breast cancer. The Moores Cancer Center utilizes two electronic health records, Epic (Epic, Verona, WI) and ARIA oncology information system (Varian Medical Systems, Inc., Palo Alto, CA), for radiation specific visits. Charts for all patients who received breast cancer brachytherapy from January 2016 to April 2020 were reviewed to determine patient eligibility. Patients were included in this study if they were age ≥ 18 years with early-stage unilateral breast cancer (biopsy-proven) and received radiation via three-fraction brachytherapy. Other inclusion criteria were cancer positive for estrogen or progesterone receptors and lymph nodes negative for cancer. Patients receiving more than three-fractions of brachytherapy or with any lymph node positivity were excluded. This retrospective study was approved by the UC San Diego Institutional Review Board (#200600CX), with a waiver of informed consent.

APBI procedure

Patients in this series were treated using brachytherapy devices or interstitial catheter placement. Brachytherapy devices used included the multilumen Strut Adjusted Volume Implant device (Cianna Medical, Alisa Viejo, CA), the multilumen Contoua device (Hologic, Marlborough,

Table 1
Characteristics of patients receiving three-fractioned APBI brachytherapy and tumor pathology

Demographic	Patients N=30 (%)
Age	
Mean (STD)	65 (6.4)
Comorbidities	
Prior breast cancer	3 (10.0)
Diabetes/pre-diabetes	5 (16.7)
Current/former smoker	11 (36.7)
Histology	
DCIS	4 (13.3)
Invasive ductal carcinoma	23 (76.7)
Invasive lobular carcinoma	1 (3.3)
Invasive mammary carcinoma	1 (3.3)
Invasive mucinous adenocarcinoma	1 (3.3)
Tumor Location	
UIQ	5 (16.7)
UOQ	19 (63.3)
LIQ	3 (10.0)
LOQ	2 (6.7)
Multifocal	1 (3.3)
Tumor Size, mm	
Median (STD)	10.0 (6.0)
<5	2 (6.7)
≥ 5 -<10	11 (36.7)
≥ 10 -<20	12 (40.0)
≥ 20 -<30	5 (16.7)
Tumor Margins	
Negative	30 (100)
Close (<2 mm)	0
Positive	0
Receptor Markers	
Estrogen Receptor +	30 (100)
Progesterone Receptor +	30 (100)
HER2+	1 (3.3)
Post Radiation Therapy	
Anti-estrogen therapy ^a	29 (96.7)
Chemotherapy ^b	2 (6.7)

DCIS = ductal carcinoma *in situ*; LIQ = lower inner quadrant; LOQ = lower outer quadrant; UIQ = upper inner quadrant; UOQ = upper outer quadrant.

^a Four patients stopped anti-estrogen treatment early due to adverse side effects of the medications.

^b Both patients also received anti-estrogen therapy.

MA), or the multilumen MammoSite device (Hologic). The brachytherapy treatment modality was chosen based on the discretion of the treating radiation oncologist.

Devices were implanted into individual patient's lumpectomy cavities by the radiation oncologist in the clinic, followed by immediate CT simulation for brachytherapy treatment planning. All patients had received prophylactic antibiotics.

Treatment planning, dosimetric constraints, and delivery

Treatment plans were generated using Varian Medical System's BrachyVision software using dosimetric constraints identical to those used in the TRIUMPH-T trial (1).

Table 2
Dosimetry data

Characteristic	Result
Minimum skin spacing, mm	
Mean (STD)	10.4 (10.7)
Median	7.2
Range	2.7–51.2
Minimum rib spacing, mm	
Mean (STD)	18.3 (14.7)
Median	13.7
Range	2.3–65.8
Skin bridge <5 mm	
Yes	10
No	20
Rib distance <5 mm	
Yes	5
No	25
Both skin bridge and rib distance <5 mm	
Yes	3
No	27
Skin dose, % of PD	
Median	88.8
Range	27.5–108.6
Rib dose, % of PD	
Median	64.8
Range	9.6–142
V150 (cm ³)	
Mean (STD)	24.2 (8.4)
Median	22.9
Range	8.41–53.69
V200 (cm ³)	
Mean (STD)	10.0 (3.1)
Median	10.5
Range	2.25–14.12
V100%	
Mean (STD)	88.6 (4.2)
Median	88.2
Range	76.27–94.33
V95%	
Mean (STD)	92.8 (3.3)
Median	92.9
Range	83.95–98.07
V90%	
Mean (STD)	95.6 (2.5)
Median	95.8
Range	90.03–99.1
Volume of PTV eval (cm ³)	
Mean (STD)	60.9 (24.5)
Median	52.4
Range	27.0–117.8

PD = prescribed doses; PTV = planning target volume.

