

# Partial breast irradiation versus whole breast irradiation after breast-conserving surgery in early-stage breast cancer: a systematic review

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## Abstract

**Introduction:** Adjuvant radiotherapy for early-stage breast cancer has progressively shifted toward less extensive treatment approaches. Partial breast irradiation (PBI) has emerged as a safe and effective option for appropriately selected patients.

**Aim:** To systematically compare PBI versus whole breast irradiation (WBI) in early-stage breast cancer with respect to acute and late toxicity, cosmetic outcomes, quality of life, local disease control, and survival.

**Methods:** We conducted a systematic review of randomized clinical trials evaluating PBI delivered by any technique versus WBI in early-stage breast cancer. Searches were performed in CENTRAL/CCTR, EMBASE, MEDLINE, CINAHL, ISRCTN, and ClinicalTrials.gov, following PRISMA 2020 guidelines. Risk of bias was assessed using the Cochrane RoB 2 tool. Trials with low risk of bias were further evaluated. The CONSORT 2010 statement was used to guide standardized reporting, without influencing study selection.

**Results:** Of 340 records identified, 55 were randomized trials. After applying eligibility criteria and excluding studies with high or unclear risk of bias, 15 low-risk trials were included. Overall, PBI demonstrated comparable oncologic outcomes to WBI, with reduced treatment-related burden and improved quality of life in selected patients. However, results varied by technique and fractionation schedule. Notably, the RAPID trial reported higher rates of acute and late skin toxicity and worse cosmetic outcomes with twice-daily 3D external beam PBI, highlighting the importance of technique optimization and appropriate patient selection.

**Conclusions:** PBI is a safe and effective alternative to WBI in carefully selected patients with early-stage breast cancer, offering meaningful reductions in toxicity and treatment burden without compromising disease control. Technique-specific considerations remain critical to maximizing both clinical and cosmetic outcomes.

**Keywords:** breast cancer, breast neoplasm, adjuvant radiotherapy, brachytherapy, radiation

### Implications for Practice

Partial breast irradiation (PBI) is a safe and effective alternative to whole breast irradiation (WBI) for carefully selected patients with early-stage, low-risk breast cancer. Randomized trials have demonstrated comparable local control and survival, with reduced acute toxicity, improved cosmetic outcomes, and better quality of life. In addition, PBI shortens treatment duration and decreases the number of hospital visits, which can be particularly advantageous for older patients, those with limited access to treatment centers, or individuals seeking to minimize treatment burden. Optimal patient selection and the use of well-established techniques, such as multicatheter brachytherapy or modern external beam radiotherapy, are essential to ensure oncologic safety and maximize cosmetic and functional outcomes.

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## Background

Management of early-stage breast cancer has progressively evolved toward less invasive surgical and radiotherapeutic strategies. Beginning with Halsted's radical mastectomy in the late 19th century, treatment shifted over the course of the 20th century to breast-conserving surgery supplemented by adjuvant radiotherapy, which was shown to reduce local recurrence while preserving breast tissue.<sup>1-3</sup> Whole breast irradiation (WBI) after lumpectomy subsequently became the standard adjuvant approach for early-stage disease.<sup>4,5</sup>

In the 1990s and 2000s, partial breast irradiation (PBI) was introduced to target the tumor bed (the site where most recurrences occur) while sparing uninvolved breast tissue. Accelerated PBI (APBI) further reduced treatment time to less than one week and has demonstrated comparable local control to WBI in appropriately selected patients, with lower treatment-related toxicity and improved cosmetic and quality-of-life outcomes in several randomized trials.<sup>6-8</sup>

Advances in EBRT (3D-CRT, IMRT, VMAT, stereotactic) improved dose conformity and reduced exposure to organs at risk.<sup>9-11</sup> Other established PBI approaches include intraoperative radiotherapy (IORT)<sup>12</sup> and brachytherapy techniques, particularly interstitial multicatheter brachytherapy and balloon-based devices, both of which deliver high-dose radiation directly to the surgical cavity with favorable tolerability and cosmetic outcomes.<sup>13-16</sup>

Guideline statements from ASTRO<sup>17,18</sup> and GEC-ESTRO<sup>13,19</sup> have refined patient selection criteria for PBI, incorporating clinical and biological risk factors to identify patients most likely to benefit. The most recent consensus recommendations broaden eligibility to many patients aged  $\geq 40$  with small, node-negative, hormone receptor-positive tumors and adequate surgical margins, and recognize multiple EBRT and brachytherapy techniques as appropriate options in such cases.<sup>19</sup>

Despite growing acceptance of PBI, randomized trials have shown heterogeneous results depending on technique, dose, fractionation, and planning quality. Therefore, determining which patients benefit most, and under what technical conditions, remains clinically relevant.

This systematic review synthesizes evidence from randomized clinical trials comparing PBI and WBI after breast-conserving surgery in early-stage breast cancer. Using a prespecified PICO framework, we address the primary question: Is PBI as effective and safe as WBI in women with early-stage breast cancer treated with breast-conserving surgery? Secondary aims are to compare acute and late toxicity, cosmetic outcomes, quality of life, local control, and survival across different radiotherapy techniques and fractionation schedules.

This comparison remains clinically relevant because, despite numerous randomized trials and meta-analyses, results have been heterogeneous across techniques, doses, and schedules. This review integrates the existing randomized evidence on PBI using all available techniques.

