Radiotherapy and Oncology 108 (2013) 197–202

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Phase III randomised trial

Breast-conserving therapy with partial or whole breast irradiation: Ten-year results of the Budapest randomized trial

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ARTICLE INFO

Article history:
Received 18 January 2013
Received in revised form 3 May 2013
Accepted 11 May 2013
Available online 3 June 2013

Keywords:
Breast-conserving therapy
Accelerated partial breast irradiation
Brachytherapy
Randomized trial

ABSTRACT

Background and purpose: To report the long-term results of a single-institution randomized study comparing the results of breast-conserving treatment with partial breast irradiation (PBI) or conventional whole breast irradiation (WBI).

Patients and methods: Between 1998 and 2004, 258 selected women with pT1 pN0-1mi M0, grade 1–2, non-lobular breast cancer without the presence of extensive intraductal component and resected with negative margins were randomized after BCS to receive 50 Gy WBI ($n = 130$) or PBI ($n = 128$). The latter consisted of either 7×5.2 Gy high-dose-rate (HDR) multi-catheter brachytherapy (BT; $n = 88$) or 50 Gy electron beam (EB) irradiation ($n = 40$). Primary endpoint was local recurrence (LR) as a first event. Secondary endpoints were overall survival (OS), cancer-specific survival (CSS), disease-free survival (DFS), and cosmetic results.

Results: After a median follow up of 10.2 years, the ten-year actuarial rate of LR was 5.9% and 5.1% in PBI and WBI arms, respectively ($p = 0.77$). There was no significant difference in the ten-year probability of OS (80% vs 82%), CSS (94% vs 92%), and DFS (85% vs 84%), either. The rate of excellent-good cosmetic result was 81% in the PBI, and 63% in the control group ($p < 0.01$).

Conclusions: Partial breast irradiation delivered by interstitial HDR BT or EB for a selected group of early-stage breast cancer patients produces similar ten-year results to those achieved with conventional WBI. Significantly better cosmetic outcome can be achieved with HDR BT implants compared with the outcome after WBI.

Over the last three decades, breast-conserving therapy (BCT) including surgical removal of the primary tumor and whole breast irradiation (WBI) consisting of 5 weeks of external beam radiotherapy (EBRT) with or without an additional 1–2 weeks of boost irradiation to the tumor bed, became the standard of care for the treatment of early-stage breast carcinoma [1–3]. However, the necessity of giving WBI for all patients as a part of BCT has been questioned, and accelerated partial breast irradiation (APBI) has been tested in multiple clinical trials as an alternative treatment option [4–31]. The results of multiple phase I–II trials showed that APBI using interstitial multi-catheter brachytherapy (BT) using adequate patient selection and quality assurance (QA) yields similar results to those achieved with conventional WBI [4,11–14,19,20,23–25,28]. However, two randomized APBI trials conducted in the late eighties showed inferior results with partial breast irradiation (PBI) using less sophisticated EBRT techniques and limited QA procedures [7,15]. Therefore, the hypothesis that PBI produces similar results to those achieved with standard WBI should be proved in prospective randomized trials.

At the Hungarian National Institute of Oncology, a prospective phase III clinical trial comparing PBI with multi-catheter interstitial high-dose-rate (HDR) BT or EBRT with WBI for a selected group of early-stage breast cancer patients was conducted between 1998 and 2004. Five-year results of this study have been published elsewhere, and this is the first report of the ten-year results [18].

Materials and methods

Study design

Between July 1998 and May 2004, 258 patients with stage I–II breast cancer who underwent breast-conserving surgery (BCS) were randomized to receive WBI ($n = 130$) or PBI ($n = 128$). Patients were eligible if they met all the following conditions: wide excision with microscopically negative surgical margins; unifocal tumor; primary tumor size $\leqslant 20$ mm (pT1); cN0, pN0, or pN1mi (nodal

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http://dx.doi.org/10.1016/j.radonc.2013.05.008
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micrometastasis ⩽2 mm) axillary nodal status; and histological grade 1–2. Exclusion criteria included prior breast cancer or other malignancies (except skin basalioma); bilateral breast carcinoma; pure ductal or lobular carcinoma *in situ* (pTis); invasive lobular carcinoma; lymphovascular invasion; or the presence of an extensive intraductal component. Young women aged ⩽40 years were also excluded after a protocol amendment performed in 2001.

