Brachytherapy in accelerated partial breast irradiation (APBI) – review of treatment methods

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Abstract
Breast conserving surgery (BCS) with following radiotherapy (EBRT) of the conserved breast became widely accepted in the last decades as the treatment of early invasive breast cancer. In an early stage of breast cancer, research has shown that the area requiring radiation treatment to prevent cancer from local recurrence is the breast tissue that surrounds the area where the initial cancer was removed. Accelerated partial breast irradiation (APBI) is an approach that treats only the lumpectomy bed with 1-2 cm margin, rather than the whole breast and as a result allows accelerated delivery of the radiation dose in four to five days. Published results of APBI are very promising. It is evident that APBI will play a role in the management of a selected group of early breast cancer. We discuss current status, indications, technical aspects and recently published results of APBI using different brachytherapy techniques.

Key words: APBI, balloon, brachytherapy, breast cancer, interstitial.

Purpose
Breast cancer is the most frequently detected cancer in women in developed countries and its incidence ranges from 25% to 30% of all cancers in women. Average age of breast cancer patients range between 45 and 65, however, in recent years is noticeable that the average age of incidence tend to lower [1]. With the prevalence of screening and increasing awareness of the disease, more and more women may be treated with breast-conserving surgery (BCS) with a complementary external beam radiation therapy (EBRT) and tumor’s bed dose increasing (‘boost’). Results of conservative treatment supplemented by radiation therapy are as good as the results obtained after mastectomy [2-6]. Further advances in radiotherapy techniques and knowledge of the biology of breast cancer, in addition to the standard methods of combination therapy (WBRT and ‘boost’), increases the application of APBI as a radical treatment in particular cases [7-11]. This method of radiation therapy is used in a selected group of patients in the early stages of the disease [3,12-17]. The main reason for APBI introduction was the assumption that it leads to obtain an equivalent local control rates with less toxicity of treatment compared with whole breast irradiation technique (EBRT) after BCS in the selected group of patients. The results of studies comparing the effectiveness of BCS + WBRT and APBI have shown that a very large percentage of local recurrence (more than 80-90%) occurs in the immediate vicinity of the original location of the tumor.

This was the primary cause for the use of brachytherapy alone after breast-conserving therapy in a strictly selected group of patients. The advantage of this method is also shorter time of treatment from 5-7 weeks (WBRT + boost), to 4-5 days of APBI. It is supposed to be capable of reducing the rate of complications: radiation-induced reactions, telangiectasia and fibrosis. Due to increasing use of APBI methods we present the most recent reports on this subject. We describe the treatment techniques, principles of patient selection for this method, the results of treatment and current recommendations of GEC-ESTRO (Groupe Européen de Curietherapie – European Society for Therapeutic Radiology and Oncology), ABS (American Brachytherapy Society) and ASTRO (American Society for Therapeutic Radiology), three major world societies of radiation oncologists.

Rationale for use of APBI
The results of studies examining the efficacy of BCS followed by whole breast radiotherapy (WBRT) showed that a very large percentage of local recurrence arises in the immediate vicinity of the original location of the tumor (Fig. 1). At least five prospective randomized studies examining the percentage of local recurrence after radiotherapy the whole breast were published and it was found that 69% to 90% recurrences occur in immediate vicinity of the primary tumor (Table 1). In other studies, the percentage of recurrences in other quadrants than in being treated or contralateral...
breast was 0.9% to 3.5% in prospective studies and 2% to 5% in retrospective studies (Table 2). This was the basic cause for the use of brachytherapy alone after BCS treatment in a strictly selected group of patients [5,10,15,26-28]. Another advantage of this method pointed out by many authors is also shortening the treatment duration from 5-7 weeks (conventional EBRT) to 4-5 days, what, particularly for working women, living far away from the cancer center and older patients is important. Offeresen et al. [29] in the summary pointed out that in the U.S. socio-economic factors affect the type of surgery – poorer women (eg, paying a lower insurance premium) and/or living far from the radiotherapy center choose mastectomy, even after qualifying for the BCS. In some areas, up to 25% of older women after BCS are not irradiated from these reasons. After examination of 175 000 patients with early breast cancer (SEER database) it was found that in 1992-2003 the percentage of BCS increased from 41% to 60%, while the proportion of patients irradiated after BCS decreased from 79% to 71%. Undoubtedly it affects the increased risk of local recurrences after BCS. Similar conclusions were reached by Njeh et al. [30] – in this article, they exchanged the factors affecting to decide RT: convenience, accessibility, cost, distance from the center of RT, lack of transportation, lack of social support, movement difficulties of patients doctor bias, age of the patient and fear of radiation. Also in Japan, only about 70% of patients are treated with radiotherapy after BCS, for similar reasons as in the U.S.