## Methods

This systematic review was conducted in accordance with the PRISMA 2020 guidelines<sup>20</sup> and registered in the Open Science

Framework (OSF; DOI: 10.17605/OSF.IO/BJP6X), ensuring transparency and accessibility. An initial unrestricted exploratory search was performed to ensure completeness. The final search was limited to studies published between 2000 and 2025, as the most methodologically robust randomized controlled trials (RCTs) on partial breast irradiation (PBI) were conducted during this period. Randomized controlled trials comparing PBI versus whole breast irradiation (WBI) for early-stage breast cancer were subsequently identified and evaluated according to predefined eligibility criteria.

## Eligibility criteria

Randomized controlled trials (RCTs) comparing PBI versus WBI for early-stage breast cancer were eligible for inclusion. Eligible studies enrolled women aged  $\geq 18$  years with histologically confirmed invasive breast carcinoma treated with breast-conserving surgery and negative margins. Eligible tumors were unifocal pT1-2 pN0-1mic M0; patients had ECOG 0-2, no neoadjuvant therapy, and diagnosis confirmed by imaging.

Eligible PBI techniques included external beam radiotherapy (3D-CRT, IMRT, VMAT, SBRT), interstitial multicatheter or balloon-based brachytherapy (e.g., MammoSite), and intraoperative radiotherapy (IORT with electrons or low-energy X-rays). WBI was delivered via EBRT using 3D-CRT or IMRT. Trials that did not specify radiotherapy technique, fractionation schedule, or follow-up duration were excluded.

## Data sources and search strategy

A systematic search<sup>21</sup> of MEDLINE (PubMed), EMBASE (Ovid), CINAHL (EBSCOhost), ISRCTN, CENTRAL/CCTR, and ClinicalTrials.gov was conducted from January 1, 2000, to May 29, 2025. This time frame was selected because the large randomized trials with greater statistical power comparing WBI and PBI began after 2000, whereas between 1987 and 2000 the literature consisted mainly of preliminary experimental and small clinical studies exploring interstitial partial-breast brachytherapy as an alternative to whole-breast irradiation, based on the observation that most local recurrences occurred near the original tumor site. Search strategies used MeSH descriptors and Boolean operators combining "Breast Neoplasms," "Radiotherapy," "Brachytherapy," and "Randomized Controlled Trials."

Search strings and filters were peer-reviewed according to the PRESS guideline,<sup>22</sup> and the complete strategies and record counts are detailed in Supplementary Methods (see online supplementary material). Reference lists of relevant reviews and included studies were screened to ensure completeness.

## Study selection and data extraction

Two reviewers independently screened titles/abstracts and full texts using Rayyan QCRI,<sup>23</sup> applying predefined inclusion and exclusion criteria. Discrepancies were resolved by consensus. Data extraction was performed using a standardized form capturing PICO elements, patient and tumor characteristics, treatment details, outcomes, and risk-of-bias assessments. Extracted data were cross-checked for accuracy by both reviewers.

## Risk of bias and reporting quality assessment

Methodological quality was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.<sup>24</sup> Reporting quality was guided by the CONSORT 2010 statement (Table 1) to ensure adequate reporting standards.<sup>25</sup> Only trials with low or moderate risk of bias (some concerns) were included in the final synthesis, ensuring methodological reliability. Risk of bias assessments are presented in Supplementary Table S1 (see online supplementary material).

## Outcome measures

Primary outcomes were selected for clinical relevance and patient-centeredness: (I) acute and late toxicity, (II) cosmetic outcome, (III) body image, and (IV) quality of life. These outcomes directly reflect treatment burden and functional/cosmetic sequelae in early breast cancer survivors, highlighting the importance of patients' long-term well-being through validated cosmetic assessments and quality-of-life instruments. Secondary outcomes were (I) local control, (II) overall survival, and (III) disease-free survival, capturing oncologic efficacy and allowing correlation between patient-centered outcomes and tumor control, confirming that improved tolerance and quality of life do not compromise oncologic results.

### Primary

- 1) **Toxicity:** acute and late effects. Studies used RTOG (Radiation Therapy Oncology Group)<sup>19</sup> and CTCAE v4.0 (Common Terminology Criteria for Adverse Events).<sup>26</sup> Late effects were evaluated clinically through signs such as skin thickening, scar tissue, asymmetry, hyperpigmentation, and edema. Radiologists assessed fibrosis, architectural distortion, tissue retraction, and liponecrosis on follow-up mammograms.
- 2) **Cosmetic outcomes:** assessed with the Harvard scale and EORTC Cosmetic Rating System<sup>27</sup> by both patients and clinicians.
- 3) **Body image:** evaluated using the EORTC QLQ-BR23 (BRBI domain).<sup>19,26</sup>
- 4) **Quality of life (QoL):** defined as the period during which patients maintained or improved ECOG/Performance Status, measured by the ECOG scale validated by the WHO. Patient-reported outcomes were also assessed through the EORTC QLQ-C30 and QLQ-BR23<sup>19,26</sup> and the FACIT-Fatigue scale,<sup>28</sup> administered before, during, and after treatment.