Randomization was done by the principal investigator. Patients were randomly allocated to treatment options by a sealed-envelope system in blocks of ten. Blinding of physicians performing treatments and follow-up and of patients was not possible for technical reasons. No stratification was used. The primary endpoint for analysis was the appearance of local recurrence (LR) as a first event. The scientific hypothesis was "non-relevant non-inferiority" of PBI with regard to LR. The difference in LR between the two arms that we considered clinically non-relevant for our sample size calculation was 6% (e.g. 10% after PBI vs 4% after WBI at five years). The 4% figure was considered as the low ceiling of five-year LR rates reported in modern breast-conserving series using WBI. The originally planned sample size ($n = 570$) was calculated to detect this 6% difference in LR rate at five years between the two treatment arms with a statistical power of 80% and at a significance level of 5%. Accrual was stopped prematurely at a sample size of 258 patients, because since June 2004 all eligible patients have been offered to participate in the European multicentric GEC-ESTRO (Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology) phase III APBI trial. One patient in the WBI arm developed distant metastasis before RT and did not receive the assigned treatment. Another patient in PBI arm refused her assigned therapy and underwent mastectomy without RT. However, all patients were analyzed according to the intent to treat policy (Fig. 1). The trial protocol was accepted by the ethics committee of the National Institute of Oncology, Budapest, and informed consent of the patients was required.

Surgery

All patients underwent BCS with axillary dissection ($n = 160$) or sentinel lymph node biopsy ($n = 93$), while surgical axillary staging was omitted in 5 cases, based on the surgeon's preference. During surgery, the boundaries of the excision cavity were marked with titanium clips. All breast specimens were inked and oriented by the pathologist to define microscopic margins. Patient and tumor characteristics are listed in Table 1.

Radiotherapy

Eighty-eight out of 128 (69%) patients in the PBI arm were assigned to be treated with 7×5.2 Gy b.i.d. HDR multi-catheter interstitial BT alone, but the protocol allowed 50 Gy limited-field EB irradiation for patients who were technically unsuitable for interstitial implantation ($n = 40$; 31%). Implantations were performed four to six weeks after BCS under local anesthesia. Patients were treated with HDR remote after-loading equipment using a ^{192}Ir stepping source. The traditional Paris system guidelines were used for the planning of the implant geometry [32]. A preimplant radiograph simulation was performed by using a template placed on the breast to determine the entrance and exit points of the needles from the "needle-eye" view. Planning target volume (PTV) was defined as the excision cavity delineated by the surgical clips plus a margin of 2 cm. However, only a 1–1.5 cm safety margin was applied when excision cavity was close to the skin surface or chest wall. Four to thirteen (median: 9) guide needles were inserted into the tumor bed in a triangular geometry using template guidance. The spacing between the needles was 13 or 15 mm. Then, the guide needles were replaced with flexible plastic catheters, which were fixed with buttons. Single-, double-, triple-, and four-plane implants were performed at 1 (1%), 47 (54%), 38 (44%), and 1 (1%) patients, respectively. The Paris system rules were not used for dose prescription [32]. Our own planning concepts have been established to achieve more conformal coverage of the PTV. The treatment planning was based on a three-dimensional reconstruction of the locations of the catheters, surgical clips, and skin points digitized from two postimplant radiograph films taken with the variable-angle reconstruction technique. The active source positions and reference dose points were defined individually in each catheter, and the optimization of the dwell times to dose points and geometry was performed. The most peripheral active source

