CT-image based conformal high-dose-rate brachytherapy boost in the conservative treatment of stage I – II breast cancer – introducing the procedure

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SUMMARY

AIM: Breast-conserving surgery (BCS) followed by radiotherapy (RT) has become the standard treatment for the majority of patients with early breast cancer. With regard to boost technique some disagreements are found between groups that are emphasizing the value of electron boost treatment and groups pointing out the value of interstitial brachytherapy (BT) boost treatment. We present the preliminary results in treating selected patients with early-stage breast cancer using high-dose-rate brachytherapy (HDR-BT) as a boost after breast conservation therapy (BCT).

MATERIALS/METHODS: Between January 2006 and August 2007, a total of 58 female patients with first and second stage breast cancer underwent BCT. This therapeutic procedure involves BCS, whole breast radiation therapy (WBRT) and additional irradiation to the tumour bed (boost) using interstitial HDR-BT via flexible implant tubes. A 10 Gy boost dose was received by all patients. The treatment planning was based on CT-guided 3D (three-dimensional) reconstruction of the surgical clips, implant tubes and critical structures localization (skin and ribs). The accuracy of tumour bed localization, the conformity of planning target volume and treated volume were analyzed.

RESULTS: The evaluations of implant parameters involved the use of: dose volume histogram (DVH), the volume encompassed by the 100% reference isodose surface (V100%), the high dose volume calculation (V150%, V200%, V300%), the dose non-uniformity ratio (DNR), and the conformity index (COIN). Our results were as follows: the mean PTV volume, the mean high dose volume (V150%; V200%; V300%), the DNR and COIN mean value were estimated at 57.38, 42.98, 21.38, 7.90, 0.52 and 0.83 respectively.

CONCLUSIONS: CT-guided 3D HDR-BT is most appropriate for planning the boost procedure after BT especially in large breast volume, in cases with a deep seated tumour bed, as well as in patients with high risk for local recurrences. This technique reduces the possibility of geographical miss. Moreover, better conformity could be achieved between planning the target volume and the treated volume, even at the cost of worse dose homogeneity. The irregular 3D shape of the target volume and the normal tissue structures can be correctly localized on the basis of visual information obtained from cross-sectional CT imaging. Better local control rate with fewer side effects might be achieved with this technique based on CT imaging.

KEY WORDS: breast-conserving therapy, radiotherapy, HDR brachytherapy, boost, CT-based treatment planning.

BACKGROUND

Over the past century, breast cancer treatment has experienced a lot of significant and historic changes. From radical Halsted mastectomy to the current era of breast conservation surgery, RT has steadily integrated itself into the management of breast cancer [1–3]. Today with the availability of modern diagnostic imaging facilities allowing detection of early stages of breast cancer, along with the integration of sophisticated RT techniques, BCT is widely accepted as an alternative to mastectomy in the management of early breast cancer [4]. Even the concept of tumour bed RT alone (partial breast irradiation, PBI) as an alternative to whole breast RT in BCT, was evaluated in patients with low risk of relapse [5, 6]. The standard procedure of BCT involves conservation surgery (tumourectomy, lumpectomy, quadrantectomy and axillary sampling), radiation of residual breast tissue (with or without regional nodal irradiation) and – if needed – additional systemic therapy. The main purpose of radiation in BCT is to prevent any local recurrence without effecting cosmetic outcome [7–14]. Conventionally RT in BCT includes WBRT that is usually delivered by tangential beams. A supplementary tumour bed boost dose of 10–20 Gy (either through electrons, photons or an interstitial implant) is added to decrease the rate of local recurrence. A considerable number of scientific discussions have been focused on the optimal technique of delivering the radiation boost [15]. Moreover, the role of boost dose in a patient with negative margins of resection was questioned [16]. However, the use of BT as additional irradiation to the tumour site with early stage breast cancer has increased significantly over the past several years [7, 8, 17–19]. With regard to boost technique, there are certain disagreements between groups emphasizing the value of electron boost treatment and groups pointing out the value of interstitial boost therapy [11, 15, 20]. However, there are patients for whom electrons may be less appropriate. They include patients with large breasts and deep tumour location where electron boosting may result in excessive skin dose or even increased dose to the underlying lung. The big advantage of BT over external beam radiotherapy (EBRT) is the much smaller and more conformal irradiation to the target volume due to the rapid dose fall-off [11, 15, 21, 22]. Nowadays the indication of the boost after BCT and selection of the proper technique in order to deliver an extra dose should depend on clinical and morphological criteria as well as patients' agreement. At present there are several techniques used in maintaining better coverage of the target volume. However, the irregular 3D shape of the excision cavity and the normal tissue structures can only be accurately localized by visual information acquired from cross-sectional imaging. The use of surgical clips and CT at the same time seems to be the best method to determine the target volume, since both titanium clips and borders of the excision cavity can be visualized exactly from slice to slice [23–25]. A CT scan with visible clips is presented in Figure 1.