### Secondary

- 1) **Local control (LC):** rate of locoregional or distant recurrence.
- 2) **Overall survival (OS):** time from surgery or randomization to death.
- 3) **Disease-free survival (DFS):** time from surgery or randomization to first locoregional/distant recurrence or second tumor.

## Synthesis methods and heterogeneity management

A meta-analysis was pre-specified; however, substantial clinical heterogeneity across PBI modalities, fractionation schedules,

target delineation, and outcome timing precluded meaningful quantitative pooling. Consistent with SWiM guidance,<sup>29</sup> a structured narrative synthesis was performed, stratified by PBI technique and outcome domain. Effect direction and consistency were summarized across trials, considering the assessed risk of bias.

## Outcome harmonization

Toxicity was abstracted as graded by RTOG or CTCAE and harmonized into acute ( $\leq 90$  days from treatment) and late ( $> 90$  days) periods. Cosmetic outcomes were harmonized by dichotomising Harvard/EORTC scales into good-excellent vs fair-poor when required. Quality of life was extracted from EORTC QLQ-C30/BR23 and FACIT-Fatigue; we prioritized prespecified global and breast-specific domains and change-from-baseline when available. Local control and survival endpoints were recorded per trial definitions and analysed on an intention-to-treat basis. When metrics were incomparable, we reported effect direction and narrative comparison rather than pooled estimates.

## Data availability

Full search strategies, de-duplicated record counts, data extraction forms, and RoB 2 assessments are available in Supplementary Methods, Table S1 (see online supplementary material) and within the Open Science Framework (OSF) repository (DOI: 10.17605/OSF.IO/BJP6X), ensuring transparency and reproducibility.

## Results

The search identified 340 articles, 55 of which were RCTs. After removing duplicates and applying the Cochrane risk of bias assessment tool, a preliminary sample of 30 RCTs was obtained. Inclusion criteria were applied, and high-risk studies per RoB 2 were excluded. Reporting completeness was guided by the CONSORT 2010 statement (Table 1), which served only as a framework for standardized reporting and not as a quality assessment tool. Finally, 15 RCTs were included in this systematic review, together with their respective updated versions (Figure 1).<sup>6-12,14,30-37</sup>

## PBI compared to WBI; results from each RCT

Fifteen RCTs<sup>6-12,14,30-37</sup> (Table 2), published in 22 articles including updates, with a total of 15 592 patients [Interquartile range (IQ): 54-4216] evaluated PBI versus WBI]. PBI modalities included 3D radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), intraoperative radiotherapy (IORT), and multicatheter or balloon interstitial brachytherapy (BT; MammoSite). The mean age was 62.4 years (IQ range: 44-78 years) and the average tumor size was 1.1 cm; 95% of patients had tumor grades 1-2; 10% had invasive lobular carcinoma; 90% had no lymph node involvement (pN0); and 96% were estrogen receptor (ER) positive. The median follow-up ranged from 2.3 to 16 years.

Dodwell et al. compared WBI with PBI using RTE; toxicity, QoL, and cosmetic outcomes were not detailed, and PBI showed

**Table 1** CONSORT 2010 Statement: guidelines for reporting parallel group randomized trials.<sup>25</sup>

Section/Topic	Item no	Checklist item
<b>Title and Abstract</b>	1a	Identification as a randomized trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions
<b>Introduction</b>	2a	Scientific background and explanation of rationale
<b>Background and objectives</b>	2b	Specific objectives or hypotheses
<b>Methods</b>	3a	Description of trial design (such as parallel, factorial) including allocation ratio
<b>Trial design</b>	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
<b>Participants</b>	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
<b>Interventions</b>	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
<b>Outcomes</b>	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
<b>Sample size</b>	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
<b>Randomization:</b>		
<b>Sequence generation</b>	8a	Method used to generate the random allocation sequence
	8b	Type of randomization; details of any restriction (such as blocking and block size)
<b>Allocation concealment mechanism</b>	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
<b>Implementation</b>	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
<b>Blinding</b>	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
<b>Statistical methods</b>	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
<b>Results</b>	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomization, together with reasons
<b>Recruitment</b>	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
<b>Baseline data</b>	15	A table showing baseline demographic and clinical characteristics for each group
<b>Numbers analysed</b>	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
<b>Outcomes and estimation</b>	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
<b>Ancillary analyses</b>	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
<b>Harms</b>	19	All important harms or unintended effects in each group
<b>Discussion</b>	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
<b>Limitations</b>		
<b>Generalisability</b>	21	Generalisability (external validity, applicability) of the trial findings
<b>Interpretation</b>	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
<b>Further information</b>	23	Registration number and name of trial registry
<b>Registration</b>		
<b>Protocol</b>	24	Where the full trial protocol can be accessed, if available
<b>Funding</b>	25	Sources of funding and other support (such as supply of drugs), role of funders