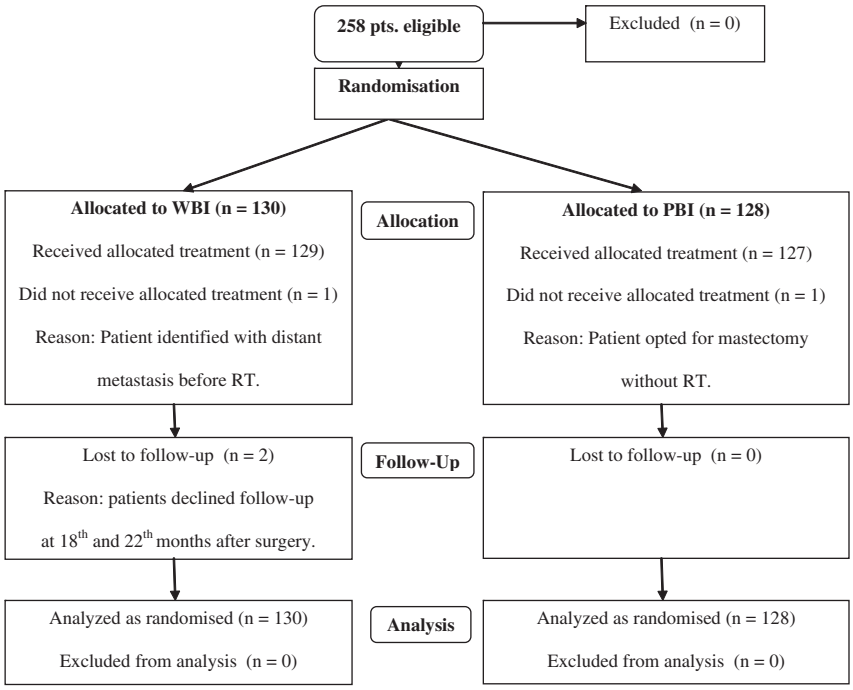

Fig. 1. CONSORT trial flow diagram. *Abbreviations:* WBI – whole breast irradiation; PBI – partial breast irradiation; RT –radiotherapy.

Table 1
Patient and tumor characteristics by treatment arms.

Characteristic	PBI (n = 128)	WBI (n = 130)	p-Value
Mean age (years)	59	58	0.31[b]
Range	30–84	31–80	
Age groups (years)			0.23
⩽40	3 (2.4)	6 (4.6)	
41–50	26 (20.3)	26 (20.0)	
51–60	41 (32.0)	50 (38.5)	
>60	58 (45.3)	48 (36.9)	
Premenopausal	27 (21.1)	28 (21.5)	0.93
Pathological tumor size (mm)			0.14
⩽5	8 (6.2)	3 (2.3)	
>5 but ⩽10	39 (30.5)	35 (26.9)	0.13[b]
>10 but ⩽20	81 (63.3)	92 (70.8)	
Median	13	13	
Pathological nodal status			0.25
pN0	121 (94.5)	123 (94.6)	
pN1mi	3 (2.3)	6 (4.6)	
Not known (no axillary surgery)	4 (3.2)	1 (0.8)	
Surgical margins			0.78
Close (<2 mm)	0 (0)	1 (0.8)	
Clear (⩾2 mm)	123 (96.1)	123 (94.6)	
Clear (NSABP)[a]	5 (3.9)	6 (4.6)	
Histologic type			0.52
Ductal	103 (80.5)	108 (83.1)	
All others	25 (19.5)	22 (16.9)	
Tumor grade			0.03
1	81 (63.3)	65 (50)	
2	47 (36.7)	65 (50)	
ER status			0.42
Positive	116 (90.6)	113 (86.9)	
Negative	10 (7.8)	16 (12.3)	
Unknown	2 (1.6)	1 (0.8)	

Abbreviations: PBI – partial breast irradiation; WBI – whole breast irradiation; ER – estrogen receptor. Data are n (%).
[a] National Surgical Adjuvant Breast and Bowel Project criteria, no tumor on ink.
[b] Mann–Whitney two-sample test. All other variables were tested with the chi-square test.

positions were kept at a minimum of 10–15 mm from the skin surface, limiting the maximal skin dose to 60% of the prescribed dose. The distances of the dose points from the catheters were 4–12 mm and could vary from catheter to catheter. The prescribed BT dose, calculated to the 100% isodose surface was 36.4 Gy and delivered with seven fractions of 5.2 Gy, each given at least six hours apart within four days. For the assessment of implant quality, cumulative dose-volume histograms and dose-nonuniformity ratios (DNR) were used [33]. The mean volume encompassed by the 100% isodose surface (V_{ref}) was 63 cm^3 (range: 27–120 cm^3). The mean DNR was 0.38 (range: 0.21–0.63). Postimplant CT scans were performed for only 17 of 87 patients (20%) to document PTV coverage and to develop CT-image based BT planning techniques later [33]. Eighty-five out of 88 patients (97%) received the intended dose of BT. At one patient only six fractions of 5.2 Gy were delivered because of grade 3 acute skin toxicity. Another patient was treated with an off-protocol fractionation scheme (five fractions of 6.64 Gy b.i.d.) based on the decision of the treating radiation oncologist. One patient refused BT, as she opted for mastectomy instead of RT. All BT patients received antibiotics during the treatment period plus two days, thereafter. After the last treatment fraction the catheters were removed.

