BreastCare

Review Article

Breast Care 2018;13:157–161
DOI: 10.1159/000489638

Published online: May 29, 2018

The Role of Brachytherapy in the Treatment of Breast Cancer

Daniela Kauer-Dorner Daniel Berger

Department of Radiotherapy, Medical University of Vienna, Vienna, Austria

Keywords

Breast cancer · Brachytherapy · Partial breast irradiation · Boost therapy

Summary

Radiotherapy plays an important part in the management of breast cancer. Especially after breast-conserving surgery, external whole breast irradiation, occasionally with an additional local boost, is an integral part of breast conservation. Besides external radiation techniques, brachytherapy (BT) has long been among the treatment options, especially with regard to local boost application. With the emerging implementation of accelerated partial breast irradiation (APBI), BT in general and interstitial multi-catheter BT in particular, are gaining an increasing role in the management of a selected group of early breast cancer patients. APBI is an approach to reduce the irradiated area to the former tumor bed rather than treating the whole breast tissue in patients with a low baseline local recurrence risk. After a variety of phase I–III clinical studies, it is clearly evident that APBI will play a role in the treatment of this selected patient group. In this review, we focus on the clinical development and different available techniques of breast BT and provide a preview of prospects for its use.

Introduction

With an estimated 1,676,600 new cases and 521,900 deaths, breast cancer is the most frequent malignant tumor in women worldwide [1]. Breast-conserving surgery (BCS) followed by external whole breast irradiation (WBI), frequently including a local boost therapy, is accepted as standard therapy in the breast-conserving management of early breast cancer (stage 0–II) [2]. Since the late 1990s, a new approach of fractionation has been established in the postoperative treatment. Hypofractionation with a reduced total dose of 39–42.6 Gy in 13–16 fractions administered within 3 weeks is now widely accepted as a standard method for WBI [3, 4]. Besides external beam irradiation, brachytherapy (BT) represents an important radiotherapeutic modality in breast cancer treatment. In the beginning, breast BT was mainly used for local boost therapy. However, in trying to de-escalate treatment time and treatment volume while maintaining the local control rates of WBI, accelerated partial breast irradiation (APBI) has quickly evolved as an attractive new approach. From the beginning of APBI, BT has played a role as the oldest and best investigated technique of delivering radiation doses to the breast. In this review, we focus on the role of BT in modern breast cancer treatment and on the different techniques, and provide an overview of outcomes and future trends.

Brachytherapy

BT is a type of radiotherapy in which tiny amounts of radioactive material sealed in catheters, wires, needles, or seeds are placed directly into the tumor tissue or the former tumor bed if used as postoperative treatment. Because of the precise positioning of the radiation sources into the tumor or the tumor bed, high doses can be applied to small areas. Furthermore, due to Newton's inverse-square law, which applies to ionizing radiation, the dose accordingly decreases with the distance to the center of the source, and high doses can be applied to target areas while avoiding high dose levels at nearby organs at risk (OAR). BT is commonly used in the treatment of cervical, prostate, and breast cancer as monotherapy or as a boost therapy in addition to external beam therapy. However, it may also be used as part of the treatment procedures in several other tumors, such as carcinoma of the head and neck region, respiratory tract, digestive tract, and soft tissue sarcoma [5].

KARGER

Fax +49 761 4 52 07 14
Information@Karger.com
www.karger.com

Accessible online at:
www.karger.com/brc

Dr. Daniela Kauer-Dorner
Department of Radiotherapy
Medical University of Vienna
Währinger Gürtel 18–20, 1090 Wien, Austria
daniela.kauer-dorner@meduniwien.ac.at

BT can be delivered as intracavitary, intraluminal, or multicatheter interstitial BT (MIB) as a temporary application or as a permanent seed application.