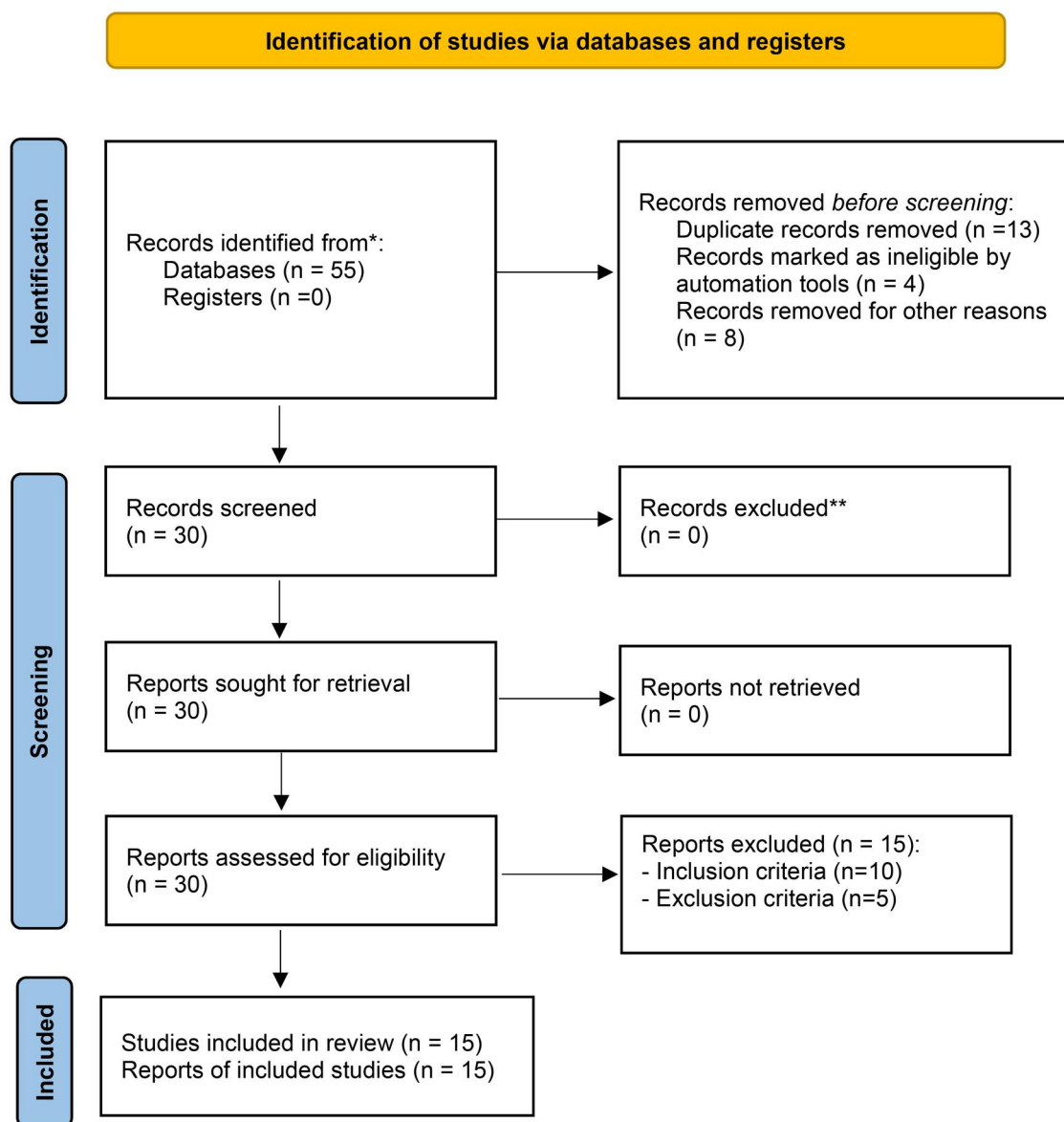


Figure 1 PRISMA 2020 flow chart for systematic reviews.<sup>20</sup>

higher local recurrence, although OS and distant recurrence were not significantly different.<sup>6</sup>

The BUDAPEST trial by Polgar et al. compared APBI with BT versus WBI; over 20 years, APBI showed significantly lower late toxicity, better cosmetic outcomes, and similar OS, DFS, and LC, confirming non-inferiority.<sup>35,38,39</sup>

Rodríguez et al. compared PBI with 3D-CRT versus WBI; PBI had lower acute toxicity and reduced skin elasticity loss, with good cosmetic results in >75% of patients, and no recurrences at 5 years; OS and DFS were comparable.<sup>8</sup>

In the ELIOT trial, Veronesi et al. compared APBI with RIOE versus WBI; PBI showed lower skin toxicity and better cosmesis, but higher local recurrence, while OS and DFS were similar.<sup>33</sup>

The RAPID trial by Olivotto et al. compared PBI with 3D-CRT BID versus WBI; PBI caused higher acute and late toxicity, worse cosmetic outcomes, and a nonsignificant trend toward higher recurrence, but OS and DFS were similar.<sup>9</sup>

The TARGIT-A trial by Vaidya et al. compared APBI with RIO versus WBI; PBI showed lower acute/late toxicity and fewer non-breast cancer events, but higher local recurrence (3.3% vs 1.3%). The 2020 update (median 8.6 years) confirmed non-inferiority, although recurrence remained higher and noncancer mortality lower, without significance.<sup>34,40</sup>

In the GEC-ESTRO study, Strnad et al. compared APBI with multicatheter BT versus WBI; APBI showed significantly lower acute and late toxicity, better QoL (EORTC QLQ-C30/BR23), and superior cosmetic outcomes, with confirmed non-inferiority in LC, OS, and DFS.<sup>41</sup>

Polgár et al. reported a late-toxicity analysis showing lower grade  $\geq 2$  skin toxicity with APBI (6.9% vs 10.7%,  $P = .020$ ), with no significant differences in fibrosis or fat necrosis; cosmetic outcomes at 5 years were comparable.<sup>38</sup>

Säfer et al. assessed QoL in the same trial, finding better functional/emotional profiles, less body image distortion and

Table 2. Characteristics of the clinical trials included and updates.