Electron beam PBI (n = 40) was performed using 6–15 MeV en face electron fields to the tumor bed extended with a margin of 2 cm. In the case of deep-seated tumor bed a smaller safety margin was used in the direction of the pectoral muscle to avoid irradiation of the lung tissue. Adequate field size and beam energy were defined by CT-based treatment planning and/or simulation radiographs. The median total dose was 50 Gy (range: 42–50 Gy) using conventional fractionation (2 Gy/day, five fractions/week).

In the control arm, WBI was delivered with telecobalt (n = 29) or 6–9 MV photon (n = 100) beams using wedged tangential fields with 2 Gy daily fractions over five weeks. Two dimensional CT-based treatment planning was used for all patients. Three dimensional conformal (3D-CRT) or intensity modulated radiotherapy (IMRT) were not available in that era. One patient (0.8%) was identified with distant metastasis and received palliative systemic treatment instead of WBI. The median total dose of WBI for the other 129 patients was 50 Gy (range: 42–50 Gy). Only one patient (0.8%) received 16 Gy additional electron boost to the tumor bed. Regional nodal irradiation was not given.

Adjuvant systemic therapy

Adjuvant systemic therapy was given according to the actual institutional treatment protocol. Since 1999, all patients with tumor size >10 mm received adjuvant systemic therapy. Eighty-nine of 128 (70%) PBI and ninety-four of 130 (72%) WBI patients received chemo- and/or hormone therapy (p = 0.37). Hormone therapy consisted of aromatase inhibitors in 23 (18%) and 24 (18%) patients, or tamoxifen in 64 (50%) and 68 (52%) women with goserelin acetate in 15 (12%) and 13 (10%) cases, respectively. Only 7 patients received adjuvant chemotherapy including 6 cycles of CMF in 1 (0.8%) and 2 (1.5%) patients or 4 cycles of AC in 1 (0.8%) and 3 (2.3%) women, respectively. An additional patient in the WBI arm was identified with distant metastasis and received palliative chemo- and hormone therapy instead of RT.

Follow-up

Patients were seen every three months in the first two years after RT, every six months in the next three years, and annually thereafter. Baseline mammography was performed six months after completion of RT and yearly, thereafter. Local recurrence was defined as any detection of cancer in the treated breast occurring as a first event, proved by histological examination in every case. An elsewhere breast failure (EF) was defined as ipsilateral LR detected at least 2 cm from the surgical clips. All other LR was classified as true recurrence/marginal miss (TR/MM). Cosmetic outcome was assessed by the treating radiation oncologist and/or the principal investigator at each follow-up. The cosmetic results were scored using the Harvard criteria for those patients who received at least one fraction of the assigned treatment (n = 256) [34]. The last available follow-up data were used for the analysis of cosmetic results. Data on cosmetic outcome were available for 241 patients (94%), and registered at a median follow-up of 124 months (range: 18–162 months).

Statistical methods

Survival analyses were based on the intent to treat principle with event-free intervals defined as the time between the date of surgery and the date of event or last follow-up. The statistical test used to perform power calculation for "non-relevant non-inferiority" was one-sided. Accrual was closed before reaching the originally planned sample size (n = 570). According to our reanalysis of power for the actual sample size (n = 258), our study has an 80% power to detect a 10% difference between the arms.

Discrete pretreatment variables of the two arms were compared using the chi-square test. Continuous variables were evaluated using the Mann–Whitney two-sample test. Survival curves were calculated using the Kaplan–Meier method and compared with two-sided log-rank test. A probability level of 0.05 was considered to be statistically significant. The probability of events obtained

from the Kaplan–Meier estimates was given with 95% confidence intervals (CI). Differences in cosmetic outcome between treatment groups were compared using the Fisher's exact test. The SOLO software (Department of Biometrics, University of California, Los Angeles, CA) was used for statistical analyses.