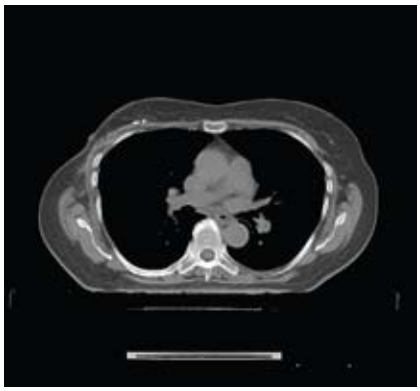

Fig. 1. TK image showing surgical clips necessary for tumour bed localization

AIM

We present the preliminary findings of our treatment protocol that involves radiation boost after breast conservation therapy (BCT) in selected patients with early-stage breast cancer using high-dose-rate brachytherapy (HDR-BT). We also review the current status, indications, technical aspects and future prospects of boost irradiation after BCT.

MATERIALS

Patients and tumour characteristics

Between January 2006 and August 2007, 58 female patients with stage I and II breast cancer underwent BCT. This therapeutic proce-

dure comprises BCS, WBRT and a boost of additional irradiation to the tumour bed using interstitial HDR-BT via flexible implant tubes. Most of the patients were premenopausal, with high risk for local recurrence as a consequence of a close, positive margin and extensive intraductal component (EIC) presence. None of the patients were showing symptoms of systemic metastasis based on clinical examination, liver function test, chest X-ray and ultrasound abdomen at the time of BCT. Patients with indications of bone pain underwent a skeletal survey. All patients were subjected to a mammogram test in order to rule out multicentric ipsilateral disease as well as contralateral breast cancer. Post-operative specimen analysis revealed invasive ductal carcinoma in 32 of the patients, invasive lobular carcinoma in 13 and other types of cancer in 10 cases, where a positive margin was noted in 8 of them. EIC defined as more than 25% of tumour composition and intraductal component was present in 15 patients with negative resected margin. In Table I summarized clinical data are presented.

Table 1. Patient and tumour characteristics

Clinical data	Number of patients
Age (years):	
< 40	4
41–50	28
51–60	18
> 60	8
All:	58
Menopausal status:	
Premenopausal	32
Postmenopausal	26
Pathological stage:	
Tumour (pT):	
pT1a	5
pT1b	15
pT1c	20
pT2	15
pTx	3
Node involvement (pN):	
pNo	45
pN+	13
Histology:	
DCIS	3
IDC	32
ILC	13
others	10
Grading:	
G1	10
G2	28
G3	20
EIC present	15
Receptor status:	
Positive	48
Negative	10
Surgical margin:	
Clear	29
Close < 2mm	18
Positive	8
Not available	3

DCIS: ductal carcinoma in situ; IDC: infiltrative ductal carcinoma; ILC: infiltrative lobular carcinoma; EIC: extensive intraductal component

METHODS

Treatment procedure

Surgery

All of the patients underwent BCS, of which there was: tumourectomy, lumpectomy, quadrantectomy with 15, 16 and 27 patients, respectively. During surgery, the margins of the excision cavity were marked with 2 to 6 titanium clips. Axillary dissection was performed in all patients with cancer stage I and II. Five of the patients underwent re-excision in an attempt to achieve a clear margin. A total of 18 of the cases reported the final margin status at less than 2 mm. The data of six patients were ultimately documented with a focally positive margin.