Trial median follow-up (months)	Treatment arms	Sample size (n) N = 16 925	Mean age (years)	Tumor size	Lymph node stage	Hormone receptor positivity	Histology and grade
Strnad et al. 2016 GEC-ESTRO 60 months	APBI: 32 Gy (8 FX 4 Gy) o 30.1 Gy (7 fx × 4.3 Gy) WBI: mean 50 Gy (2-50 Gy) (2 Gy/fx)	1184	62	Tis: 5.1% Tmic: 0.3% T1a: 4.3% T1b: 31.2% T1c: 48.6% T2 (<3 cm): 10.6%	N0: 96% N1mi: 0.5%	ER +: 91%	Grade 3: 7% IDC: 74%
Livi et al. 2015 60 months	APBI: 30 Gy (5 fx × 6 Gy, nonconsecutive) WBI: 50 Gy (2 Gy/fx) + 10 Gy boost in 5 fx	520	60-69	Tis: 10.6% T1a: 8.8% T1b: 35.8% T1c: 39.2% T2 (<2.5 cm): 5.6%	N0: 85.6% N1: 10% Unknown: 4.4%	ER +: 95.6% HER2 +: 4%	
Vaidya et al. 2014 TARGIT 29 months	APBI IORT low-energy photons: 20 Gy WBI: 40-56 Gy in 15-25 fx +/- 10-16 Gy boost in 5-8 fx	3451	61-70	T1ab: 39.2% T1c: 47.9% T2: 12.9%	N0: 83.9% N1: 13.8% N2: 2.3%	ER +: 93% HER2 +: 11.6%	Grade 3: 15.2% IDC: 100%
Olivotto et al. 2013 RAPID 103 months	PBI: 38.5 Gy (3.75 Gy/fx) WBI: 42.5-50 Gy in 16-25 fx +/- boost 10 Gy in 4-5 fx	2135	61	T < 1.5 cm: 61.3% T > 1.5 cm: 38.7%	N0: 100%	ER +: 84%	Grade 3: 17.2% IDC: 82%
Veronesi et al. 2013 ELIOT 69.9 months	APBI IORT electrons: 21 Gy WBI: 50 Gy (2 Gy/fx) + 10 Gy boost in 5 fx	1305	60-69	T1ab: 30.4% T1c: 55.2%	N0: 73.4% N1: 21.3% N2: 5.3%	ER +: 90.8% HER2 +: 3.4%	Grade 3: 21.7% IDC: 80.2%
Rodriguez et al. 2013 60 months	PBI: 37.5 Gy (3.75 Gy/fx) WBI: 48 Gy in 24 fx +/- boost 10 Gy	102	68.6	T1a: 3.9% T1b: 45.2% T1c: 44.1%	N0: 100%	ER +: 98% HER2+: 1%	Grade 3: 0% Lobular excluded
Polgar et al. 2013 122.4 months	APBI: 36.4 Gy (7 fx × 5.2 Gy). BT WBI: mean 50 Gy (2-50 Gy) (2 Gy/fx)	258	58	T2 (<3 cm): 6.8% T1a: 4.3% T1b: 28.7% T1c: 67%	N0: 95% N1mi: 3.5% Unknown: 1.5%	ER +: 88.7%	Grade 3: 0% IDC: 81.8%
Dodwell et al. 2005 96 months	PBI: 55 Gy in 20 fx (2.75 Gy/fx) WBI: 40 Gy (at 2.67 Gy/fx) + boost max 15 Gy	174	52	2 cm	N0: 97%	ER +: 95%	Grade 3: 24% IDC: 85%
Burkon et al. 2023 24 months	APBI: 30 Gy (6 Gy/fx) (total 10 days), SBRT WBI: 40.05 in 15 fx (2.67 Gy/fx) + 10 Gy boost	57	65	T1: 100% Tis: 5.3% T1a: 7% T1b: 53% T1c: 35%	N0: 100%		Grade 3: 0% IDC: 70%
Li et al. 2021 123.6 months	PBI: 37.5 Gy at 3.75 Gy/fx 3D-RT WBI: 50 Gy in 25 fx	102	68	pT1a: 13.7% pT1b: 39.2% pT1c: 42.2% pT2: 4.9%	N0: 100%	ER +: 100% HER2 +: 14%	Grade 3: 0% Grade 3: 0% IDC: 70%

(continued)

Table 2 (continued)