Results

Median follow-up of all and surviving patients were 10.2 years (range: 1.5–13.5 years) and 10.8 years (range: 7.6–13.5 years), respectively. During the follow-up period 48 patients (19%) have died, and only 2 (0.8%) have been lost to follow up. Overall, 7 (5.5%) and 6 (4.6%) patients developed LR as a first event in the PBI and WBI arm, respectively. The crude rates of first events according to treatment arms are summarized in Table 2. The five- and ten-year actuarial survival rates are presented in Table 3. The ten-year probability of LR-free survival was similar in the two treatment arms (Fig. 2). The ten-year actuarial rate of LR, TR/MM, and EF was 5.9% (95% CI 1.6–10.2%), 2.4% (95% CI 0–5.1%), and 3.5% (95% CI 0.1–6.9%) after PBI, whereas it was 5.1% (95% CI 1.1–9.1%), 3.4% (95% CI 0.1–6.7%), and 1.6% (95% CI 0–3.9%) after WBI, respectively. The ten-year probability for developing regional recurrence after PBI and WBI was 2.5% (95% CI 0–5.3%), and 1.7% (95% CI 0–4.0%), respectively. Overall survival (OS), cancer-specific survival (CSS), and disease-free survival (DFS) at ten years for PBI was 79.7% (95% CI 72.5–86.9%), 94.4% (95% CI 89.9–98.9%), and 85.3% (95% CI 79.0–91.6%), respectively, whereas for WBI it was 82.1% (95% CI 75.5–88.7%), 91.7% (95% CI 86.8–96.6%), and 83.6% (95% CI 77.0–90.2%).

Six out of seven patients with LR in the PBI group were salvaged with repeated BCS. Four of them received WBI up to a total dose of 45–50.4 Gy. One patient developed subsequent lung metastasis

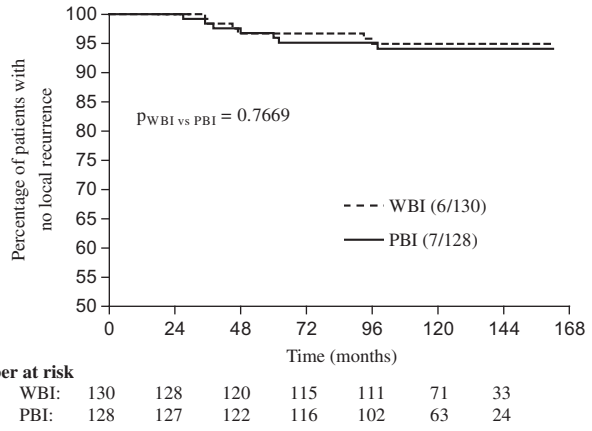

Fig. 2. Time to local recurrence by Kaplan–Meier estimates. *Abbreviations:* WBI – whole breast irradiation; PBI – partial breast irradiation.

treated with hormone therapy and was alive with stable disease at the time of analysis. Second LR occurred only for one patient, treated with chemotherapy followed by trastuzumab yielding partial response and breast cancer death later. The other four patients were alive without any further relapse. In the PBI group only one woman underwent successful salvage mastectomy.

Among the six patients with LR in the WBI group, three were salvaged with lumpectomy, and three with mastectomy. One of them developed distant metastasis and died of the disease later. The other five women were alive without any further relapse. Second LR did not occur.

Cosmetic outcome according to the RT technique is listed in Table 4. The rate of excellent-good cosmetic result was 81% in the PBI arm and 63% in the WBI arm ($p < 0.01$). The rate of excellent-good cosmesis in the PBI group was 85% after HDR BT and 72.5% after EB ($p = 0.97$), whereas in the WBI group it was 67% using 6–9 MV photons and 48% using telecobalt ($p = 0.08$). Excluding EB PBI and telecobalt WBI patients from the analysis, significantly more patients treated with HDR BT had excellent-good cosmetic result compared to those treated with 6–9 MV photon WBI (85% vs 67%; $p < 0.01$). Analysis of late radiation side effects will be reported elsewhere.