EBRT

All patients received EBRT to the entire breast using wedge tangential 6 MV photon fields. Three schedules of external beam radiotherapy (EBRT) were applied before patient admission to the Department of Brachytherapy (Table 2). For patients with negative axillary lymph nodes (pN0) or with metastasis < 2mm (pN1a), regional nodal ir-

Table 3. Description of applications

Number of applications	Total	58
Number of applicators	Median	7
	Range	3–12
PTV [cm^3]	Median	57.38
	Range	15.77–177.48
Reference Dose [Gy]		10
Optimization	Manual	23
	On reference points	29
	Geometrical	5
PTV – planning treatment volume		

radiation (RNI) was omitted. The remaining patients received RNI by an anterior supraclavicular/axillary field on account of risk of subclinical involvement of regional lymph nodes. After receiving EBRT with one to a few days' break, the brachytherapy boost treatment was delivered.

HDR-BT

The HDR-BT was preferred as a boost particularly for a deeply seated tumour bed in large volume breasts (deeper than 10 mm under the epidermis) and in cases of high risk of local recurrence (close or positive surgical margin with EIC present). During the procedure after breast conservation surgery the patients were subjected to tumour bed implantation with a flexible implant, guided by an individually created template for each patient, based on the patient's breast volume and tumour characteristics. An example of the procedure is presented in Figure 2. Two sets of pre- and post-implant CT scans were performed. The HDR-BT was delivered with an HDR Microselectron unit. A dose of 10 Gy was given in one fraction.

Indications for interstitial HDR-BT were as follows: 1. Interstitial HDR-BT of the primary tumour site after breast conserving surgery and/or chemotherapy and WBRT. 2. Interstitial HDR-BT of the primary tumour bed after neoadjuvant chemotherapy, BCS in the high risk group for local recurrence group and WBRT.

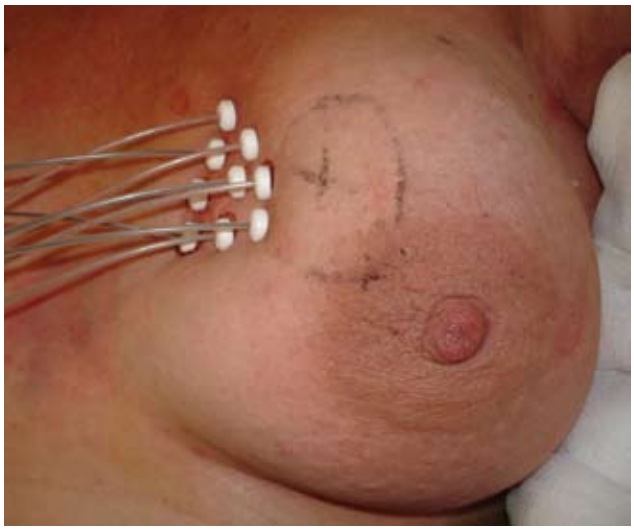

Fig. 2. Interstitial applicators inserted into breast, 9 applicators visible

Contraindications for interstitial boost irradiation included: 1. multicentric breast cancer; 2. Paget's disease alone or in association with a breast lump; 3. superficially located tumour bed in small breasts; 4. lack of patient agreement and preference for EBRT boost method.

Systemic therapy

Adjuvant chemotherapy consisted of AC (adriamycin-cyclophosphamide) in 33 of the patients, CMF (cyclophosphamide-methotrexate-5 FU) in 8, neoadjuvant chemotherapy according to AC programme in 2 of the cases, respectively. A total of forty-eight patients received adjuvant hormone therapy.

CT-based treatment boost planning – target volume delineation

Every individual case of BT target volume was based on combined information from the pathologic evaluation (factors considered included excision specimen size, tumour location within the resected specimen, characteristics of surgical margins, histological type) mammographic and ultrasound findings, clinical examination (scar position, size and location of any palpable seroma), localization of surgical clips, as well as CT pre-implant cross-sectional imaging (both exact visibility of titanium clips and borders of the slice to slice excision cavity). The clinical target vol-

ume (CTV) was defined by a margin of 2 cm of breast tissue of the primary tumour, since this area contains 80% of the microscopic tumour extensions. The planning target volume (PTV) was comparable to the CTV for the reason that extra margin added in case of organ motion or set-up errors is not required in interstitial BT. The CTV of boost irradiation was not focused on such critical structures as the ribs and breast skin with tissues beyond the fascia such as thoracic wall muscle. The minimum distance from the PTV to skin and underlying ribs was 10 mm. This helped to define the dimensions of the boost volume, as well as the choice between electron beam boost and interstitial implants.