Trial median follow-up (months)	Treatment arms	Sample size (n) N = 16 925	Mean age (years)	Tumor size	Lymph node stage	Hormone receptor positivity	Histology and grade
Meattini et al. 2020 FLORENCE TRIAL 128 months	APBI: 30 Gy in 5 fx IMRT WBI: 50 Gy in 25 fx with boost 10 Gy	520	60	Tis: 10 % T1: 84 % T2: 15 %	N0: 80 % N1: 10 %	ER +: 95 %	Grade 3: 10 %
Forster et al. 2020 COSMOPOLITAN 60 months	APBI IORT electrons: 21 Gy WBI: 40.05 Gy in 15 fx	202	55	T1: 100%	N0: 100%	ER +: 100%	Grade 3: 0% IDC: 100%
Franceschini et al. 2020 HYPAB 36 months	APBI: 30 Gy in 5 fx VMAT (total 10 days) WBI: 50 or 40.05 Gy in 15 fx	172	64	T1a: 3%. T1b: 37%. T1c: 59%. T2: 1%	N0: 100%	ER +: 90%	Grade 3: 3% IDC: 74%
Vicini et al. 2019 NSABP B-39/RTOG 0413 122 months	PBI: 34 Gy (3.4 Gy/fx) balloon BT or RTE IMRT or 3D (where 3D dose, 38.5 Gy in 3.85 Gy/fx) WBI: 50 or 50.4 Gy in 25-28 fx +/- boost	4216	54	Tis: 24%	N0: 65% N1: 10%	RH+: 81%	Grade 3: unknown
Schäfer et al. 2018 GEC-ESTRO (update) 79 months	APBI: 32 Gy (8 Gy/fx) WBI: 50 Gy in 25 fx + boost 10 Gy	1206	62	T1: 87 % T2: 14 %	N0: 97 % N1mi: 0.5 %	ER +: 91 % HER2 +: 5.6 %	Grade 3: 10 % IDC: 74%
Coles et al. 2017 IMPORT 71.1 months	PBI: 40 Gy in 15 fx IMRT (only partial breast) WBI: 40 Gy in 15 fx IMRT	1343	62	Median 1-2 cm (0.8-1.6)	N0: 97 % N1: 3 %	ER +: 95.1 % HER2 +: 4%	Grade 3: 9.5 % IDC: 85.4%

Abbreviations: ER+, estrogen receptor positive; Fx, fractions; Gy, Grays; HER2+, overexpression of human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma. Tumor size: Tis (*in situ*), T1a (>0.1 cm and ≤0.5 cm), T1b (>0.5 cm and ≤1 cm), T1c (>1 cm and ≤2 cm), T2 (>2 cm and ≤5 cm); Nodal involvement: N0 (no lymph node involvement), N1mi (micrometastases in lymph nodes).

fatigue, and fewer breast/arm symptoms in the APBI group, while overall QoL remained stable; treatment-related changes were fewer immediately and at 3 months post-treatment.<sup>30</sup> The 2023 update confirmed equivalence in cancer control and toxicity after >10 years, supporting APBI with BT as a safe, effective, and well-tolerated alternative for selected patients.<sup>42</sup>

In the FLORENCE trial, Livi et al. compared APBI with RTE-IMRT versus WBI; APBI showed significantly better QoL (EORTC QLQ-C30/BR23), including body image, breast/arm symptoms, and prognosis, with sustained benefits over time.<sup>12</sup>

Meattini et al. reported the 10-year update, confirming equivalent LC (1.2% both arms,  $P=.99$ ), but significantly better toxicity and cosmetic outcomes for APBI in both physician (0% vs 1.9%,  $P<.0001$ ) and patient (0.8% vs 14.6%,  $P<.0001$ ) assessments, supporting superior tolerance without compromising LC, OS, or DFS.<sup>32</sup>

The IMPORT LOW trial by Coles et al. evaluated three arms (WBI, WBI + boost, and PBI with IMRT); PBI showed lower toxicity, fewer skin side effects, better cosmesis, and improved QoL, particularly regarding breast appearance, with similar OS, DFS, and LC across groups and very low recurrence at 5 years.<sup>7</sup>

The NSABP B-39/RTOG 0413 trial (Vicini et al.) compared PBI with 3D-CRT or balloon brachytherapy versus WBI; APBI showed fewer skin effects and better cosmetic outcomes, with comparable OS and DFS, and a nonsignificant trend toward higher local recurrence.<sup>14</sup>

In the HYPAB trial, Franceschini et al. compared APBI with VMAT versus WBI; APBI showed lower acute and late toxicity, suggesting improved QoL, with low and similar recurrence rates, but the trial closed early due to poor recruitment, limiting OS/DFS analysis.<sup>10</sup>

In the COSMOPOLITAN trial, Forster et al. compared APBI with electron RIO versus WBI; APBI showed lower acute toxicity and improved fatigue scores (FACIT-Fatigue), with favourable QoL, while OS, DFS, and LC are still under evaluation as the trial remains ongoing.<sup>31</sup>

Li et al. compared PBI with 3D-CRT-type RTE versus WBI; efficacy outcomes (OS, DFS, LC) were equivalent, toxicity was slightly higher with PBI (grades 1-2 fibrosis), but cosmetic outcomes were similarly rated as good/excellent in both groups (38).

