

Healthcare Professional Guide

Brachytherapy:

The precise answer for tackling breast cancer



Because life is for living

Radiotherapy: a cornerstone of early breast cancer care

Breast cancer is the most commonly diagnosed malignancy in women worldwide and the global incidence is rising.¹ Rates are especially high in developed countries (approximately 80–90 per 100,000).¹ Although the incidence of breast cancer has increased over recent decades, mortality has declined in developed countries. The high survival rates are largely due to early diagnosis through effective screening programs.¹ However, significantly, improvements in treatment mean **many women can now achieve excellent cancer control and preservation of their breast.**

In recent years, breast cancer treatment goals have moved from **life preservation** to **cure with breast conservation.**

Radiotherapy plays an important role in early breast cancer management and has achieved remarkable progress during the last two decades. Current clinical efficacy and safety are, to a large extent, attributable to scientific and technical advances in imaging modalities, computerized planning, dose delivery and innovative applicators. Radiotherapy therefore remains a cornerstone of early breast cancer treatment, alongside surgery, chemotherapy and hormone therapy.

Brachytherapy: treating breast cancer ‘from the inside, out’

Radiotherapy can be divided into radiation ‘from the outside, in’, i.e. **external beam radiotherapy** (EBRT), and ‘from the inside, out’, frequently referred to as **brachytherapy**. Unlike EBRT, brachytherapy involves placing a radiation source internally, into the breast. This precise, targeted approach allows radiation to be delivered direct to the target area, while sparing surrounding tissues and structures.^{2,3}

This guide provides an overview of the benefits of brachytherapy that make it an important treatment option for many women with early breast cancer as part of their treatment plan.

Benefits of brachytherapy in early breast cancer; delivering radiation from the ‘inside, out’:

- **Demonstrated efficacy:** Cancer control and long-term survival rates similar to EBRT.⁴⁻⁶
- **Precision:** Radiation dose delivered precisely to the tumor site.^{7,8}
- **Minimized risk of side effects:** Surrounding healthy tissue is spared from unnecessary radiation reducing toxicity/damage to healthy breast tissue and nearby structures such as the chest wall, heart, lungs or skin.⁶⁻⁹
- **Excellent cosmesis:** Limited fibrosis and skin toxicity, providing excellent cosmetic results.^{6,9}
- **Convenience:** Short treatment times of up to 5 days allow patients to get back to their everyday life sooner.¹⁰
- **Cost-effective:** Favorable investment, maintenance and cost-effectiveness profile.¹¹



Treating early breast cancer

Treatment options

Treatment of early breast cancer requires a multi-modal approach with combinations determined by tumor stage as well as patient factors such as age, general health status and treatment acceptance. The main treatment options include **surgery, radiotherapy, chemotherapy and hormonal therapy.**

Surgical options

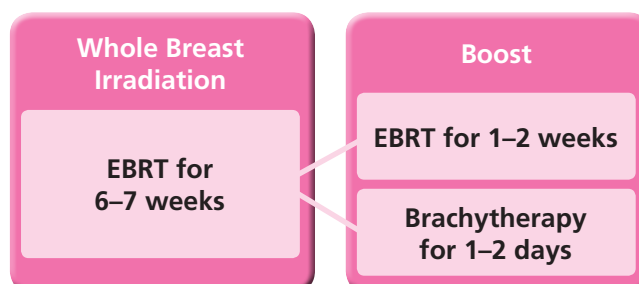
Following the diagnosis of early breast cancer, mastectomy was historically considered the standard treatment. However, the removal of the whole breast can have significant negative physical, psychological and economic effects on women.¹² More recently, breast conserving therapy (BCT) involving lumpectomy followed by radiotherapy (often in combination with chemotherapy or hormone therapy) has become standard of care. BCT provides comparable efficacy to mastectomy, but with vastly improved cosmetic results.

