



## Original article

## ESTRO-ACROP guideline: Interstitial multi-catheter breast brachytherapy as Accelerated Partial Breast Irradiation alone or as boost – GEC-ESTRO Breast Cancer Working Group practical recommendations

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## ABSTRACT

**Purpose:** This consensus statement from the Breast Cancer Working Group of Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO) aims at generating practical guidelines for multi-catheter image-guided brachytherapy in the conservative management of breast cancer patients used for either Accelerated Partial Breast Irradiation (APBI) or for a breast boost. **Methods:** Recent advances in techniques of multi-catheter brachytherapy were summarized and all the relevant literature was reviewed by a panel of experts. Panel members of the GEC-ESTRO experts participated in a series of conferences, supplemented their clinical experience, were surveyed to determine their current practices and patterns, performed a literature review, and formulated recommendations for implementing APBI with multi-catheter brachytherapy, focusing on treatment planning issues, catheter insertion, dosimetry and quality assurance. This document was reviewed and approved by the full panel, the GEC-ESTRO executive board and by the ACROP (Advisory Committee on Radiation Oncology Practice).

**Results:** Three-dimensional (3D) treatment planning, catheter insertion techniques, dosimetry and methods of quality assurance for APBI and boost with multi-catheter image-guided brachytherapy after breast conserving surgery are described. Detailed recommendations for daily practice including dose constraints are given.

**Conclusions:** Recent standards and guidelines for the use of APBI with different multi-catheter image-guided brachytherapy techniques have been defined. Different techniques are used to insert the catheters. Guidelines are mandatory to assure precise catheter insertion for coverage of the target volume and to guarantee high-quality dosimetry. The same rules apply for brachytherapy based boost irradiation for breast cancer after whole breast irradiation as well as for partial breast re-irradiation.

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Interstitial multi-catheter brachytherapy in the context of breast conserving therapy (BCT) represents one of the most highly published irradiation techniques for Accelerated Partial Breast Irradiation (APBI) alone, Salvage-APBI and Boost after whole breast irradiation (WBI) [1–4]. Generally, this technique delivers a high-dose to a precise, strictly limited in-breast target volume, avoiding to the greatest possible extent, exposure of adjacent organs at risk

(OARs) thus resulting in excellent local control with low rates of side effects [1,5–12]. To date, APBI using multi-catheter brachytherapy is the only method of breast irradiation with a treatment duration of merely 4–5 days with level 1 evidence showing it to be a valid treatment alternative to WBI after breast conserving surgery (BCS) for low-risk breast cancer patients which is used in clinical routine [1,4,9–12]. Sole APBI based on multi-catheter brachytherapy is intended first to shorten treatment duration compared with the WBI regimen (40–50 Gy over 3–6 weeks) and second to reduce late side effects to OARs such as the heart,

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lung and skin while achieving similar rates of local control, disease-free survival and overall survival. As a consequence, sole APBI with multi-catheter brachytherapy is also a unique treatment technique for re-irradiation after re-excision (Salvage-APBI, Accelerated Partial Breast Re-Irradiation – APBrI) after previous BCS and WBI with an exceptionally low rate of side effects and with local recurrence rates comparable to salvage mastectomy alone [2].

Recently, guidelines for patient selection and target definition for APBI after both breast conserving closed and open cavity surgery as well as dose recommendations according to risk factors were provided by the Breast Cancer Working Group of GEC-ESTRO [13–15]. Similar guidelines for patient selection were also published by numerous USA societies [16–18]. Guidelines for treatment planning using different techniques for APBI were provided by the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39/Radiation Therapy Oncology Group (RTOG) 0413 Protocol [19]. The NSABP B-39 protocol included criteria for target coverage as well as for sparing OARs.

The aim of this consensus statement of the GEC-ESTRO Breast Cancer Working Group is to generate detailed practical guidelines for APBI, boost after WBI or APBrI with multi-catheter image-guided brachytherapy for the conservative management of breast cancer patients in daily practice.

## Methods

The authors evaluated the relevant literature, identified established and controversial topics via working conferences, circular emails, meetings, conference calls and supplemented this information with their clinical experience to formulate the current guidelines. A consensus decision was made to incorporate strategies using 3D image guidance for interstitial brachytherapy based APBI. Specific commercial equipment, instruments, and materials are described only when necessary. Such identification does not imply recommendation or endorsement by the presenter nor imply that the identified material or equipment is necessarily the best available for these purposes.