Burkon et al. evaluated APBI with SBRT versus WBI; APBI showed significantly lower acute and late toxicity, fewer skin side effects, better cosmetic outcomes (assessed by physicians, nurses, and patients), and improved QoL due to lower toxicity, with equivalent OS, DFS, and LC.<sup>11</sup> A 2025 QoL analysis of the same trial, using EORTC QLQ-C30 and QLQ-BR45 up to 24 months, found that APBI yielded better outcomes in breast symptoms, systemic side effects, and pain at treatment end, higher global health status (GHS) at 6 months, and more stable physical function, while WBI patients showed gradual recovery of breast symptoms but greater functional decline; overall, APBI demonstrated non-inferior QoL with milder acute effects and better symptom control.<sup>43</sup>

## Analysis of the effectiveness of PBI according to the type of technique applied

Given modality-specific physics, dosimetry, and radiobiology, results are presented by PBI technique (IORT, brachytherapy,

EBRT) before their overall cross-technique interpretation in the Discussion section. Due to methodological heterogeneity, a detailed cross-technique comparison was not feasible. Therefore, results were grouped into three main categories (IORT, BT, and EBRT) to facilitate comparison with WBI according to the predefined objectives of this review.

### PBI using IORT compared to WBI

IORT was associated with a statistically significantly higher risk of local recurrence than WBI, but with lower acute and late toxicity. However, differences in OS and DFS were not statistically significant.<sup>31,33</sup>

### PBI using BT compared to WBI

The available evidence suggests that APBI using multicatheter interstitial brachytherapy is effective in selected patients. Patients meeting the following criteria: female gender, age < 50 years, tumors smaller than 3 cm, negative surgical margins, and no lymph node involvement. Advantages include lower skin toxicity, better cosmetic outcomes, and reduced treatment duration.<sup>41,42</sup>

However, some studies suggest a slight increase in local recurrence rates among certain subgroups, which highlights the importance of careful patient selection. The availability of technology and the experience of the treatment team also influence the application of this technique.<sup>41</sup>

### PBI using RTE (3D-CRT, IMRT, VMAT, and SBRT) compared to WBI

Current evidence shows that PBI with modern external radiotherapy techniques achieves oncological outcomes comparable to WBI in selected patients, with advantages in toxicity, cosmesis, and treatment convenience, particularly with IMRT, VMAT, and SBRT. Technique choice must consider long-term toxicity, dose distribution, and evidence strength, since 3D-CRT is associated with the most late adverse effects. In early-stage breast cancer, PBI with RTE yields similar LC and OS to WBI, although toxicity, cosmesis, and QoL vary by technique. The RAPID trial (3D-CRT, BID schedule) reported higher acute  $\geq$ G2 skin toxicity, subcutaneous fibrosis, and worse long-term cosmesis versus WBI, mainly due to accelerated fractionation (38.5 Gy/10 BID fractions) and limited use of advanced imaging, although LC and DFS were non-inferior; younger patients, those with small breasts, or upper/inner quadrant tumors showed higher late toxicity and poorer outcomes.<sup>9</sup>

IMRT-based PBI improves dose conformity and reduces irradiation of healthy tissue, leading to lower acute toxicity, better cosmesis, and improved short-term QoL, with preliminary data showing equivalent LC and survival.<sup>7,32</sup>

VMAT-based PBI provides homogeneous dose distribution and shorter treatment times, with similar LC and acute toxicity to WBI, favourable QoL, and reduced heart/lung irradiation, although concerns remain about slightly increased integral volume exposure.<sup>10</sup>

SBRT-based PBI, delivered in 2-5 fractions, shows high precision, minimal acute toxicity, and excellent short-term cosmesis, but long-term data on late toxicity, LC, and survival are limited; early-phase studies are encouraging, although large randomized trials versus WBI are lacking.<sup>11,43</sup>

## Discussion

In this systematic review of 15 randomized trials and updates comparing accelerated partial breast irradiation (PBI/APBI) with whole breast irradiation (WBI) after breast-conserving surgery in early-stage breast cancer, PBI generally reduced acute toxicity and improved cosmetic outcomes and quality of life (QoL) without compromising oncologic efficacy. Local recurrence (LR) rates were similar to WBI in most studies, except for intraoperative radiotherapy (IORT), which showed higher LR despite comparable overall survival (OS) and disease-free survival (DFS). Late toxicity was similar or lower with modern PBI techniques, whereas twice-daily 3D-CRT regimens, such as RAPID, showed higher skin reactions and poorer cosmesis. These findings support PBI as a safe and effective option for carefully selected patients, while emphasizing that technique, planning quality, and fractionation schedule are major determinants of outcomes. Differences in trial design and endpoints limit comparability and require cautious interpretation.

### Interpretation in the context of contemporary WBI

The landscape of breast radiotherapy has evolved markedly with the widespread adoption of moderately hypofractionated WBI ( $\approx 40\text{--}42.5$  Gy in 15–16 fractions). This modern standard achieves excellent tolerance and reduced treatment burden compared with historical 5–6-week regimens. Thus, the advantage of PBI over modern hypofractionated WBI is smaller and future trials should compare them directly.

### Heterogeneity and methodological considerations

Results across studies were influenced by substantial heterogeneity in technique, dose schedule, eligibility criteria, and follow-up duration ( $\approx 2\text{--}16$  years). Differences in target definition and planning margins may explain trial discrepancies. Differences in outcomes, particularly in toxicity and cosmesis, closely paralleled the technical evolution of PBI delivery. Once-daily IMRT/VMAT and brachytherapy achieved favorable results, whereas BID 3D-CRT caused higher toxicity. This heterogeneity limits the generalizability of findings and underscores the need for harmonized eligibility criteria, dose prescription, and outcome definitions in future studies.