Radiotherapy options

A wealth of evidence confirms the efficacy of radiotherapy in reducing recurrence rates, especially in the area of the tumor bed where the majority of local recurrences occur.^{5,13}

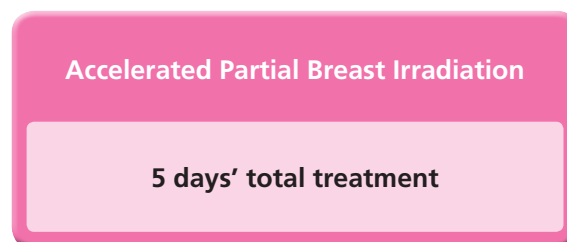
After lumpectomy, two different radiotherapy options are available:

1. Whole Breast Irradiation (WBI):



EBRT is administered to the whole breast followed by a 'boost' dose of radiation given either by EBRT or brachytherapy. Adding an additional 'boost' dose of radiation to the tumor bed has been proven to increase efficacy and reduce local recurrence rates in the long term.¹⁴

2. Accelerated Partial Breast Irradiation (APBI)

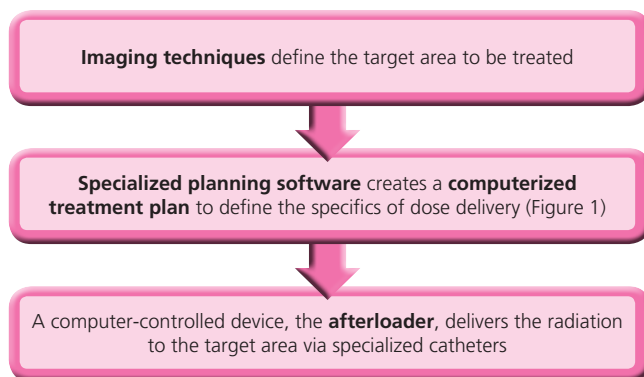


Based on the rationale that the majority of recurrences occur in the tumor bed and the whole breast may not require irradiation to achieve the same efficacy, **APBI delivers high dose rate radiation to the specific target tissue in a short timeframe.** Delivering comparable efficacy to WBI but with a **reduced treatment period of 5 days**, APBI means that women who are suitable for this treatment option can opt for BCT and complete the radiotherapy regimen in a short convenient time frame.^{15,16} **APBI allows women to get back to their everyday lives quickly.**

Brachytherapy for early breast cancer

Brachytherapy delivery

Brachytherapy, via modern and specialized imaging, computer-based treatment planning and specific dose delivery, **delivers tailored radiation doses direct to the target tissue with high precision**. Importantly, this ensures that surrounding healthy tissues and organs, such as the heart, lungs and skin are spared from potentially harmful radiation, **limiting the risk of associated toxicity and improving cosmetic outcomes**. It has been shown that brachytherapy is associated with the benefits of targeted precision and reduction in radiation exposure to healthy tissue and organs at risk.^{7,8}



Brachytherapy modalities

Two main brachytherapy modalities are used:

1. Interstitial multicatheter brachytherapy

- Used either as boost following WBI or as APBI.
- Multiple catheters are inserted into the breast and the radiation dose is delivered via the afterloader.
- Multiple treatment sessions are required (1–2 days for boost and 5 days for APBI) in an outpatient setting to deliver the total prescribed radiation dose.
- The catheters are removed following the last treatment session.

2. Intracavitary brachytherapy

- Used as APBI e.g. MammoSite®, SAVI®.
- A single tube is inserted into the breast and inflated/expanded.
- The tube contains a single channel or multiple channels.
- The radiation dose is delivered via the afterloader.
- Multiple treatment sessions over 5 days in an outpatient setting are required to deliver the pre-planned total dose.
- The tube is removed following the last treatment session.

Delivery of brachytherapy may be carried out at different dose rates: a high dose rate (**HDR**: a high dose over a short time), pulsed dose rate (**PDR**: a high dose over a series of short pulses) or low dose rate (**LDR**: a lower dose over a longer period).¹⁰

HDR brachytherapy is used most prevalently and is incorporated into treatment guidelines for both boost treatment following WBI, and APBI.¹⁷