Concerning the treatment of breast cancer, MIB has been investigated for a long time with extensive follow-up [6, 7]. For this technique, between 14 and 20 flexible, afterloading catheters are placed in the breast closely around the lumpectomy cavity. Application is free-hand or template-guided, mostly under general anesthesia. The change from 2-dimensional (2D) reconstruction of the implant geometry and treatment planning based on X-ray reconstructions to computed tomography(CT)-based 3D planning has significantly improved implant quality. In modern BT, a computer program (treatment planning system) is used to calculate the exact dose delivered by a radioactive sealed source (usually Ir-192) inside the breast area requiring treatment. A small radiation source, motor-controlled and dwelling within the applicators (needles or tubes), is used to deliver the treatment using a so-called afterloader device: Radiation is delivered via applicators for the shortest possible time while the patient remains in a shielded room. This ensures maximal radiation protection of the personnel. A major part of the planning process is the applicator reconstruction where the implant geometry is digitized onto 3D images on which the target volume can be defined. Inserted catheters are numbered, positioned, and placed relative to the surrounding tissue and other catheters. As mentioned above, if 2D treatment planning is employed, applicators are visualized by using radiographs and then projected onto CT simulation scans (fig. 1). The assessment of accurate implant geometry [8] for individualized treatment planning has always been an essential part of quality assurance in the planning process in order to limit the irradiated volume as much as possible and to limit the dose to adjacent OAR like skin, lungs, and heart [9]. To avoid any necrosis in the implanted tissue from radiation, the dose nonuniformity ratio (DNR) is monitored and kept below 35%. The DNR is the ratio of the target which receives a dose equal to or higher than 150% of the reference dose to the target which receives a dose equal to or higher than the reference dose [10]. Before the year 2000, implant geometry was thus mainly defined on radiographs, while after that period, CT-based simulation emerged in BT planning where the implant is directly visualized as located in the target tissue. This technological progress has resulted in better reconstruction accuracy (<1 mm spatial resolution) and a significant reduction in the treated volume by 30–40% in breast BT over the last 10 years at the Medical University of Vienna (unpublished).

Using MIB, the dose can be delivered using low dose rate (LDR), pulsed dose rate (PDR), or high dose rate (HDR) techniques, depending on the length of time the radioactive source remains in place [11]. In LDR BT, radiation sources deliver doses continuously with dose rates between 0.4 and 2 Gy/h over a few days. LDR regimens were mainly used in early APBI trials where doses of up to 45 Gy in 4.5 days were used [12]. While radiobiologically advantageous, LDR cannot be delivered in an afterloading setup. In HDR BT, a single radiation source delivers the dose to the application site using the above described afterloading setup. Doses are delivered at a rate of 12 Gy/h or higher to the so-called dwell positions so that large doses can be administered within a few minutes. PDR BT, which is also administered using an afterloading setup, uses dose rates of up to about 3 Gy/h, and the dose needed is administered (pulsed) every hour, 24 h per day. In this way, it combines the physical and radioprotection advantages of HDR with the radiobiological advantages of LDR [13].

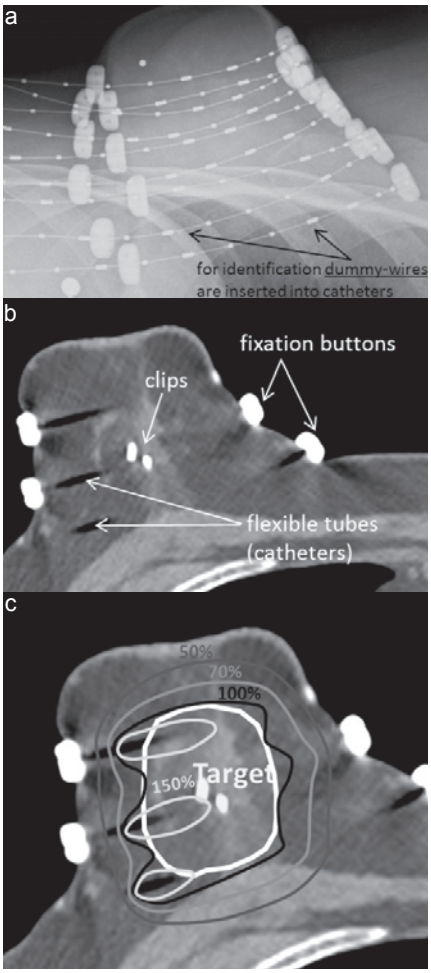

Fig. 1. Development from **a** X-ray-based catheter visualization to **b** computed tomography-based brachytherapy planning and **c** dose distribution in an APBI (accelerated partial breast irradiation) patient.