Data collection

After eligibility was determined, patient charts were manually reviewed. Patient information was abstracted from both Epic and Varian ARIA oncology information system. Patient demographics, tumor indices (size, margins, grade), radiation treatment information, toxicity evaluations, cosmetic evaluations, and cancer outcomes were abstracted from the medical record. Dosimetry data, including skin and rib dose, were obtained from the BrachyVision radiation treatment planning system (Varian Medical Systems, Inc., Palo Alto, CA).

Outcomes

The primary outcomes of this study included acute toxicities (<6 weeks), late toxicities (≥6 weeks), cosmesis, and cancer outcomes. Toxicity grades were based on NCI CTCAE Version 4.0 toxicity scales. Acute toxicities included: radiation dermatitis, breast pain, fatigue, skin erythema, pruritus, desquamation, infection, and rash. Late toxicities included: seroma formation, breast pain, hyperpigmentation, breast edema, tissue fibrosis, fat necrosis, and a non-healing wound. All toxicity events were included in this study, even if the symptom resolved according to later follow-up notes.

Cosmetic outcomes were noted to occur if they were indicated on a radiation oncology physician note at any time following radiation therapy. The cosmetic indices included breast texture changes, thickening, hyper or hypopigmentation, telangiectasias, breast asymmetry, tissue retraction, and nipple/areolar deformation. Harvard Criteria was also evaluated (18). Cancer outcomes examined included local recurrence (marginal and elsewhere), contralateral recurrence, regional recurrence, metastases, and death.

Statistical analysis

Following data abstraction, all variables were analyzed to determine the frequency of each event. Cancer-specific outcomes (overall survival, local recurrence-free survival, and locoregional recurrence) were determined via the Kaplan-Meier method. All data analysis was performed using SPSS v27 software (Armonk, NY).

Results

A total of 30 consecutive patients received three-fraction APBI between January 2016 and April 2020. Nineteen of the 30 patients were originally treated as part of the TRIUMPH-T trial (1). Demographic information for the patient population is presented in Table 1. All women had stage T2 or lower invasive breast cancer or ductal carcinoma *in situ* (DCIS) and the median age of diagnosis was 65 years (range 51–77 years).

All treatment plans included in this study met the dosimetric constraints used in the TRIUMPH-T trial. Once the radiation plan was approved, patients received the first (and possibly second) fraction of APBI that same day. Patients then returned the next day to complete their treatments. All treatments were administered at least 6 h apart and the devices were all removed in their entirety after the third APBI treatment.

Table 3
Acute (<6 weeks) and late (≥ 6 weeks) toxicity events in patients receiving three-fractioned APBI brachytherapy

Outcome	Patients N = 30 (%)		
	Grade 1	Grade 2	Grade 3
Acute			
Radiation dermatitis	1 (3.3)	0	0
Acute breast pain	7 (23.3)	0	0
Fatigue	4 (13.3)	1 (3.3) ^a	0
Erythema	15 (50)	0	0
Pruritus	3 (10)	0	0
Desquamation	2 (6.7)	0	0
Rash	2 (6.7)	0	0
Infection	0	0	0
Late			
Seroma – asymptomatic	2 (6.7)	0	0
Seroma – symptomatic	0	0	0
Long term breast pain	12 (40)	0	0
Hyperpigmentation	8 (26.7)	0	0
Tissue fibrosis	16 (53.3)	3 (10)	1 (3)
Breast edema	0	0	0
Fat necrosis	0	0	0
Non-healing wound	0	0	0

^a Likely attributable to antibiotics, adrenal insufficiency, or anastrozole.

All patients received 2250 cGy in three-fractions via brachytherapy over a time period of 2 d. Treatments were administered as outlined in the TRIUMPH-T trial, with a minimum of 6 h between applications.¹ Radiation was delivered via either the Strut Adjusted Volume Implant device (76.7% of patients), Contura device (13.3%), interstitial catheter (6.7%), or ML MammoSite device (3.3%). The median time to last follow-up was 22 months (mean 27 months). Following radiation therapy, 29 (96.7%) patients were started on an anti-estrogen therapy, though 4 (13.3%) stopped anti-estrogen treatment early due to adverse side effects of the medications. Two (6.7%) patients also received chemotherapy. Dosimetry data is demonstrated in Table 2. Skin spacing ranged from 2.7 to 51.2 mm, rib spacing ranged from 2.3 to 65.8, and V150 and V200 ranged from 8.41 to 53.69 and 2.25–14.12, respectively.