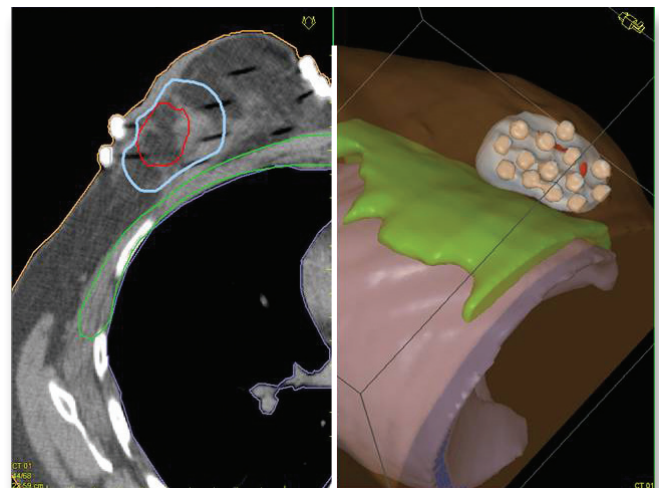


Figure 1. Modern 3D treatment planning: interstitial multicatheter brachytherapy

Interstitial multicatheter brachytherapy as boost

As a boost dose to the tumor bed, brachytherapy offers **exceptional efficacy, similar to EBRT boost**. In addition, brachytherapy has the benefit of **tissue sparing, and good cosmesis, together with logistical and lifestyle advantages** since it shortens boost treatment schedules from a couple of weeks to a couple of days.

Efficacy

Interstitial multicatheter brachytherapy as a boost provides excellent long-term efficacy with recurrence rates of <10% after 5 and 10 years' follow-up typically reported.⁵

When comparing efficacy against EBRT boost, **no significant difference in local tumor control or overall survival rates between the two modalities** have been found. Seven year local recurrence-free rates of 93.7% for brachytherapy and 93.9% for EBRT ($p=0.53$), and overall survival rates of 81.4% and 83.1%, respectively were reported ($p=0.77$).⁴

Side effects and cosmesis

Boost therapy is **generally well tolerated**, although an increased risk of adverse effects, such as fibrosis, has been observed compared with patients not receiving boost treatment.¹⁸ This is attributed more to the increased radiation dose than to how the radiation is delivered.

Interstitial multicatheter brachytherapy boost is a precise treatment, irradiating a small volume of normal healthy tissue and the **risk of associated side effects is therefore reduced and cosmesis improved.**⁹

“In addition to external beam boost modalities, multicatheter brachytherapy remains a standard treatment option to deliver an additional dose to the tumor bed after breast conserving surgery and whole breast irradiation”¹⁹



Brachytherapy as APBI

APBI addresses some of the biggest patient concerns with respect to radiotherapy, including treatment times and side effects. For suitable early breast cancer patients (based on selection criteria from professional organizations such as ASTRO, ABS and GEC ESTRO), brachytherapy as APBI provides an **equally efficacious treatment to whole breast irradiation but with the benefits of minimal side effects and reduced treatment time of up to 5 days**.

Efficacy

Interstitial multicatheter brachytherapy

APBI using interstitial multicatheter brachytherapy remains the technology with the largest evidence and experience base for APBI, providing **exceptional local tumor control and survival rates** (Table 1).

Study	N	Median f/u (months)	IBFR (%)	EFR (%)
King, 2000	160	84	2.5	1.2
Vicini, 2003	199	65	2.5	1.5
Arthur, 2003	44	42	0.0	0.0
Strnad, 2010	274	63	2.9	2.9

Table 1. Summary of selected interstitial multicatheter brachytherapy APBI studies^{15,20-22}

f/u: follow-up; IBFR: ipsilateral breast failure rate; EFR: elsewhere failure rate

These treatment responses are maintained in the long term with excellent 12-year follow-up rates for actuarial recurrence (9.3%), disease-free survival (DFS; 75.3%), cancer-specific survival (CSS; 91.1%) and overall survival (88.8%) being reported.⁶

Importantly, these long-term efficacy results are **equivalent to those achieved with whole breast irradiation (with or without boost)**, demonstrating that reducing the overall target treatment volume does not negatively impact efficacy outcomes (7-year relapse-free survival rates for APBI: 79.8%, WBI: 73.5%, WBI + boost: 77.7%).²³

The efficacy of 3D conformal radiotherapy (3D CRT) and intensity modulated radiation therapy (IMRT) is less well established than is the case for brachytherapy. The average follow-up reported for 3D CRT and IMRT in the ASTRO consensus statement was 1 year, compared

to 5 years for brachytherapy (335 versus 7,133 patient years respectively).²⁴ Longer term results have been reported in a prospective study of 52 patients treated with APBI using 3D CRT, with 4-year local recurrence rates of 6%.²⁵ The results achieved with brachytherapy, over similar or longer follow-up (Table 1), thus compare favorably.