Technique of implantation

BT catheter placement and treatment delivery were conducted on an outpatient basis. Equipment used in implantation included: 16–20 cm long implantation needles (guide needles), templates in different sizes (channels in square or triangular arrangement and with distances of the channels in the range 12–20 mm) depending on the thickness of the breast (the thicker the breast, the larger the template and spacing used), ruler for measurement of the skin distance, plastic tubes, and buttons to immobilize inserted catheters. The treatment procedure was performed under general anaesthesia. The patient was placed in a supine position with ipsilateral arm in 90 abduction. Once the PTV was defined, the implant geometry was designed according to the rules of the Paris System:

1. Needles were implanted parallel and equally distant from each other. The direction of implant depended on tumour cavity localization and it was selected in such a way as to enable adequate PTV covering and at the same time to avoid overlapping of source positions in critical structures (minimum 1 cm distance from critical structures was taken into account). In most cases, the needles were inserted in a lateral-medial direction. When the PTV localization was in the upper outer quadrant, 45-degree angle needle implantation was frequently applied.

2. Needles in two planes were usually required to cover the PTV procedure. A single plane was sufficient in the case of flat breast target thickness of less than 12 mm. Three planes were required in a large breast target thickness of more than 30 mm. In the case of implantation on two or more planes, needles were disposed either in a triangular or a square pattern. Moreover, the triangular configuration was better adopted to follow the breast skin contour whenever the PTV was placed close to the skin.

3. The first needle (the so-called guidance or reference needle) was placed within the deepest place of the tumour bed and in the centre of the lowest level of the implant. The rest of the needles were inserted in order to adequately cover the PTV. To ensure that the following needles would be implanted parallel and equally distant from each other, an appropriate size template was placed over the guidance needle. Number and spacing between template size needles was chosen to cover sufficiently the width and the thickness of the PTV. Guide needles were replaced by plastic tubes immobilized by buttons at both sides of the breast.

4. Positioning verification of the plastic tubes with the help of the CT unit. A CT post-implant scan was performed every 3 mm during the procedure and transferred directly to the PLATO System. The CT-based planning allowed surgical clips to be localized and a sufficient distance to be maintained between implant tubes and overlying skin and underlying ribs. In our study after the pre-implant simulation 3 to 14 (mean 7) guide needles were inserted into the previously targeted area in a triangular or square setting with template guidance. Single, double and triple plan implant was performed in 6, 40 and 20 cases, respectively. We used three methods of dose optimization: manual – 23 cases; on dose points – 29; and geometrical – 5 of the patients.

CT-based treatment planning procedure

3D treatment planning based on a CT cross-sectional image was performed in all cases. The main aspect of our practice was to achieve such dose distribution that all surgical clips would receive at least 85% of the prescribed dose. Our planning concepts were based on the 3D reconstruction of the catheters, tumour bed clips maintaining proper distances (at least 10 mm) from critical structures

(skin, ribs). Some examples of 3D treatment plans are presented in Figures 3–7. The active source positions, dwell times and reference dose points were defined individually in each catheter as well as dose optimization. To avoid skin and rib injury, the most peripheral active source positions were kept at a minimum of 10 mm distance from the skin and rib surface.

Follow-up and treatment assessment

All patients completed the boost treatment and were placed on follow-up (operating for over a year). The first control visit was one month after completion of the BCT procedure. Subsequent visits were scheduled once every 3 months until the end of the first year of follow-up. During the visits, certain important factors were evaluated such as: local control

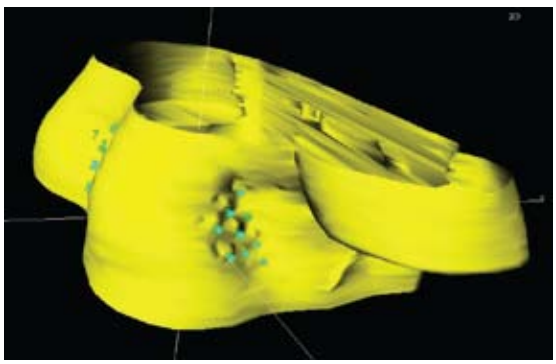

Fig. 3. 3D imaging of chest and interstitial applicators. Yellow colour – chest contour