Indications for APBI

Recommendations of the American Brachytherapy Society (ABS) and the American Society of Breast Surgeons (ASBS) on the qualifications for APBI are shown in Table 3 [31], while the GEC-ESTRO (Groupe Européen de Curie-thérapie European Society for Therapeutic Radiology and Oncology) recommendations are posted in Table 4 [32].

Contraindications for APBI

It lists: clinical stage III or IV, no evaluation of surgical margins, presence of extensive intraductal component (EIC), Paget’s disease, infiltration or other changes in skin, present contralateral breast cancer (or in the past), previous others cancers (within 5 years from eligibility for the study) with the exception of skin cancer and 0 or I stage FIGO cervical cancer (previous), pregnancy or lactation period, connective tissue disorders, collagen diseases, genetic or metabolic proceeding with hypersensitivity to radiation such as Ataxia teleangiectasia or similar, disorder or mental diseases, anticipated difficulties with carrying out brachytherapy [3,6,10,11].

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Table 1. Spatial pattern of ipsilateral breast relapse (IBTR) in patients enrolled in randomised trials testing the effect of whole breast radiotherapy [11]

| Trial (time of primary treatment) | Median follow-up (range) | Recurrence number/ Total number of patients | Pattern of IBTR |
|---------------------------------|--------------------------|---------------------------------------------|-----------------|
| NSABP B-06 (1976-1984) [12]     | 39 (5-95) months         | 110 (1108)                                  | 86% within or close to the quadrant of the index cancer 14% more diffuse within the breast |
| Uppsala-Orebro (1981-1988) [13] | 10 years                 | 57 (381)                                    | 69% in the surgical field 3.6% in the cuticular scar 3.6% in the skin overlying the surgical field 23.6% in the breast parenchyma outside the field of surgery |
| Ontario Clinical Oncology Group (1984-1989) [14] | 43 months               | 131 (837)                                  | 86% (83% with RT) at the site of primary surgery |
| Milan III (1987-1989) [15]     | 9 years                  | 75 (579)                                    | 85% (84% with RT) in the scar area 15% (16% with RT) in other quadrants |
| SweBCG 91-RT (1991-1997) [16]  | 5 years                  | 104 (1178)                                  | 90% in the same quadrant as the previous tumour 10% in other quadrants |
In APBI currently are applied several techniques: 1) Interstitial brachytherapy (HDR, PDR, permanent implants); 2) Brachytherapy using the balloons (Mammosite, Contura); 3) Hybrid brachytherapy devices (SAVI applicator); 4) External beam radiotherapy (3D, IMRT); 5) IORT (intraoperative radiotherapy) with electrons or X-rays. Below we will discuss the basic principles of brachytherapy techniques.

**Patient qualification for brachytherapy techniques**

Before preparing the treatment plan, a careful evaluation of tumor size and location should be made (clinical examination, mammography, ultrasonography (US), magnetic resonance (MRI)), determination of the stage of disease according to TNM and detailed histopathological examination should be performed. In the course of conservative treatment it is advisable to leave 4 to 6 clips on the border of tissue removed in the axis of anterior-posterior, posterior-medial, sagittal, up and down, which will facilitate the preparation of the brachytherapy treatment plan. Clipping of tumor bed is considered by many authors as the most precise factor determining the accuracy of brachytherapy.

Below we will discuss the basic principles of brachytherapy techniques.
Interstitial multicatheter brachytherapy

Currently, two brachytherapy techniques are used in breast cancer brachytherapy: HDR (high dose rate) and PDR (pulsed dose rate). Some clinical studies are published on using permanent implants (I125, Pd103) [33,34].