Role of Brachytherapy in Local Boost Therapy

The treatment intention of adjuvant breast irradiation is to minimize the risk of local recurrence after BCS. It is well known that especially the tissue immediately surrounding the primary tumor (bed) is at highest risk of giving rise to recurrence. Clinical and pathological findings have clearly documented high rates of failure patterns in the closest vicinity of the primary index lesion [14–17]. This strongly supports dose escalation to the tumor bed after WBI. Several randomized studies have already demonstrated an evident benefit of local boost therapy with reduced 5-year local recurrence rates from 7.3–13.3% in the non-boost groups to 3.6–6.3% in the boost groups [18–22]. The randomized boost versus non-boost EORTC 22881-10882 trial is the landmark study proving the significant benefit of a local boost after WBI in terms of local control rates, however, without any measurable effect on long-term overall

survival. After 20 years of follow-up, the actuarial overall rate of ipsilateral breast tumor recurrence (IBTR) was 16.4% in the no-boost group versus 12% in the boost group [23]. Interstitial BT is one of the oldest and time-tested techniques of boost application and has been used by several institutions participating in the EORTC 22881-10882 trial. Besides interstitial BT, there are other methods of administering local boost therapy, in particular, external beam irradiation and intraoperative radiotherapy. Limited data are available comparing advantages and disadvantages of brachy boost therapy and the other techniques [24, 25]. Until now, no significant difference could be identified in terms of local control and side effects like fibrosis between BT and other modalities. All show excellent or good cosmetic outcome; however, prospective head-to-head comparisons are not available. Arguably, treatment volumes are always lower with BT, giving BT an advantage over external beam or intraoperative electron therapy. Besides local control and cosmetic outcome, the dose to OAR has been intensively investigated as it is the surrogate parameter of treatment toxicity. Terheyden et al. [26] could demonstrate a significant dose reduction with HDR BT to the investigated OAR such as lung, ribs, skin, and heart for right-sided breast cancer compared to external beam radiotherapy, while left-sided irradiation did not show a difference in the maximum dose to the heart. Regarding the dose to the lung, it is well established that the pneumonitis risk due to radiation is proportional to the mean dose to the lung, and the long-term risk of secondary malignancy induction seems to be related to the lung dose [27–29]. A brachy boost delivers a lower dose to the lung compared to external techniques, but further studies are needed to confirm any advantage translating into favorable long-term clinical outcome.

Role of Brachytherapy in Accelerated Partial Breast Irradiation

Looking at local control after BCS followed by WBI, several prospective trials demonstrated that a very large percentage of local recurrences (69–90%) arises in the very close vicinity of the initial tumor area [30–32]. Therefore, concentrating the required total dose to the area of highest risk of an ipsilateral in-breast recurrence, a lot of normal breast tissue at greater distance from the index tumor and OAR like lung, heart, and skin could be spared from acute and chronic side effects, which also could eventually favorably influence cosmetic outcome. The biological model of the linear quadratic equation, on which the estimation of radiation effects is based, formed the basis of the fractionation scheduling of accelerated delivery in partial breast irradiation. Based on the concept of radiobiological equivalence, shortening a treatment course requires decreasing the total dose, and the reduction in treated volume permits an increase in the dose per fraction to achieve the same clinical outcome as with a longer treatment course. BT, which has been in use for boost radiation after WBI as described above, provides an excellent technique to deposit a high radiation dose into the small area of the former tumor bed with a rapid dose falloff around the target volume. At the beginning of the APBI trials, the only form of BT was MIB using multiple catheters to deliver radiation to the lumpectomy cavity [33–36]. One of the earliest trials using MIB for APBI was started in the late 1980s by Guy's Hospital using LDR MIB for monotherapy in 27 non-randomized patients, followed by the Ontario trial performed at the London Regional Cancer Center with 39 patients. Both studies included patients with unfavorable risk factors like positive resection margins, large tumors, and node-positive disease, resulting in high ipsilateral in-breast recurrence rates (37%/16.2%) These discouraging results triggered the discussion of proper selection criteria for patients suitable for APBI, establishing risk factors for local recurrence like young age, tumor size, node-positive disease, positive or unknown resection margins, high nuclear grade, lymphovascular invasion, and extensive intraductal component. Furthermore, the development of image-based catheter implantation, implant reconstruction, and dose planning replaced 2D orthogonal-based treatment planning and resulted in a marked improvement in tumor dose coverage. All these efforts promoted the initiation of several prospective trials of modern MIB with strict patient selection criteria [37–41]. The key study to establish MIB APBI as a single treatment option after BCS is a randomized, non-inferiority phase III trial including 1,184 patients from multiple centers in Europe, which was recently published by the GEC-ESTRO Breast Cancer Working Group [42]. 5-year local control, disease-free survival, and overall survival were similar for MIB APBI and external WBI after BCS in early breast cancer patients with comparable early toxicity and patient compliance [43], and the trial proved non-inferiority of the de-escalation of treated volume, total dose, and overall treatment duration with MIB APBI compared to WBI. Patients included in the largest randomized trial of APBI versus WBI, NSABP B39/RTOG 0431, including MBI are still in follow-up and results are pending.