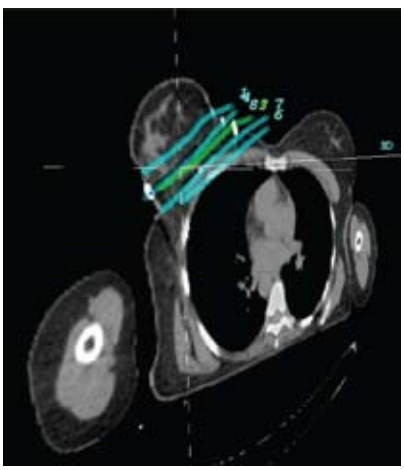

Fig. 4. TK image with applicators (blue and green colour) before planning – first stage

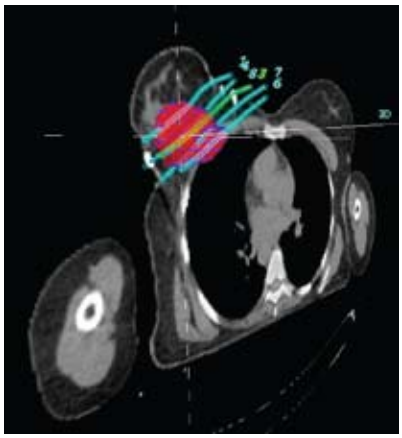

Fig. 5. TK image with applicators (blue and green colour) – after optimization (blue points), red colour – reference isodose

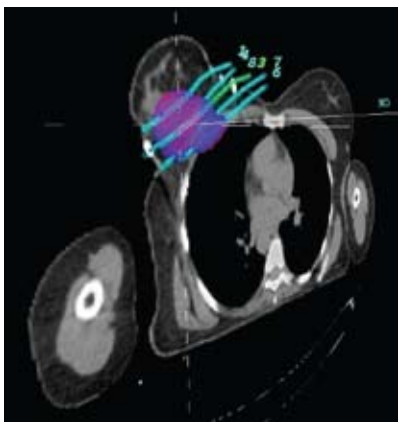

Fig. 6. The same image as Fig. 5, dwell-steps visible

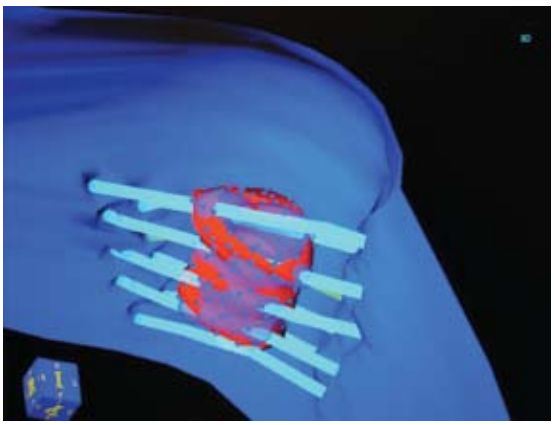

Fig. 7. 3D image of treated target (tumour bed with margin) – red colour

(LC), disease-free survival (DFS), cosmetic result and quality of life according to the general questionnaire EORTC Q-30 and the module EORTC QLQ-BR-23 specific for breast cancer. Tumour control was assessed by clinical examination, serum biochemistry, radiological investigations (annual X-ray, abdomen USG, mammogram – the first time six months after completion of BCT). Cosmetic result was scored objectively by the treating physician and subjectively by the patient. Clinical examination and taking a photograph of the patient's breasts were the basis for the objective cosmetic evaluation. The overall cosmetic outcome was scored according to the scale: excellent (perfect symmetry, no visible distortion), good (slight distortion of nipple/skin with visible telangiectasia and mild hyperpigmentation), acceptable (moderate distortion, breast asymmetry, moderate hyperpigmentation, prominent skin retraction or telangiectasia), poor (marked distortion of nipple, breast asymmetry, oedema, fibrosis, severe hyperpigmentation).

RESULTS

Preliminary results are promising. None of the patients have experienced local relapse to date and local control in this study was achieved in 100%. Only one patient developed a distant metastasis during follow-up and subsequently received appropriate palliative RT along with second line chemotherapy (at the time of this report the patient is still alive). Acute toxicity including transient erythema, breast swelling and skin reaction at the needle puncture sites was healed subsequently with conservative treatment. None of the patient experienced local infection. However, after removing catheters, two patients acquired breast haematoma. So, in order to avoid late toxicity some cases required longer follow-up.