Techniques
Perioperative application of catheters

Brachytherapy using interstitial applicators can be performed in two ways. Perioperative brachytherapy involves the assumption of flexible applicators during surgery in place of the tumor bed. In this method, BT is applied immediately during BCS. The advantage of a perioperative technique is a need for only one general anesthesia (implantation of applicators takes place during surgery), resulting in reducing overall treatment time and the ability to precisely determining the location of the tumor visible during surgery. Throughout lumpectomy/quadrantectomy, the surgeon provides surgical clips (should be 6) to determine the tumor bed (the clips are helpful later in treatment planning). Applying of applicators requires precision, experience and basic knowledge in the field of radiation from the surgeon. The limitation of perioperative “boost” is the lack of the final histopathological examination - the risk of incorrect BT qualification can be leveled by precise clinical staging before procedure, intraoperative histological examination and the necessary implementation of the Sentinel-Lymph-Node Biopsy (SLN). The irradiated area is limited to the surgical bed with 1-1.5 cm margin depending on technique.

Application of catheters after BCS

Applicators are often implanted after healing of the surgical scar and after receiving the final histopathological diagnosis in 2-4 weeks after surgery. Radiation oncologist inserts applicators after visualization of the tumor bed using X-ray (the location of surgical clips) and ultrasound (in general) or local anesthesia (depending on the experience of the center). Location of applicators on the skin with subcutaneous tissue and part of the breast is anesthetized with lidocaine or Xylocaine (2%) solution, while analgesics are intravenously administered. General anesthesia involves standard procedures. After determining the shape and position of the tumor bed, the correct template and number of planes is selected, as well as the distance between the applicators.

Fig. 2. Interstitial brachytherapy for breast cancer – implantation of 7 flexible applicators attached to the skin with buttons, the tumor bed localized by ultrasound.
plicators and the active length for stepping source. The num-
ber of implanted applicators has to be determined indi-
vidually, depending on breast size, location of the tumor
bed and type of surgery (tumorectomy, quadrantectomy).
Frequently it is from 7 to over a dozen. Figure 2 shows im-
ages of applicators implanted in a patient with breast can-
cer after quadrantectomy, covering the upper external quad-
rant. Figures 3-5 present examples of treatment plan and
applicators used in interstitial BT.

Balloon brachytherapy (MammoSite, Contura)
and hybrid SAVI applicators

This technique was intended to reduce the technical dif-
ficulties associated with EBRT treatment planning and ap-
plication of many interstitial applicators. The balloon ap-
plicator consists of a silicone balloon catheter, containing
a channel for filling the balloon and 1 to 8 channels to in-
troduce radioisotope (Figs. 6A-B, 7A-B). SAVI applicator
does not include a balloon, but only applicators to adapt
to the shape of the box (Figs. 8A-D). Balloon technique in
principle is applicable in APBI without WBRT after surgery.
HDR sources are used in this technique. Balloon applica-
tors may be placed in the bed of the tumor during the BCS
(rarely) or 2-4 weeks after surgery with the help of ultra-
sound. Previously published results suggest a satisfac-
tory treatment outcome (as measured by the percentage of
local failure) and good cosmetic results (80% to 93% of pa-
tients) [36-43]. So far, we do not have randomized studies
comparing this technique treatment with interstitial BT.
The possible response will bring the results of Phase III Trial (NSABP B-39/RTOG 0413) conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the Radiation Therapy Oncology Group (RTOG). The objective of this trial is to compare the results of different treatment methods: WBRT, APBI with MammoSite or multicatheter interstitial BT 3D EBRT in stage 0, I and II of breast cancer [38].

Balloon brachytherapy was developed as an alternative to interstitial brachytherapy. Interstitial brachytherapy requires the experience in setting up many interstitial applicators, while using balloon brachytherapy is simpler in the application. Cosmetic results after balloon brachytherapy techniques seem to be very acceptable [37,40,43-45] with a high rate of satisfactory or excellent results. To achieve such results, the proper selection of patients (large breasts, central location of the primary tumor) is significant.