Discussion

APBI is an attractive treatment approach that shortens the 5–7 week course of conventional WBI to one week or less focusing ionizing radiation just to the vicinity of the tumor bed and avoiding irradiation of the surrounding healthy breast tissue. The acceleration of RT eliminates some of the disadvantages of the extended treatment period, especially for elderly patients, working women, and those who live at a significant distance from the RT facility.

Table 2
Incidence of first events according to treatment arms.

Event	PBI ($n = 128$)	WBI ($n = 130$)
Ipsilateral breast failure	7 (5.5)	6 (4.6)
Tumor bed recurrence/marginal miss	3 (2.4)	4 (3.1)
Elsewhere breast failure	4 (3.1)	2 (1.5)
Regional failure	3 (2.3)	1 (0.8)
Axillary failure	2 (1.5)	1 (0.8)
Supraclavicular failure	1 (0.8)	0 (0)
Distant metastasis	7 (5.5)	11 (8.5)
Any first relapse[a]	17 (13.3)	18 (13.8)
Contralateral breast cancer	9 (7.0)	8 (6.2)
2nd Primary tumor	7 (5.5)	6 (4.6)
Non-breast cancer death	10 (7.8)	10 (7.7)

Abbreviations: PBI – partial breast irradiation; WBI – whole breast irradiation. Data are *n* (%).
[a] Local, regional, or distant failure, whichever came first.

Table 3
Actuarial 5- and 10-year survival rates by treatment arm.

Event	PBI vs WBI 5-year rate	PBI vs WBI 10-year rate	*p*-Value
Ipsilateral breast failure	4.0% vs 3.3%	5.9% vs 5.1%	0.77
Tumor bed recurrence/marginal miss	1.6% vs 1.6%	2.4% vs 3.4%	0.72
Elsewhere breast failure	2.4% vs 1.6%	3.5% vs 1.6%	0.41
Contralateral breast cancer	6.4% vs 2.4%	8.3% vs 6.4%	0.56
Regional failure	1.6% vs 1.7%	2.4% vs 1.7%	0.65
Distant metastasis	6.4% vs 6.3%	7.3% vs 11.5%	0.61
Disease-free survival	88.8% vs 90.5%	85.3% vs 83.6%	0.97

Table 4
Cosmetic outcome.

Harvard cosmetic score	PBI – HDR BT ($n = 85$)[a]	PBI – EB ($n = 40$)[a]	WBI – photons ($n = 93$)[a]	WBI – cobalt ($n = 23$)[a]
Excellent	29 (34.1)	7 (17.5)	16 (17.2)	3 (13.1)
Good	43 (50.6)	22 (55.0)	46 (49.5)	8 (34.8)
Fair	11 (12.9)	11 (27.5)	22 (23.6)	11 (47.8)
Poor	2 (2.4)	0 (0)	9 (9.7)	1 (4.3)

Abbreviations: PBI – partial breast irradiation; HDR BT – high-dose-rate brachytherapy; EB – electron beam; WBI – whole breast irradiation. Data are *n* (%).
[a] *n* = patient number with data available on cosmetic outcome.

In the last two decades APBI using interstitial BT implants and EBRT techniques has been intensively evaluated in prospective clinical studies as a possible alternative to WBI (Table 5). The results of these trials were controversial. Majority of phase II BT trials – using strict patient selection criteria and proper treatment technique – were successful in yielding an annual LR rate in the range of 0–1.2% [4,11–14,19,20,23–25,28]. On the other hand, results of early trials using out-of-date BT or EBRT techniques without rigorous QA procedures for mainly unselected patients were poor [7–9,15,17,22]. These results suggest that APBI is a reasonable approach at least for a properly selected subgroup of early-stage breast cancer patients, provided that meticulous attention is paid to QA [21].

In the last decade, based on the promising results with accelerated multi-catheter partial breast BT, new APBI techniques including external beam three-dimensional conformal radiotherapy (3D-CRT), intraoperative RT, and intracavitary BT have been developed and implemented [5,6,10,16,26,27,29]. According to the first published series, the five-year results are encouraging with both 3D-CRT and intracavitary balloon BT (Table 5) [5,10,16]. On the other hand, in a recent large retrospective population-based cohort study, treatment with breast BT compared with WBI was associated with significantly higher five-year incidence of subsequent mastectomy (4% vs 2.2%), and postoperative complications (28% vs 17%) [30]. In addition to the limitations associated with such retrospective comparative effectiveness studies, it should be noted that 77% of BT patients were treated with intracavitary BT using single-entry balloon applicators. In contrast, in our prospective randomized trial only one patient (0.8%) in the PBI arm, and three (2.3%) in the WBI arm underwent subsequent mastectomy. Therefore, the results and conclusions obtained from the retrospective study of Smith et al. [30] should not be used to disparage APBI using interstitial multi-catheter BT, if properly performed [4,11–14,19,20,23–25,28].