In the analysis of conformity of the PTV and treated volume we involved the use of: cumulative dose-volume histograms (DVH), high dose volumes calculation (V150%, V200%, V300%) as recommended by ICRU Report 58 [26], the mean volume encompassed by the 100% reference isodose surface (V100%), the dose uniformity ratio (DNR), defined as the ratio of the 150% high dose volume (V150%) to the 100% reference dose volume (V100%), conformity index (COIN), optimization of dose distribution (three methods of optimization: manual, on reference points, geometrical). Results of evaluated parameters are presented in Tables 3–4.

DISCUSSION

BCT has become widely accepted in the last decades as the treatment of early invasive breast cancer [1–3]. The rationale of boosting the primary tumour bed up to 60–70 Gy is based on evidence that the majority (50–80%) of local recurrences appear in or close to the same quadrant where the primary tumour was located [8, 9]. A clear dose-local control relationship for doses > 45 Gy was found by several authors [3, 8, 13, 19, 22, 24, 27, 28]. Institutional experience and a large randomized trial suggested improved local control which resulted from boosting the area of the tumour bed with an adequate safety margin (Table 5). However, the precise indications for boost irradiation are not well established. Factors including insufficient surgical margins, young age, unfavourable histopathologic criteria such as EIDC, high grade of malignancy, tumour necrosis and endolymphatic extension were described as the predisposing circumstances to develop local recurrences [14, 15, 16]. Re-excision is considered in the case of negative margins measuring less than 2 mm and focally positive margins. Whenever

Table 2. Treatment strategy

Treatment strategy	Number of patients
Surgery:	
Tumourectomy	15
Lumpectomy	16
Quadrantectomy	27
WBRT (total dose in Gy, dose per fraction, number of fractions)	
42.5 / 2.5 / 17	30
45 / 2.25 / 20	20
50 / 2 / 25	8
Regional nodal irradiation	10
Adjuvant Chemotherapy	45
Adjuvant Hormone therapy	48

Table 4. Physical factors appraised in treatment plan

	Mean	SD	Range
D90	8.64	1.68	0.93–10.74
D100	4.30	1.68	0.50–8.33
V100	82.04	1.68	41.96–95.24
V150	42.98	1.68	10.04–60.90
V200	21.38	8.14	10.53–37.79
V300	7.90	3.03	3.74–17.27
DNR	0.52	0.11	0.14–0.68
C1	0.82	0.09	0.43–0.95
C2	0.82	0.07	0.63–1.00
COIN	0.83	0.10	0.33–0.87

D90 – the dose value which covers 90% of PTV volume [Gy]
D100 – the dose value which covers 100% of PTV volume [Gy]
V100 – the mean volume encompassed by the 100% reference isodose surface (V100%)
V150 – the mean volume encompassed by the 150% reference isodose surface (V100%)
V200 – the mean volume encompassed by the 200% reference isodose surface (V100%)
V300 – the mean volume encompassed by the 300% reference isodose surface (V100%)
DNR – the dose uniformity ratio defined as the ratio of the 150% high dose volume (V150%) to the 100% reference dose volume (V100%),
C1 – the fraction of PTV that is enclosed by the reference dose
C2 – the fraction of reference dose volume that is covered by PTV
COIN – conformity index

additional surgery is not considered appropriate, a boost dose even up to 20 Gy should be delivered either with electrons or interstitial BT. The optimal boost technique (electron vs. brachytherapy) and its impact on local tumour control and cosmetic result [15, 28, 31, 32] is creating some controversy. Based on the results of numerous retrospective and recently published forthcoming trials, the European Brachytherapy Society (GEC-ESTRO) and the American Brachytherapy Society (ABS) have issued their guidelines regarding these subjects [33, 34], which will help clinicians in their medical decisions. In the generally accepted treatment plan all patients should be routinely boosted where the 5-year local recurrence rate after BCS and whole breast RT is assumed to be > 5%. This high risk subset of patients involves all women aged less than 50 years, with a positive or close resection margin, and with EIC. Moreover, demarcation of the excision cavity by intraoperative clips should be routinely used as a minimum requirement for target volume definition. The ABS also published their guidelines specifically for selective use of BT as a boosting technique where delivering the boost irradiation with electrons can be problematic (large breasts, deep tumour location, worse prognostic factors including close, positive, or unknown margins, EIC, and young patient). Interstitial BT offers a conformal dose delivery method with the ability to reduce the dose of unwanted irradiation to the skin and ribs. Satisfactory results of local control and positive cosmetic outcome were documented in performing this technique. The advantages of HDR brachytherapy include: outpatient treatment, control of patient positioning in order to ensure accuracy of treatment delivery, ability to optimize dose distribution, improvement in staff protection during radiation, much smaller and more conformal irradiated volume to the target volume due to the rapid dose fall off [15, 33–36]. It is known from clinical practice that deeply seated target volumes can be covered more accurately by interstitial implants than by electron beams. The latter method is not only associated with larger treatment volumes, resulting in higher rate of breast fibrosis, but also results in an