**Technique**

The balloon applicator consists of a silicone balloon with catheter to fill the balloon with fluid and 1 to 8 channels, where a radioactive source is placed. For the greater precision, in most centers using this method, the balloon is fixed

![Fig. 7. A) Contura balloon applicator (SenoRx®) [30]. B) Contura balloon applicator on CT section with the distribution of isodoses, 5 channels for iridium visible](image1)

![Fig. 8. A) Applicator SAVI (Strut Adjusted Volume Implant) with expanded channels (Cianna Medical®) [30]. B) SAVI applicator X-ray images showing surgical clips (arrows) [35]. C) SAVI applicator, a balloon with a visible isodoses [35]](image2)
in the operating room under ultrasonography. Then the applicator is fluid-filled to a volume strictly adhering to the walls of the tumor bed. Afterwards, a cross-section CT is made in order to prepare a treatment plan. Target (CTV) includes the volume of the balloon with a margin of 1 cm. Critical organs include the skin and lungs. In this technique HDR sources are used.

**Doses**

The most common treatment schemas of APBI techniques are: 1) fraction dose of 3.4 Gy two times daily with an interval of 6 hours, 10 fractions in 5 days to a total dose of 34 Gy; 2) fraction dose of 4 Gy two times daily – 8 fractions to 32 Gy; 3) fraction dose of 4.3 Gy two times daily – 7 fractions to 30.1 Gy [31,32].

**Electronic brachytherapy [30]**

A platform for delivering HDR brachytherapy radiation has been developed that involves the electronic generation of kV X-rays instead of using a radioactive source. The Axxent X-Ray Source manufactured by Xoft, Inc. was approved by the FDA for the treatment of breast cancer in January 2006 (Figs. 9A-C). The Xoft Axxent produces X-rays ranging from 20 to 50 kV, although only the 50 kV X-ray setting is used in breast brachytherapy. Using the 50 kV setting, the average energy of the X-rays is 28 keV; the radial dose function lies between those of 125I and 103Pd sources [46]. The Xoft Axxent Electronic Brachytherapy source is used in conjunction with a balloon applicator. The disposable source is intended to be used for a maximum of 10 fractions. Testing of the inter-source consistency performed by Rivard et al. shows that individual sources produce predictable energy spectra, anisotropy functions and radial dose functions. As such, independent dosimetric verification is not necessary for each source. Instead, prior to each treatment, a single measurement of the source air-kerma strength is the only requirement [46].

The low energy photons emitted from the kV brachytherapy source (KVB) have a limited range that obviates the need for a shielded radiation vault. This expands the settings in which the source could be used and may increase the availability of PBI. Additionally, the difference in photon energy between a KVB source and an 192Ir source has dosimetric implications. Dickler et al. found that the %V90 and %V100 do not appear to differ between KVB and MammoSite, demonstrating that KVB offers comparable target volume coverage. Due to its rapid dose fall-off, KVB provides a mean ipsilateral lung %V30 of 1.1% compared to 3.7% for MammoSite. Using KVB, the volume of the PTV receiving 200% of the prescription dose slightly exceeded the volume associated with an increased risk of fat necrosis in a previous study by Wazer et al. [44]. Similarly, a phantom study of KVB by Smitt et al. found that in order to achieve 90% coverage of the PTV, the V200 varied from 16 to 22 cm³ [48]. These figures are far higher than those of MammoSite and approach the dose-volume constraints that have been shown to be correlated with fat necrosis in studies of interstitial multicatheter brachytherapy [49]. However, it is unclear if dosimetric parameters that predict fat necrosis in multicatheter procedures are applicable to balloon applicator procedures. The effect of chemotherapy on the development of fat necrosis also remains to be clarified.

**Fig. 9.** A) Axxent Electronic Brachytherapy System, the control unit (Xoft®) [30]. B) Axxent Electronic Brachytherapy System, X-ray source HDR (Xoft®) [30]. C) Axxent Electronic Brachytherapy System, a balloon applicator (Xoft®) [30]
**Table 5. Comparison of APBI techniques – from Offersen [29] and Sarin [50]**