Vaidya et al. [26] recently reported the interim results of an international randomized trial comparing targeted intraoperative RT (TARGIT) with WBI. At a median follow-up of two years, the four-year estimate of LR was 1.2% in the TARGIT, and 0.95% in the WBI group. The authors concluded that a single dose of RT delivered at the time of surgery should be considered as an alternative to WBI. Another randomized trial (ELIOT Trial, Milan) was currently being conducted using single-fraction intraoperative RT [27]. However, further follow-up of the TARGIT and ELIOT trials is necessary to prove the long-term efficacy of single-fraction intraoperative RT.

Our single-institution randomized trial represents the first phase III study proving that long-term results of PBI are similar to WBI. At a median follow-up of 10.8 years, we failed to demonstrate any statistically significant difference in the ten-year actuarial rates of LR, DFS, OS, and CSS between the two treatment arms. However, with the LR rate of 5.9% (95% CI 1.6–10.2%) in the PBI arm and 5.1% (95% CI 1.1–9.1%) in the WBI arm, we cannot exclude that the PBI arm is inferior (or superior) for our sample of 258. Although our results should be confirmed by ongoing multicentric phase III trials with larger sample size, our findings reinforce the hypothesis that an accelerated RT regimen confined to a limited volume is safe, and more favorable cosmetic outcome can be achieved with carefully designed multi-catheter BT implants compared to the outcome after WBI. A detailed analysis of late side-effects will be published elsewhere. However we assume that the smaller irradiated volume and fibrosis confined to the tumor bed yielded less diffuse fibrosis and retraction in the APBI arm. In addition, skin side-effects using properly performed interstitial implants practically could be avoided. However, it should be emphasized that the lack of modern teletherapy techniques (e.g. 3D-CRT and IMRT), and the use of cobalt units also contributed to the worse cosmetic outcome in the WBI arm.

The main limitation of the present study is that due to the relatively small sample size the statistical power might be limited for the detection of small possible differences in local tumor control between the two treatment arms. In spite of this limitation, the ten-year results of our randomized study provide a strong basis for other ongoing phase III APBI trials. Patient accrual for the GEC-ESTRO multicentric phase III APBI trial was completed in 2009, and results are awaited to be published within two years. Recruitment for the ongoing North-American NSABP B-39/RTOG 0413 APBI Trial was started in 2005. While the GEC-ESTRO Trial compares WBI to APBI exclusively with multi-catheter interstitial BT, the North-American Trial compares WBI to three different APBI techniques including multi-catheter BT, single-catheter balloon BT, and 3D-CRT. Recently, two additional phase III APBI trials have been activated using 3D-CRT (the RAPID trial in Canada), and intensity modulated RT (the IMPORT LOW trial in the UK) in the PBI arm. Unfortunately, enrollment for the RAPID trial has been prematurely closed.

In conclusion, the ten-year results of our randomized study suggest that PBI using interstitial BT implants or electron beams to deliver radiation to the tumor bed alone for a selected group of early-stage breast cancer patients produce similar long-term results to those achieved with conventional WBI. Significantly better cosmetic outcome can be achieved with carefully designed HDR multi-catheter BT implants compared with the outcome after WBI. Long-term results of other ongoing phase III APBI trials are needed to define the role of different APBI techniques in the treatment of early-stage breast cancer. As data from these trials mature, they will hopefully support the integration of APBI into routine clinical practice.

Conflict of interest statement

The authors state no conflict of interest.

Acknowledgments

We acknowledge the contributions of colleagues who previously worked on the trial, treated patients, and contributed to follow-up and data collection, including K. Lövey, L. Mangel, G. Németh, Z. Orosz, A. Somogyi†, Z. Takácsi-Nagy, and N. Udvarhelyi.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.radonc.2013.05.008.

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