Table 5. Results of prospective breast boost trials

Trial	Number of Patients	Median FUP years	Boost dose (Gy), technique	Crude LR % – boost vs no boost	5-years actual LR % – boost vs no boost	5-years RFS % – boost vs no boost
Uzsoki Hospital [29]	111	3.8	10-20 (BT)	5.4 vs 10.7	NR	NR
Nice Hospital[30]	664	6	10 (EBRT)	4.3 vs 6.8	NR	NR
Lyon Hospital [8]	1024	3.3	10 (EBRT)	1.9 vs 4.0	3.6 vs 4.5	86.0 vs 82.2
EORTC [28]	5318	5.1	15-16 (EBRT/BT)	4.1 vs 6.8	4.3 vs 6.8	NR
Budapest Hospital [17]	207	4.8	12-16 (EBRT/BT)	6.7 vs 14.6	8.0 vs 15.7	79.5 vs 67.3
All	7324			3.9 vs 6.7		

FUP: follow-up period; LR: local recurrence; RFS: relapse-free survival; EBRT: external beam radiotherapy (electrons); BT: brachytherapy; NR: not reported; EORTC: European Organization for Research and Treatment of Cancer

increased rate of telangiectasia due to a higher skin dose. Applying the useful boost range concept, van Limbergen et al. calculated that the critical depth for the target volume where the interstitial implant has a definitely better ballistic selectivity compared to electron boost is 28 mm [15, 34]. It is most advisable to perform the electron boost in cases of superficial and peripheral localizations of the tumour bed. Advantages and disadvantages of different boost methods are summarized in Table 6. Adequate definition of the target volume is the crucial point in using any boost technique. The boost PTV is usually defined with a 2 cm safety margin of the tumour bed. In the past, only palpation, mammograms, surgical reports and scars were available landmarks to localize the excision cavity. Nowadays, there are several methods to maintain better coverage of the target volume. The authors of scientific publications have used ultrasound (US) examination to localize the tumour bed. DeBiose et al. emphasized that US was indeed an appropriate method for boost target definition, but only in the first 6–8 weeks after surgery [36]. Rabinovitch et al. prospectively compared the precision of different methods in a TV definition [37]. His study revealed that the ultrasound examination significantly underestimated all three dimensions of the excision cavity. Furthermore, in his general conclusion he indicated the radiographic evaluation of surgical clips to be superior to US in defining the lumpectomy cavity. Some of the authors in their research delivered the HDR-BT boost using Iridium-192 implants at the time of surgery, but before WBRT [38]. The advantage of this modality is the possibility of placing the catheters more accurately into the tumour bed. However, the limitation of this procedure is the lack of detailed histological information at the time of implantation. An intraoperative implantation demands good collaboration and time management between the surgeons and radiation oncologists. The majority of authors have suggested the best orientation given by titanium clip markers that are implanted intraoperatively [15, 24, 37]. Placing 6 clips into the walls of the excision cavity according to latero–medial, antero–posterior, inferior and superior dimensions seems to be the ideal approach. However, the titanium clips do not alter the dose distribution during RT or the quality of diagnostic MR images after the procedure. The irregular 3 dimensional (3D) shape of the target volume and the normal tissue structures can only be correctly localized on the basis of visual information obtained from cross-sectional CT imaging. In addition to this, better local control rate with fewer side effects might be achieved with these techniques based on CT imaging [24, 34, 35,

Table 6. Advantages and disadvantages of different boost methods [9]