Another development in the use of MBI in primary breast-conserving treatment is the further shortening of the treatment duration from about 10-8 fractions given over 4–5 days to single-dose irradiation. Hannoun-Lévi et al. [44] recently reported a phase I/II trial of single-dose irradiation with 16 Gy in elderly women with promising outcome in terms of local control and acceptable acute toxicity and cosmetic outcome. Besides this study, more trials are focusing on the benefit of MIB post BCS as a treatment option in elderly breast cancer patients . Treatment decisions in elderly cancer patients need to focus not only on local control and overall survival but primarily on quality of life. Sumodhee et al. [45] and Genebes et al. [46] demonstrated in their studies that MIB can perfectly apply sufficient local irradiation with maximum preservation of OAR in a very short treatment period with excellent local control and low acute and chronic side effects. This could be an ideal alternative for elderly breast cancer patients, representing a compromise between omitting radiotherapy and a whole course of WBI.

Besides the primary treatment of early breast cancer patients, APBI using MIB is gaining increasing importance in the local treatment of IBTR after a second course of BCS. Radical mastectomy is still regarded as the gold standard treatment for IBTR. However, there is an increasing philosophy for a second course of breast-conserving local treatment for IBRT including radiation

after BCS to minimize the risk of a second local recurrence. MIB is the most commonly used technique of second-course local irradiation with promising results on local control with well accepted acute and chronic side effects and a high percentage of excellent to good cosmetic results [47–49].

In the early days of APBI, MIB was the only technique to deliver APBI with promising clinical results; however, MBI is highly dependent on the operator and the center's expertise. Since 2002, balloon-based BT devices and hybrid applicators including MammoSite® (Hologic, Marlborough, MA, USA), Contura® (Hologic), and Savi® (Cianna Medical, Aliso Viejo, CA, USA) have been introduced. The 5-year analysis of treatment efficacy, cosmetic outcome, and toxicity of MammoSite breast BT from the American Society of Breast Surgeons showed excellent results comparable to other forms of APBI [50]. However, using the single-channel MammoSite carries a certain risk of dosimetric limitation resulting in limited ability to shape the radiation dose to the target volume and OAR, which may in turn result in a greater risk of healthy tissue damage. The development of multi-luminal hybrid BT devices like Contura and Savi has combined the user-friendly application of MammoSite with the dosimetric advantages of MIB [51]. These new devices provide adequate targeting of the tumor bed and better control over the radiation dose to critical structures. Further research will be needed to define the potential of these devices as well as advantages and disadvantages in terms of clinical outcome in comparison to classical MIB.