Tumor specific information is presented in Table 1. Four (13.3%) patients had DCIS and 26 (86.7%) patients had an invasive carcinoma. The median tumor size was 10 mm. All 30 (100%) patients were reported to have margins >2 mm. Thirty (100%) tumors were ER+, 30 (100%) PR+, and 1 (3.3%) HER2+.

Acute toxicity events were reported in 17 (56.7%) patients, none of which were \geq grade 3 (Table 3). The most common acute toxicity was mild erythema (15, 50.0%), followed by acute breast pain (7, 23.3%), and fatigue (5, 16.7%). One patient reported grade 2 fatigue, possibly attributable to adrenal insufficiency, diagnosed shortly after treatment. Grade 1–2 late toxicities were reported in 25 (83.3%) patients (Table 3). Mild tissue fibrosis (19, 63.3%) was the most common late toxicity reported. One

(3.3%) patient reported grade 3 tissue fibrosis. There were no other \geq grade 3 late toxicity events. No patients had breast edema, fat necrosis, or non-healing wounds. Grade 1–2 cosmetic events occurred in 14 (46.7%) patients (Table 4); patients with breast asymmetry or nipple/areolar retraction likely had these cosmetic events due to a combination of surgery and radiation. No \geq grade 3 cosmetic events occurred. Ten patients had physician notes specifically outlining the Harvard Criteria classification of the cosmetic outcomes, all of which were “good” or “excellent.” Based on retrospective review of provider notes, all additional patients met criteria for “good” or “excellent” cosmesis as well.

Finally, local recurrence-free survival was 95.8% at 22 months (Fig. 1). One patient (3.3%) with invasive ductal carcinoma on tamoxifen was diagnosed with ipsilateral marginal recurrence 1.5 years following APBI treatment and no patients were found to experience metastases or death following their radiation treatment. The patient with the marginal recurrence was treated with relumpectomy and WBI.

Discussion

This case series describes patients with early-stage breast cancer who received three-fraction APBI brachytherapy. Patients had excellent oncologic and cosmetic outcomes. No patient experienced \geq grade 3 acute toxicity and there was only one grade 3 late toxicity. We found low rates of recurrence with one patient experiencing ipsilateral marginal recurrence. Altogether, our data demon-

Table 4
Cosmetic outcomes in patients receiving three-fractioned APBI brachytherapy

Outcome	Patients N= 30 (%)		
	Grade 1	Grade 2	Grade 3
Variables			
Breast texture	1 (3.3)	0	0
Thickening of scar tissue	5 (16.7)	0	0
Color change	1 (3.3)	0	0
Telangiectasias	1 (3.3)	0	0
Breast asymmetry	4 (13.3)	1 (3.3)	0
Scar retraction	2 (6.7)	0	0
Nipple/areolar deformation	7 (23.3)	3 (10)	0
Skin changes	0	0	0
Harvard classification			
Excellent	25 (83.3)		
Good	5 (16.7)		
Fair	0		
Poor	0		

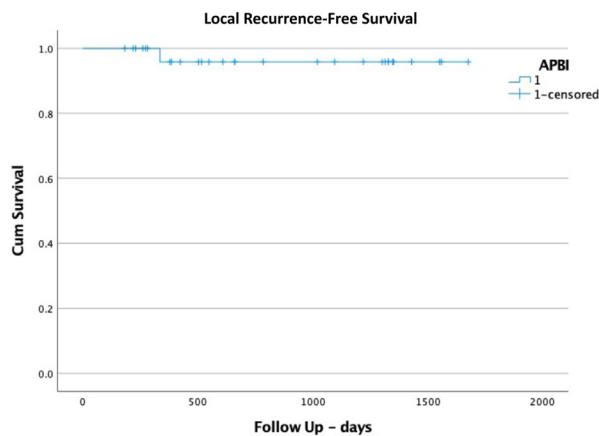


Fig. 1. Kaplan-Meier curve of local recurrence-free survival. “(For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)”

strates the safety and efficacy of the three-fraction breast brachytherapy for partial breast irradiation over a longer period than prior publications.