Intracavitary brachytherapy

The rates of **local recurrence for APBI using intracavitary brachytherapy are comparable to WBI**.

Data are currently less extensive than for interstitial multicatheter brachytherapy as follow-up times are currently shorter. The latest update from the American Society of Breast Surgeons study, involving over 1,400 patients, reported **5-year local recurrence rates of 3.8%**.²⁶ Additional results are outlined in the table below (Table 2).

Study	N	Median f/u (months)	LR (%)	EFR (%)
Voth, 2006*	55	24	3.6	1.2
Chao, 2007*	80	36	2.5	1.5
Dragun, 2007*	70	26	5.7	0.0
Goyal, 2010*	70	51.5	1.4	8.9
Yashar, 2009+	63	18	1	2.9

Table 2. Summary of selected intracavitary brachytherapy APBI studies²⁷⁻³¹

*: MammoSite balloon; +: SAVI strut device; f/u: follow-up; LR: local recurrence rate; EFR: elsewhere failure rate

Side effects and cosmesis

The precision of brachytherapy minimizes exposure of surrounding healthy breast tissue, chest wall, heart, lungs and skin to radiation – resulting in a reduced risk of acute and late toxicities and excellent cosmesis

Interstitial multicatheter brachytherapy

Toxicity and side effects: Rigorous long term follow-up studies have demonstrated a low risk of acute and late minimal side effects. A recent 5-year study demonstrated only minimal early side effects in a few patients. Long-term side effects were negligible: only 1.8% reported any skin changes (all Grade 1), fat necrosis was reported in 5.1% patients and was associated with no or minor symptoms. Fibrosis was seen in 30% patients, more than half of which were Grade 1.²²

A similar favorable long-term adverse event profile was reported in a group of patients followed for up to 12 years.⁶

Cosmesis: Long-term data demonstrate excellent cosmesis outcomes, resulting from the favorable incidence of long-term toxicities. Good-to-excellent ratings of up to 90% or greater have been reported (Table 3).

Study	N	Median f/u (months)	Excellent/good cosmesis (%)
Polgar, 2004	45	81	84
Chen, 2006	199	76	>90
Kaufman, 2007	32	60	89
Strnad, 2010	274	63	90
Polgar, 2010	45	133	78

Table 3. Reported cosmesis rates with interstitial multicatheter brachytherapy APBI^{22,23,32,33}

Intracavitary brachytherapy

Cosmesis: Similar excellent long-term cosmesis outcomes have been reported, of around 90% or greater good-to-excellent rates. Ongoing studies are providing additional evaluation (Table 4).

Study	N	Median f/u (months)	Excellent/good cosmesis (%)
Dickler, 2005	30	13	93
Sadeghi, 2006	67	13	96
Benitez, 2007	43	66	83
Vicini, 2010	95	72	85

Table 4. Reported cosmesis rates with intracavitary brachytherapy APBI (MammoSite balloon)^{12,34-36}

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For further information on brachytherapy for breast cancer, consult the following resources:

Speak to colleagues who have successfully integrated brachytherapy into their practice

ESTRO (European Society for Therapeutic Radiology and Oncology)
www.estro.org

ASTRO (American Society for Therapeutic Radiology and Oncology)
www.astro.org

GEC-ESTRO (Groupe Européen de Curiethérapie and the European Society for Therapeutic Radiology and Oncology)
www.estro.org/about/Pages/GEC-ESTRO.aspx

ABS (American Brachytherapy Society)
www.americanbrachytherapy.org

NCCN (National Comprehensive Cancer Network)
www.nccn.org



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Brachytherapy:

The precise answer for tackling breast cancer

Reasons to consider brachytherapy in breast cancer management

- Demonstrated efficacy
- Precision radiotherapy
- Minimized toxicity
- Patient-centered
- Cost-effective
- State-of-the-art

Because life is for living

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