| Coverage of target | 3D EBRT | Interstitial brachytherapy HDR, LDR, PDR | MammoSite | Target, 50 kV X-rays | IORT, electrons |
|--------------------|---------|----------------------------------------|------------|----------------------|----------------|
| Thickness of cavity wall irradiated | PTV = tumor bed + 20-25 mm to field edge from PTV | 1-2 cm | dose prescribed to 1 cm from surface of applicator | dose prescribed to 1 mm from surface of applicator | dose prescribed to 90% isodose line. 80% isodose at 13 mm (3 MeV) – 24 mm (9 MeV) |
| Dose homogeneity | best | good | good | good | good |
| Sparing of normal breast/other organs | least | good | good | best | varies with location |
| Skin dose | least | least | variable | least (can shield) | least |
| Technical feasibility for various size, shape or location of cavity | suitable for virtually all cases | not suitable if inadequate tissue or near axilla | not suitable for large/irregular cavities, or at the periphery of the breast | not suitable for large/irregular cavities, or at the periphery of the breast | not suitable for tumors near brachial lexus/axilla or skin |
| Expertise required | average | high | average | high | very high |
| Potential for wide spread use | very good | fair | very good | fair | limited |
| Main drawback | relatively higher dose to normal tissue and breathing motion | adequacy of target coverage in some cases and wider applicability | cavity shape and size. Although easy to use, stringent QA is required. Skin dose may be high | very limited depth irradiated; cavity shape and size, histology not available | wider applicability. Histology not available, based on quadrantectomy |

**Table 6. Results of recent clinical experience with interstitial brachytherapy with more than 5 years follow-up [30]**

| Author          | No of cases | Follow up interval (years) | Technique | Scheme | Total dose (Gy) | 5-year LR (%) | Good/Excellent cosmesis |
|-----------------|-------------|---------------------------|-----------|--------|-----------------|---------------|------------------------|
| Strnad et al.   | 274         | 5.25                      | PDR/HDR   | PDR – 0.6 Gy/h HDR – 4 Gy × 8 fr. | PDR = 50 Gy HDR = 32 Gy | 2.9% | 90% |
| Antonucci et al. | 199        | 9.6                       | LDR/HDR   | HDR – 0.52 Gy/h × 96 h | HDR = 4 Gy × 8 fr. HDR = 3.4 Gy × 10 fr. | 5% | 99% |
| Johansson et al. | 50          | 7.2                       | PDR       | HDR = 50 Gy/5 d | 50 Gy | 4% | 56% |
| Arthur et al.   | 99          | 7                         | LDR/HDR   | HDR = 3.5 Gy/5 d HDR = 3.4 Gy × 10 fr. | 45 Gy (LDR) HDR = 34 Gy (HDR) | 4% | n/a |
| Polgar et al.   | 128         | 6.8                       | HDR       | HDR = 5.2 Gy × 7 fr. | 36.4 Gy | 4.7% | 77% |
| King et al.     | 51          | 6.25                      | LDR/HDR   | HDR = 4 d HDR = 4 Gy × 8 fr. | 45 Gy (LDR) HDR = 32 Gy (HDR) | 3.9% | 75% |
| Otto et al.     | 274         | 5.25                      | PDR/HDR   | HDR = 5 d, 0.6 Gy/h HDR = 4 Gy × 8 fr. | 49.8 Gy (PDR) HDR = 32 Gy (HDR) | 2.9% | 92% |
| Polgar et al.   | 45          | 11.1                      | HDR       | HDR = 4.33 Gy × 7 fr. HDR = 5.2 Gy × 7 fr. | 30.3 Gy HDR = 36.4 Gy | 4.4% | 78% |

LR – local recurrence; HDR – high dose rate; LDR – low dose rate; PDR – pulsed dose rate; n/a – data not available; h – hours, d – days, fr. – fractions

Results of APBI

Comparison of different APBI techniques is posted in Table 5 [29,50]. Clinical results of APBI after various treatment techniques are presented in tables. Table 6 presents the results of interstitial brachytherapy, Tables 7, 8 – results of balloon brachytherapy.
### Table 7. Some of the recent clinical experience with MammoSite [29]