Toxicity in this case series was comparable to those reported for 10-fraction APBI brachytherapy (11,19), supporting the use of three-fraction APBI as an alternative treatment. The absence of \geq grade 3 acute toxicity events demonstrates that this treatment regimen was very well tolerated by patients within the weeks following the procedure. Fifty seven percent of patients experienced any acute toxicity, all grades 1–2. Furthermore, the only grade 2 toxicity was fatigue, likely attributable to a concurrent medical condition in that patient. A prior study by Wallace *et al.* used four-fractioned APBI brachytherapy and demonstrated similar results, though with a higher incidences of grade 3 acute toxicities and breast pain (10). Khan *et al.* reported a slightly lower acute toxicity rate (38.5% of pa-

tients), though with more grade two events (1). Our study also found that the rate of significant (\geq grade 3) late toxicities was very low (3.3%), indicating safety of this treatment regimen over the study period. Prior publications on 10-fraction APBI brachytherapy demonstrate grade 3 toxicities of 10%, higher than the rates found in this study for three-fraction APBI brachytherapy (11,19).

Cosmetic outcomes were very favorable, with all patients achieving good/excellent cosmesis. This is similar to the outcomes reported in a prior study of three to four fraction brachytherapy which found 97.5% of patients to have good/excellent cosmesis, as well as other studies analyzing abbreviated schedules of APBI brachytherapy (12,15). Though nearly half the patients in this case series experienced a grade 1–2 cosmetic toxicity, certain cosmetic outcomes such as nipple/areolar retraction or breast asymmetry are likely attributable to the combined effects of surgery and radiation therapy.

Additionally, at this early juncture there were acceptable oncologic outcomes with three-fraction APBI brachytherapy. Only one patient had an ipsilateral marginal tumor recurrence. No distant metastases or deaths were observed at a median follow up of 22 months. Studies on 10-fraction APBI brachytherapy have demonstrated an ipsilateral tumor recurrence rate between 2.5–4% (11,19).

Though longer follow up is needed in future studies evaluating APBI for early-stage breast cancer, the early results are encouraging in demonstrating both efficacy and tolerability of three-fraction breast APBI brachytherapy techniques.

The ability to perform complete adjuvant radiation treatment within 2 d has significant advantages in patient quality of life, convenience, and access to care. It also expanded the use of brachytherapy to those at increased risk of infection, such as diabetics, that were excluded from brachytherapy with 5–7 d of an indwelling device (1,10).

By limiting the number of treatment days women may more easily complete the full course of radiation while balancing other responsibilities. The three-fraction breast APBI brachytherapy technique may also expand the accessibility of radiation therapy for people in rural locations. Additionally, the increased efficiency of abbreviated schedules may provide the opportunity for medical institutions to perform breast radiation on an increased number of women, leading to improved breast cancer care (20).

While this study showed promising results, there are some limitations. Primarily, this retrospective study had a relatively small sample size and was limited to one institution. Further analysis of three-fraction APBI at other institutions is important for generalizability of our results. However, the concordance between this study and prior works evaluating the safety and outcomes of APBI brachytherapy provides reassurance in the results. Additionally, due to the retrospective nature of this study, the devices used during treatments were selected by the practitioner based on patient-specific needs. Therefore, target volumes and dosimetric requirements were based on standard guidelines for each technique. As both interstitial and single-entry devices were included in the TRIUMPH-T trial evaluating the three-fraction regimen, a similar structure was used in this study. A further limitation is the relatively short median follow-up time (22 months) (1,10). Finally, assessment of adverse events was determined via physician-reported outcomes, as opposed to patient-reported outcomes.

Conclusion

This study analyzed the efficacy of three-fractioned APBI brachytherapy for the treatment of early-stage low risk breast cancer following lumpectomy. This treatment regimen had favorable cancer related outcomes, very few \geq grade 3 toxicities, and excellent cosmesis. Abbreviated schedules of APBI brachytherapy have the potential to improve access to care and quality of life for breast cancer patients needing radiation therapy and may become a feasible treatment alternative.

Disclosures

One author has received honoraria from Varian Medical Systems for speaking engagements. One author's husband holds stock in a medical device company, Viewpoint Medical.

References

- [1] Khan AJ, Chen PY, Yashar C, et al. Three-fraction accelerated partial breast irradiation (APBI) delivered with brachytherapy applicators is feasible and safe: first results from the TRIUMPH-T trial. *Int J Radiat Oncol Biol Phys* 2019;104:67–74. doi:10.1016/j.ijrobp.2018.12.050.