Conclusion

Radiotherapy plays an essential part in breast-conserving treatment, and external beam irradiation is the most widely used modality. However, BT can deliver radiation doses to the target volume in a highly conformal way, thereby minimizing exposure of normal surrounding structures and OAR. The use of modern imaging technologies like CT, or even ultrasound and MRI, together with highly sophisticated treatment planning software, have further improved the accuracy of individualized treatment planning. However, there are still unanswered questions concerning the use of breast BT as a boost therapy or for APBI in primary or recurrent breast cancer: There is a variety of options for delivery with external and internal techniques for boost application and partial breast irradiation, but data are not sufficient to clearly favor any particular technique. Further research is required firstly to determine the optimal technique with regard to long-term local control and side effects, and secondly to define the best approach for individual patients. Patients with small breasts and planned eventual oncoplastic surgery might be the best candidates for external or intraoperative electron radiotherapy [52] as a boost or partial breast irradiation, while women with larger breasts might benefit more from different invasive techniques like MIB or balloon-based BT. Long-term follow-up data of BT, especially periods exceeding 10 years, are not currently available but are needed to support the efficacy of breast BT given the high survival rate of these patients. Finally, consensus guidelines on suitable patient selection criteria are available from national and international societies like ESTRO, ASTRO, and DEGRO but should be harmonized between countries and even different techniques. Proper patient selection criteria suitable for APBI and harmonized biologically equivalent dose schedules will simplify the comparison of data from different trials. A potential barrier to the wide adoption of MIB for APBI might be the complex and difficult handling of interstitial BT. MIB is technically demanding and operator- and center-dependent, and therefore it may be a less popular technique compared to other BT modalities. A lot of effort has already been put into giving general recommendations for performing MIB for APBI and boost therapy, but more clinical research is needed.

Disclosure Statement

The authors declare that they have no conflicts of interest.

References

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A: Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.
2 Early Breast Cancer Trialists' Collaborative Group (EBCTCG): Effect of radiotherapy after breast-conserving surgery on 10-yearrecurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials. Lancet 2011;378:1707–1716.
3 Haviland JS, Owen JR, Dewar JA, et al.; START Trialists' Group: The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol 2013;14:1086–1094.
4 Whelan TJ, Pignol JP, Levine MN, et al: Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med 2010;362:513–520.
5 Gerbaulet A, Pötter R, Mazeron J-J, Meertens Harm, van Limbergen E (eds): The GEC ESTRO Handbook of Brachytherapy. Leuven, Belgium, European Society for Therapeutic Radiology and Oncology, 2002.
6 Njeh CF, Saunders MW, Langton CM: Accelerated partial breast irradiation (APBI): a review of available techniques. Radiat Oncol 2010;5:90.
7 Offersen BV, Overgaard M, Kroman N, Overgaard J: Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: a systematic review. Radiother Oncol 2009;90:1–13.
8 Kellermeier M, Fietkau R, Strnad V, Bert C: Assessment of the implant geometry in fractionated interstitial HDR breast brachytherapy using an electromagnetic tracking system. Brachytherapy 2018;17:94–102.
9 Berger D, Kauer-Dorner D, Seitz W, Pötter R, Kirisits C: Concepts for critical organ dosimetry in three-dimensional image-based breast brachytherapy. Brachytherapy 2008;7:320–326.
10 Saw CB, Suntharalingam N, Wu A: Concept of dose nonuniformity in interstitial brachytherapy. Int J Radiat Oncol Biol Phys 1993;26:519–527.
11 International Commission on Radiation Units and Measurements: Dose and Volume Specification for Reporting Intracavitary Therapy in Gynecology. Report 38. Bethesda, 1985.
12 White J, Winter K, Kuske RR, et al: Long-term cancer outcomes from study NRG Oncology/RTOG 9517: a phase 2 study of accelerated partial breast irradiation with multicatheter brachytherapy after lumpectomy for early-stage breast cancer. Int J Radiat Oncol Biol Phys 2016;95:1460–1465.
13 Skowronek J, Malicki J, Piotrowski T: Values of biologically equivalent doses in healthy tissues: comparison of PDR and HDR brachytherapy techniques. Brachytherapy 2010;9:165–170.