| Institution/Study | No. of cases | Follow-up (years) | Inclusion criteria and definition of target | Ipsilateral breast recurrence |
|-------------------|--------------|-------------------|-------------------------------------------|-------------------------------|
| American Society of Breast Surgeons, MammoSite Breast Brachytherapy Trial [59-64] | 1255 | 2.5 | > 45 years, T6, 2 cm, N0, negative margins, ductal only, applicator placement < 10 weeks postoperative, cavity P3 cm in one dimension, no EIC | 2 years – 1.11%, 3 years – 1.79% |
| Texas Cancer Clinic San Antonio [65] | 67 | 1.1 | ≥ 45 years, T < 3 cm, N0, negative margins, lumpectomy cavity 3-6 cm | NA |
| Kaiser Permanente Los Angeles Medical Center [66,67] | 51 | 1.3 | ≥ 45 years, T6, 2 cm, N0, ductal only, negative margins | 0 |
| Rush University Medical Center, Chicago [68,69] | 78 | 2.2 | ≥ 45 years, T < 3 cm, N0, negative margins | 7.1% |
| Medical University of South Carolina [70] | 37 (7 with DCIS) | 0.5 | any age, pT1-2N0, negative margins | NA |
| Tufts New England [71,72] | 38 | 1.4 | any age, T < 3 cm, ductal and DCIS, N0 (solitary nodal micrometastasis accepted), negative margins > 1 mm | NA |
| European MammoSite trial [73,74] | 28 | 1.2 | ≥ 60 years, T ≤ 2 cm, ductal only, grade 1/2, margins > 5 mm, ER+, balloon-skin distance > 7 mm, lumpectomy cavity > 3 cm, no EIC | 0 |

EIC – extensive intraductal component; DCIS – ductal carcinoma in situ; ER – estrogen receptor; PR – progesterone receptor; N/A – data not available; d – days; fr – fractions

### Table 8. Local recurrences after MammoSite [31]

| Trial | No. of cases | Follow-up (months) | Local recurrences rate (%) |
|-------|--------------|--------------------|---------------------------|
| ASBS TRIAL [75] | 1440 | 30 | 1.04 |
| Tufts/Medical College Virginia/Rhode Island [71] | 28 | 19 | 0 |
| St. Vincent Cancer Center [66] | 31 | 11 | 0 |
| Rush University Medical Center [76] | 70 | 26 | 5.7 |
| Kaiser Permanente [49] | 40 | 13 | 0 |
| Medical University South Carolina [74] | 90 | 24 | 2.2 |
| ASBS DCIS TRIAL [77] | 191 | 7 | 0 |
| William Beaumont [68] | 80 | 22 | 2.5 |
| European TRIAL [73] | 44 | 14 | 0 |
| International TRIAL [78] | 23 | 20 | 0 |
| Western Pennsylvania Hospital [79] | 55 | 24 | 3.6 |
| Oscar Lambret Center [69] | 25 | 13 | 0 |

### Table 9. Rates of good and excellent cosmesis after MammoSite brachytherapy [31]

| Institution/Study | Number of patients | Follow-up (months) | Good or excellent cosmesis (%) |
|-------------------|--------------------|--------------------|-------------------------------|
| ASBS registry trial [63] | 1449 | 30 | 94 |
| FDA trial [75] | 36 | 65 | 81 |
| Tufts/medical college of Virginia/Rhode Island [46] | 28 | 19 | 93 |
| St. Vincent’s cancer center [66] | 31 | 11 | 86 |
| Rush university medical center [76] | 30 | 26 | 93 |
| Kaiser permanente [49] | 40 | 13 | 97 |
| Medical University of South Carolina [74] | 90 | 24 | 90 |
| ASBS DCIS trial [77] | 191 | 7 | 94 |
| William Beaumont [68] | 80 | 22 | 88 |
| European trial [73] | 44 | 14 | 75 |
| International trial [78] | 18 | 20 | 67 |
| Oscar Lambret center [69] | 25 | 13 | 84 |
### Table 10. Cosmesis and complications after APBI with interstitial brachytherapy [29]