- [2] Clark RM, McCulloch PB, Levine MN, et al. Randomized clinical trial to assess the effectiveness of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer. *J Natl Cancer Inst* 1992;84:683–689. doi:10.1093/jnci/84.9.683.
- [3] Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–1241. doi:10.1056/NEJMoa022152.
- [4] Darby S, McGale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011;378:1707–1716. doi:10.1016/S0140-6736(11)61629-2.
- [5] Correa C, Harris EE, Leonard MC, et al. Accelerated partial breast irradiation: executive summary for the update of an ASTRO evidence-based consensus statement. *Pract Radiat Oncol* 2017;7:73–79. doi:10.1016/j.prro.2016.09.007.
- [6] Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet* 2016;387:229–238. doi:10.1016/S0140-6736(15)00471-7.
- [7] Castaneda SA, Strasser J. Updates in the treatment of breast cancer with radiotherapy. *Surg Oncol Clin N Am* 2017;26:371–382. doi:10.1016/j.soc.2017.01.013.
- [8] Shah C, Vicini F, Shaitelman SF, et al. The American Brachytherapy Society consensus statement for accelerated partial-breast irradiation. *Brachytherapy* 2018;17:154–170. doi:10.1016/j.brachy.2017.09.004.
- [9] Shah C, Vicini F, Wazer DE, et al. The American Brachytherapy Society consensus statement for accelerated partial breast irradiation. *Brachytherapy* 2013;12:267–277. doi:10.1016/j.brachy.2013.02.001.
- [10] Wallace M, Martinez A, Mitchell C, et al. Phase I/II study evaluating early tolerance in breast cancer patients undergoing accelerated partial breast irradiation treated with the mammosite balloon breast brachytherapy catheter using a 2-day dose schedule. *Int J Radiat Oncol Biol Phys* 2010;77:531–536. doi:10.1016/j.ijrobp.2009.05.043.
- [11] Vicini FA, Cecchini RS, White JR, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *Lancet* 2019;394:2155–2164. doi:10.1016/S0140-6736(19)32514-0.
- [12] Wilkinson JB, Martinez AA, Chen PY, et al. Four-year results using balloon-based brachytherapy to deliver accelerated partial breast irradiation with a 2-day dose fractionation schedule. *Brachytherapy* 2012;11:97–104. doi:10.1016/j.brachy.2011.05.012.
- [13] Polgár C, Strnad V, Major T. Brachytherapy for partial breast irradiation: the European experience. *Semin Radiat Oncol* 2005;15:116–122. doi:10.1016/j.semradonc.2004.10.004.
- [14] Polgár C, Major T, Takácsi-Nagy Z, Fodor J. Breast-conserving surgery followed by partial or whole breast irradiation: twenty-year results of a phase 3 clinical study. *Int J Radiat Oncol Biol Phys* 2021;109:998–1006. doi:10.1016/j.ijrobp.2020.11.006.
- [15] Guinot JL, Gonzalez-Perez V, Meszaros N, et al. Very accelerated partial breast irradiation Phase I-II multicenter trial (VAPBI): feasibility and early results. *Brachytherapy* 2021;20:332–338. doi:10.1016/j.brachy.2020.10.010.
- [16] Kinj R, Chand ME, Gal J, et al. Five-year oncological outcome after a single fraction of accelerated partial breast irradiation in the elderly. *Radiat Oncol* 2019;14:234. doi:10.1186/s13014-019-1448-0.
- [17] Hannoun-Lévi JM, Cham Kee DL, Gal J, et al. Accelerated partial breast irradiation for suitable elderly women using a single fraction of multicatheter interstitial high-dose-rate brachytherapy: early results of the Single-Fraction Elderly Breast Irradiation (SiFEBI) Phase I/II trial. *Brachytherapy* 2018;17:407–414. doi:10.1016/j.brachy.2017.11.008.

- [18] Trombetta M, Julian TB, Kim Y, *et al.* The allegheny general modification of the Harvard breast cosmesis scale for the retreated breast. *Oncology (Williston Park)* 2009;23:954–956.
- [19] Chao KK, Vicini FA, Wallace M, *et al.* Analysis of treatment efficacy, cosmesis, and toxicity using the MammoSite breast brachytherapy catheter to deliver accelerated partial-breast irradiation: the william beaumont hospital experience. *Int J Radiat Oncol Biol Phys* 2007;69:32–40. doi:10.1016/j.ijrobp.2007.02.026.
- [20] Khan AJ, Rafique R, Zafar W, *et al.* Nation-Scale adoption of shorter breast radiation therapy schedules can increase survival in resource constrained economies: results from a markov chain analysis. *Int J Radiat Oncol Biol Phys* 2017;97:287–295. doi:10.1016/j.ijrobp.2016.10.002.