14 Fisher B, Anderson S, Bryant J, et al: Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. Engl J Med 2002;347:1233–1241.
15 Bartelink H, Horiot JC, Poortmans PM, et al: Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial Clin Oncol 2007;25:3259–3265.
16 Holland R, Veling SH, Mravunac M, Hendriks JH: Histologic multifocality of Tis, T1–2 breast carcinomas. Implications for clinical trials of breast-conserving surgery. Cancer 1985;56:979–990.
17 Vaidya JS, Vyas JJ, Chinoy RF, Merchant N, Sharma OP, Mittra I: Multicentricity of breast cancer: whole-organ analysis and clinical implications. Br J Cancer 1996;74:820–824.
18 Romestaing P, Lehingue Y, Carrie C, et al: Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997;15:963–968.
19 Polgár C, Fodor J, Orosz Z, et al: Electron and high-dose-rate brachytherapy boost in the conservative treatment of stage I–II breast cancer first results of the randomized Budapest boost trial. Strahlenther Onkol 2002;178:615–623.
20 Polgár C, Jánváry L, Major T, et al: The role of high-dose-rate brachytherapy boost in breast-conserving therapy: long-term results of the Hungarian National Institute of Oncology. Rep Pract Oncol Radiother 2010;15:1–7.
21 Quéro L, Guillerm S, Tari ght N, et al: 10-Year follow-up of 621 patients treated using high-dose rate brachytherapy as ambulatory boost technique in conservative breast cancer treatment. Radiother Oncol 2017;122:11–16.
22 Skowronek J, Chicheł A: Brachytherapy in breast cancer: an effective alternative. Prz Menopauzalny 2014;13:48–55.
23 Bartelink H, Maingon P, Poortmans P, et al.; European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups: Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol 2015;16:47–56.
24 Poortmans P, Bartelink H, Horiot JC, et al.; EORTC Radiotherapy and Breast Cancer Groups: The influence of the boost technique on local control in breast conserving treatment in the EORTC 'boost versus no boost' randomised trial. Radiother Oncol 2004;72:25–33.
25 Polgár C, Major T, Fodor J, et al: High-dose-rate brachytherapy alone versus whole breast radiotherapy with or without tumor bed boost after breast-conserving surgery: seven-year results of a comparative study. Int J Radiat Oncol Biol Phys 2004;60:1173–1181.
26 Terheyden MM, Melchert C, Kovács G: External beam boost versus interstitial high-dose-rate brachytherapy boost in the adjuvant radiotherapy following breast-conserving therapy in early-stage breast cancer: a dosimetric comparison. J Contemp Brachytherapy 2016;8:294–300.
27 Kwa SL, Lebesque JV, Theuws JC, et al: Radiation pneumonitis as a function of mean lung dose: an analysis of pooled data of 540 patients. Int J Radiat Oncol Biol Phys 1998;42:1–9.
28 Bledsoe TJ, Nath SK, Decker RH: Radiation pneumonitis. Clin Chest Med 2017;38:201–208.
29 Grantzau T, Overgaard J: Risk of second non-breast cancer after radiotherapy for breast cancer: a systematic review and meta-analysis of 762,468 patients. Radiother Oncol 2015;114:56–65.
30 Liljegren G, Holmberg L, Bergh J, Lindgren A, Tabár L, Nordgren H, Adami HO: 10-year results after sector resection with or without postoperative radiotherapy for stage I breast cancer: a randomized trial. J Clin Oncol 1999;17:2326–2333.
31 Fisher ER, Sass R, Fisher B, Gregorio R, Brown R, Wickerham L: Pathologic findings from the National Surgical Adjuvant Breast Project (protocol 6). II. Relation of local breast recurrence to multicentricity. Cancer 1986;57:1717–1724.
32 Fisher B, Anderson S, Bryant J, et al: Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233–1241.
33 Fentiman IS, Poole C, Tong D, et al: Iridium implant treatment without external radiotherapy for operable breast cancer: a pilot study. Eur J Cancer 1991;27:447–450.
34 Fentiman IS, Poole C, Tong D, et al: Inadequacy of iridium implant as sole radiation treatment for operable breast cancer. Eur J Cancer 1996;32A:608–611.
35 Perera F, Engel J, Holliday R, et al: Local resection and brachytherapy confined to the lumpectomy site for early breast cancer: a pilot study. J Surg Oncol 1997;65:263–267.