| Institution, Technique | Number of patients | Follow-up | Cosmesis and complications |
|------------------------|--------------------|-----------|-----------------------------|
| The William Beaumont Hospital, USA [49,80-82] HDR 32-34 Gy/8-10 fr/4-5 days LDR 50 Gy, 96 hours | 199 | 5.7 years (L.R.), 6.4 years (cosmesis) | 7% acute infection, 4% late infection, 11% fat necrosis at ≥ 5 years, good/excellent cosmesis in > 90% |
| Ochsner Clinic, USA [83] HDR 32-34 Gy/8-10 fr/4-5 days LDR 45 Gy, 4 days | 50 | 6.3 years | cosmesis scored at median 20 months: 22% grade II/III compl., 8% grade III compl., 75% had an excellent/good cosmesis, all based on² |
| Ochsner Clinic, USA [84] HDR 32-34 Gy/8-10 fr/4-5 days LDR 45 Gy, 4 days | 99 | 2.7 years | late grade III tox. 18% (LDR) and 4% (HDR), no late grade IV tox., all based on² |
| London Regional Cancer Center, Ontario [85] HDR 37.2 Gy/10 fr/5 days | 39 | 7.6 years | median overall cosmetics score 89%, 13% had fat necrosis, all based on² |
| Tufts New England [44,86-88] HDR 34 Gy/10 fr/5 days | 75 | 6.1 years | cosmesis, excellent/good/fair-poor: 67%/24%/9% at last follow-up, late skin tox. grad. I/II/III 77%, 19%, 4%, late subcutaneous tox. grad. I/II/III 55%, 15%, 12%, 18% |
| Tufts New England [89] LDR 50, 55, and 60 Gy | 48 | 1.9 years | very good/excellent cosmesis 91.8%, 12.5% perioperative complications, 25% had fibrosis, 8% moderate to severe fibrosis, based on² |
| Tufts New England [90] HDR 34 Gy/10 fr/5 days | 32 | 7 years | 18% had fat necrosis > 5 years, 35.7% moderate to severe subcutaneous fibrosis > 5 years, 89% excellent cosmesis at 5 years, toxicity based on onc, fibrosis > 5 years |
| University of Kansas [91] LDR 20-25 Gy | 24 | 3.9 years | cosmesis good to excellent in 100%, no late complications, based on² |
| Guys Hospital, London [92,93] LDR 55 Gy, 5 days | 27 | 6 years | cosmesis good to excellent in 83%, no fibrosis, based on² |
| Guys Hospital, London [94] LDR 45 Gy, 4 days | 49 | 6.3 years | abnormal breast in 58%, based on² |
| National Institute of Oncology, Hungary [95,96] HDR 30.3-36.4 Gy/7 fr/4 days | 45 | 6.8 years | cosmesis excellent/good in 84.4%, fat necrosis 20%, ≥ grade 2 late radiation reaction 26.7%, based on³ |
| National Institute of Oncology, Hungary [55,97] HDR 36.4 Gy/7 fr/4 days (n = 88) or ERBT 50 Gy/25 fr (n = 40) | 126 | 5.5 years | excellent to good in 81.2% (HDR) and 70% (electrons), based on³, 4-year actuarial fat necrosis 36.5% (HDR) and 17.7% (electrons), based on institutional scheme |
| Erlangen, Germany [57,98-100] HDR (36%) 32 Gy/8 fr/5 days; PDR (64%) 49.8 Gy in 83 consecutive fractions of 0.6 Gy each hour/5 days | 274 | 2.7 years | cosmesis excellent to good in 94%, acute toxicity in 6.6%, fat necrosis 4.7%, breast tissue fibrosis in 19.3% and telangiec-tasia in 12.8%, scoring based on²,³,⁴ |

Number of patients refers to patients diagnosed with invasive cancer². Cosmesis scored according to institutional guidelines:² Cosmesis scored according to Harvard criteria [101].³ Skin and subcutaneous toxicity scored according to Radiation Therapy Oncology Group (RTOG)/Eastern Cooperative Oncology Group system [102].⁴ Acute and late side effects based on LENT SOMA [103].

### Cosmetic effect

Cosmetic results after brachytherapy techniques seem to be very satisfactory. Draws attention to a high rate of satisfactory or excellent results. Essential to achieve such results is a proper selection of patients (large breasts, the central location of the primary tumor).

The tables below provide a summary of cosmetic results after using the balloon brachytherapy and interstitial brachytherapy (Tables 9, 10).

### Conclusions

The percentage of local recurrence and the cosmetic results are an important argument for the choice of APBI brachytherapy technique. Based on available results from prospective clinical trials where excellent results in selected groups of patients are achieved, it seems reasonable to use of APBI outside clinical trials in selected cases. These is a conclusion also of GEC-ESTRO Breast Cancer Working Group [32]. Strict criteria for selecting patients with early...
breast cancer group (low-risk group) and systematic quality control procedures (QA) must be preserved. These recommendations may be an indication for physicians and patients to choose an APBI techniques.

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