### Toxicity, cosmesis, and quality of life

Trials such as FLORENCE and GEC-ESTRO reported superior acute and late toxicity outcomes, improved physician- and patient-reported cosmesis, and higher body image scores with PBI. These improvements likely result from reduced irradiated volume and better conformity. Conversely, RAPID remains an outlier due to large margins, BID fractionation, and limited image guidance. Importantly, shorter treatment duration and fewer adverse effects translated into higher QoL, especially for elderly or comorbid patients. Nonetheless, modern hypofractionated WBI also provides excellent QoL and cosmetic outcomes,

reinforcing that the advantage of PBI is incremental rather than absolute.

### Oncologic outcomes

Fractionated external beam and multicatheter brachytherapy trials demonstrated non-inferior local control, DFS, and OS, with LR rates  $\leq 1\text{--}3\%$  in low-risk populations. Higher LR with IORT likely reflects radiobiological limitations of single-fraction delivery and potential margin undercoverage rather than an inherent weakness of PBI. Hence, fractionated, image-guided PBI remains oncologically safe when applied to well-defined low-risk cohorts.

This reinforces the principle that the efficacy of PBI depends more on technical precision, planning quality, and appropriate patient selection than on the concept itself.

### Clinical interpretation and applicability

The role of PBI must be understood within individualized care and the modern context of hypofractionation. Today, WBI can be completed in 1–3 weeks with excellent tolerance, reducing the magnitude of PBI's advantage. Nevertheless, PBI remains an attractive, patient-centered alternative for selected low-risk women prioritizing shorter treatment, reduced exposure of healthy tissue, and cosmetic preservation. Its greatest applicability lies in "suitable" profiles (age  $\geq 50$ , pT1, node-negative or pN0–1mic, ER-positive, clear margins  $\geq 1$  mm). Caution is warranted in younger patients, upper-inner quadrant tumors, or adverse histology, where evidence remains limited.

### Implications for practice and future research

PBI should preferentially be delivered using techniques supported by long-term randomized evidence, multicatheter brachytherapy and image-guided IMRT-based external beam radiotherapy with once-daily hypofractionation, ensuring rigorous planning and quality assurance. IORT may be considered only after informed discussion of its higher LR risk.

Future studies should directly compare modern PBI with contemporary hypofractionated WBI, incorporate standardized patient-reported outcomes, and provide mature long-term data for VMAT- and SBRT-based PBI. Further research should also quantify cost-effectiveness and real-world implementation feasibility, as streamlined PBI pathways could meaningfully reduce healthcare burden while maintaining oncologic safety and patient satisfaction.

### Limitations

A major limitation is heterogeneity of outcomes and radiotherapy details, limiting comparability. Few trials included patients with moderate- to high-risk disease, underscoring the need for additional evidence in this subgroup as well as for defining optimal PBI doses and delivery techniques. The lack of blinding in randomization may have influenced subjective endpoints such as cosmesis and toxicity. Technological advances in radiotherapy over the past two and a half decades also complicate cross-trial comparisons. Grey literature was not included, and no

attempts were made to contact study authors for missing data or clarifications.

Limitations further include a potential risk of performance and detection bias for subjective endpoints (toxicity, cosmesis, QoL) due to limited blinding, selective reporting of patient-reported outcomes, incomplete or nonuniform dosimetric reporting, and possible publication bias that could not be formally assessed given the heterogeneity and small sample strata. Furthermore, internal methodological inconsistencies should be acknowledged, such as the initially incorrect search period, which was subsequently corrected to accurately reflect the time frame of the included trials (2000-2025). Although this issue was amended, it highlights the need for greater methodological rigor, protocol adherence, and critical verification during the initial stages of the review process.

Acknowledging these methodological and procedural limitations enhances the transparency and credibility of this systematic review, consistent with current standards for research reporting.

## Conclusion

Randomized clinical trials demonstrate that PBI is safe, with similar or lower acute and late toxicity than WBI, and improved cosmesis and quality of life, except for the 3D-CRT BID (RAPID) regimen. Techniques such as multicatheter brachytherapy, MammoSite, and hypofractionated external-beam radiotherapy (3D-CRT, IMRT, VMAT, SBRT) achieve recurrence rates comparable to WBI, while IORT requires careful patient selection. Overall, PBI represents a standard-of-care alternative for early-stage, low-risk breast cancer, offering reduced toxicity, better cosmetic outcomes, enhanced patient-reported quality of life, and fewer hospital visits, without compromising tumor control or survival.

Conclusions are supported by consistent evidence across multiple RCTs, while recognising important exceptions (e.g., higher toxicity and poorer cosmesis with twice-daily 3D-CRT PBI, and higher local recurrence with single dose IORT). Clinical decisions should prioritise validated techniques and appropriate patient profiles.

## Author contributions

Sara Garduño-Sánchez (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing), María Isabel Villanego-Beltrán (Conceptualization, Data curation, Investigation, Validation), Francisco Javier Carrasco-Sánchez (Conceptualization, Data curation, Software, Validation, Visualization), Juan Gómez-Salgado (Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Supervision, Validation, Visualization, Writing—review & editing), and Javier Jaén-Olasolo (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing)

## Supplementary material

Supplementary material is available at *The Oncologist* online.

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## Conflicts of interest

The authors declare no conflicts of interest.

## Data availability

All data are available within this article.

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