36 Perera F, Yu E, Engel J, Holliday R, Scott L, Chisela F, Venkatesan V: Patterns of breast recurrence in a pilot study of brachytherapy confined to the lumpectomy site for early breast cancer with six years' minimum follow-up. Int J Radiat Oncol Biol Phys 2003;57:1239–1246.
37 Arthur DW, Winter K, Kuske RR, et al: A phase II trial of brachytherapy alone after lumpectomy for select breast cancer: tumor control and survival outcomes of RTOG 95-17. Int J Radiat Oncol Biol Phys 2008;72:467–473.
38 Polgár C, Fodor J, Major T, Sulyok Z, Kásler M: Breast-conserving therapy with partial or whole breast irradiation: ten-year results of the Budapest randomized trial. Radiother Oncol 2013;108:197–202.
39 Strnad V, Hildebrandt G, Pötter R, et al: Accelerated partial breast irradiation: 5-year results of the German-Austrian multicenter phase II trial using interstitial multicatheter brachytherapy alone after breast-conserving surgery. Int J Radiat Oncol Biol Phys 2011;80:17–24.
40 Polgár C, Van Limbergen E, Pötter R, et al.; GEC-ESTRO Breast Cancer Working Group: Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). Radiother Oncol 2010;94:264–273.
41 Aristei C, Maranzano E, Lancellotta V, et al: Partial breast irradiation with interstitial multi-catheter high-dose-rate brachytherapy. Long-term results of a phase II prospective study. Radiother Oncol 2017;124:208–213.
42 Strnad V, Ott OJ, Hildebrandt G, et al.; Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO): 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet 2016;387:229–238.
43 Ott OJ, Strnad V, Hildebrandt G, et al.; Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO): GEC-ESTRO multicenter phase 3-trial: accelerated partial breast irradiation with interstitial multicatheter brachytherapy versus external beam whole breast irradiation: early toxicity and patient compliance. Radiother Oncol 2016;120:119–123.
44 Hannoun-Lévi JM, Cham Kee DL, Gal J, et al: Accelerated partial breast irradiation for suitable elderly women using a single fraction of multicatheter interstitial high-dose-rate brachytherapy: early results of the Single-Fraction Elderly Breast Irradiation (SiFEBI) phase I/II trial. Brachytherapy 2018;17:407–414.
45 Sumodhee S, Levy J, Chamorey E, et al: Accelerated partial breast irradiation for elderly women with early breast cancer: a compromise between whole breast irradiation and omission of radiotherapy. Brachytherapy 2017;16:929–934.
46 Genebes C, Chand ME, Gal J, et al: Accelerated partial breast irradiation in the elderly: 5-year results of high-dose rate multi-catheter brachytherapy. Radiat Oncol 2014;9:115.
47 Hannoun-Levi JM, Resch A, Gal J, et al.; GEC-ESTRO Breast Cancer Working Group: Accelerated partial breast irradiation with interstitial brachytherapy as second conservative treatment for ipsilateral breast tumour recurrence: multicentric study of the GEC-ESTRO Breast Cancer Working Group. Radiother Oncol 2013;108:226–231.
48 Kauer-Dorner D, Pötter R, Resch A, et al: Partial breast irradiation for locally recurrent breast cancer within a second breast conserving treatment: alternative to mastectomy? Results from a prospective trial. Radiother Oncol 2012;102:96–101.
49 Trombetta M, Julian T, Bhandari T, Werts ED, Miften M, Parda D: Breast conservation surgery and interstitial brachytherapy in the management of locally recurrent carcinoma of the breast: the Allegheny General Hospital experience. Brachytherapy 2008;7:29–36.
50 Shah C, Badiyan S, Ben Wilkinson J, et al: Treatment efficacy with accelerated partial breast irradiation (APBI): final analysis of the American Society of Breast Surgeons MammoSite® breast brachytherapy registry trial. Ann Surg Oncol 2013;20:3279–3285.
51 Cuttino LW, Arthur DW, Vicini F, Todor D, Julian T, Mukhopadhyay N: Long-term results from the Contura multilumen balloon breast brachytherapy catheter phase 4 registry trial. Int J Radiat Oncol Biol Phys 2014;90:1025–1029.
52 Sedlmayer F, Reitsamer R, Wenz F, et al: Intraoperative radiotherapy (IORT) as boost in breast cancer. Radiat Oncol 2017;12:23.