Treatment option	Personal time	Volume	Total dose (Gy)/ Fraction/ Time	Side effects	Comments
BT:					
LDR	+++	+	25 / 1 / 2d	+	Application time: days
PDR	+++	+	25 / 50 / 2d	+	Application time: days, biologically comparable to LDR;
HDR	++		10 /1 / min	+	Application time minutes, assumed high biological risk, geographical mistake risk
Intraoperative catheters placement		See LDR and HDR, PDR			Histological criteria for boost indications at time of surgery in part not available
EBRT:					
Electrons	+	++/ +++	10–20 / 5-10 / 5–10d	++	High rates of side effects in deeply seated tumour bed – increased risk of induration, shrinkage, telangiectasia;
Photons	+	++/ +++	10–20 / 5-10 / 5–10 d	++ ++	High integral dose, duration treatment prolonged;
Intraoperative electrons	+++	++/ +++	10–20 / 1 / min		Histological criteria for boost indications at time of surgery in part not available

LDR: low dose rate; PDR: pulsed dose rate; HDR: high dose rate

39]. The combined use of surgical clips and CT or MRI appears to be the best method to determine the target volume, since both titanium clips and borders of the excision cavity can be visualized exactly from slice to slice. Recently Vicini et al. and Polgar et al. implemented 3D virtual brachytherapy based on two sets (pre- and post-implant) of CT scans. In their research, the 3D BT showed excellent agreement in target volume coverage between the pre-planned virtual implant geometry and the actual positioning of the final afterloading needles [40, 41].

Three dimensional (3D) treatment planning has made promising progress in the last decade of radiotherapy. Currently, conformal 3D EBRT is a permanent part of routine clinical work in most radiotherapy departments. Moreover, 3D brachytherapy treatment planning has recently become the centre of interest.

The advantages of conformal brachytherapy boost treatment planning in the management of breast cancer are as follows: 1. as a useful tool helping to avoid geographical miss, 2. the irregular 3D shape of the target volume and the normal tissue structures can only be localized correctly on the basis of visual information obtained from cross-sectional CT-imaging (better local control rate with fewer side effects might be achieved with these technique based on CT imaging), 3. the primary role of the treatment planning and dose optimization for a given implantation is to achieve as good coverage of the target volume as possible (adequate homogeneity is relatively important), 4. verification of the positioning of the plastic tubes with the CT unit [42–44]. With CT-based planning, the distances between implant tubes and overlying skin and underlying ribs are directly visible and measurable. The skin dose should not exceed 60% of the prescribed dose (executed only in the case of a superficial plane implanted at least 10 mm from the skin).

Overall, a boost after whole breast irradiation was reported to improve local tumour control in breast conservation therapy. Its efficacy is quite likely to correlate with tumour characteristics, type of surgical procedure, status of resection margin, as well as technical details of irradiation. Preliminary results along with recently developed boost techniques (IORT,

CT-image based 3D conformal BT and 3D virtual BT) are quite promising. However, more experience and longer follow-up are required in order to define whether these methods might improve local tumour control for breast cancer patients treated with BCT.

The majority of local recurrences appear in close proximity to the tumour bed; therefore the necessity of WBRT was questioned and several centres evaluated the feasibility and efficacy of tumour bed irradiation alone. Partial breast irradiation (PBI) using HDR-BT is an attractive treatment approach in a group of patients with low risk of local recurrence (T1, T2, N0, > 40 years old).

CONCLUSIONS, CONTROVERSIES, AND FUTURE PROSPECTS

1. The results of numerous retrospective and some prospective studies suggest that boost dose increases LC (local control) for a patient treated with BCT. 2. Young age, positive or close surgical margins, and EIC should be regarded as absolute indications for boost irradiation. 3. Interstitial BT boost can be applied in BCT with low incidence of late side effects and with at least similar LTC as percutaneous boost techniques. Furthermore, BT is preferable in certain anatomical situations, especially in cases of a deep-seated tumour bed in large volume breasts. 4. Two sets (preimplant and post-implant) of CT scans are required to improve the implant quality. 5. The use of appropriately placed surgical clips to demarcate the tumour bed and the use of imaging techniques such as computed tomography and ultrasound may substantially increase the accuracy in determining the boost volume. In addition, it intensifies the probability of local tumour control as well as reducing undesirable cosmetic results. 6. The external electron beam boost usually includes the skin and the subcutaneous vessels; nevertheless, the interstitial implant represents the more conformal technique, which offers lower rates of late side effects, particularly in skin telangiectasia and skin fibrosis. 7. Preliminary results with recently developed boost techniques based on CT-image 3D conformal BT (IORT, CT-image based 3D conformal BT, and 3D virtual BT) are encouraging. However, longer follow-up and more scientific experience in this matter are required to state whether these methods might improve local tumour control for breast cancer patients treated with BCT.

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