This report document was reviewed and approved by the full panel, the GEC-ESTRO executive board and by ACROP.

## Results

### Technical recommendations

#### General issues related to multi-catheter HDR-/PDR-brachytherapy

We recommend that APBI with image-guided multi-catheter brachytherapy after breast conserving surgery (BCS) should be completed preferably in less than 12 weeks and no longer than 20 weeks, as better local tumour control and survival can probably be expected than with a longer time frame [20–27]. Nevertheless a recent analysis illustrated that starting of radiation therapy shortly after BCS seems not to be associated with a better long-term outcome [28]. In Europe, the most common HDR-brachytherapy regimen used for APBI prescribes 2 fractions per day for a total of 7–10 fractions.

Patient selection for APBI alone after BCS in patients with early breast cancer should be performed according to the GEC-ESTRO- or the ASTRO guidelines [13,29]. The GEC-ESTRO panel of members holds the view that until the results of the NSABP B-39/RTOG 0413 APBI trial are available, GEC-ESTRO selection criteria should remain unchanged, particularly because current published data of phase 3 trials [1,11,30–33] so far do not allow one to analyse corresponding subgroups of interest. As far as patient selection criteria for APBrI, we suggest using the criteria as published by Hannoun-Levi et al. [2]. Furthermore we advise using criteria as

analysed and described previously for patient selection for boost [34–38].

Furthermore we advise defining the target in accordance with current published guidelines [14,15].

### Treatment planning and catheter insertion

Pre-implant treatment planning may be performed either in a separate procedure as in a pre-plan approach, or on the day of the procedure in the operating room as intra-operative preplanning. Whatever the pre-implant treatment planning and mode of catheter insertion as listed below, the following information must be available at the time of preplanning and at the time of catheter insertion: surgical report, pathological report including size of resection margins in 6 directions, knowledge about number and position of surgical clips, images of preoperative mammography, ultrasound and, if necessary, magnetic resonance imaging (MRI).

The standard procedure for catheter insertion is to use a transcutaneous approach usually in week 4 to 12–20 after BCS under computed tomography (CT) or ultrasound (US) or X-ray monitoring and template guidance (if needed). According to the Paris System, a square or triangular arrangement is reasonable [39]. Boost brachytherapy should follow WBI as soon as possible within 4 weeks depending on the extent and grade of skin inflammation after WBI. Patient positioning should coincide with the pre-implant planning study as closely as possible when a preplan approach is used. If US equipment is used a high-resolution system is recommended. When the surgeon leaves the cavity open, the seroma can easily be identified during needle insertion [40], and thus the needles cover the shape of the cavity (Image-guided Brachytherapy). After closed cavity surgery, a pre-implant CT with radiopaque marks on the skin scar and nipple is useful in order to locate the surgical scar and/or the clips. If no clips are in place and a surgical scar cannot be identified, a CTV is difficult to define so an APBI or boost cannot be easily and securely performed. Fluoroscopy (as X-ray based guidance) as a complementary imaging modality can only be used if surgical clips are present.

### CT-based pre-implant treatment planning and insertion of catheters after open cavity surgery

According to timing and number of CT imaging, various policies exist, but the catheter positions are always determined using the 3D rendering of the target volume and patient anatomy. Planning the catheter positions can be done using a plastic template on the breast during pre-implant CT imaging [41,42]. Then, using 3D rendering of patient anatomy and virtual simulation the appropriate catheter positions can be defined. A few needles (e.g. in deep plane – close to the thoracic wall) can be inserted freehand, and the remainder with a template. The template is made of plastic; it has two plates with holes arranged in regular geometry with a triangular pattern. The distance between the holes is between 12 and 20 mm (Fig. 1). Ideally, two CT image series (pre-implant and post-implant) are used for the implantation and treatment planning [41,42]. First, one day before implantation a CT-compatible plastic template is placed over the breast skin taking into account the scar position on the skin and other relevant clinical information about the tumour location. Distance between the template plates is recorded and their positions are marked on the skin. Pre-implant CT imaging is performed, the cavity is outlined in axial slices, and the target volume is created according to the contouring protocol. Using 3D rendering in the treatment planning system, the patient's image data are then rotated to the “needle's eye view”, i.e. viewing in the direction of the needles, and the target volume is projected on to the rendered template with the holes (Fig. 2). By visual inspection the holes covering the target volume are identified, and their coordinates are recorded. On the following day, another more rigid template,



Fig. 1. Template-based insertion of needles and replacement with plastic catheters.

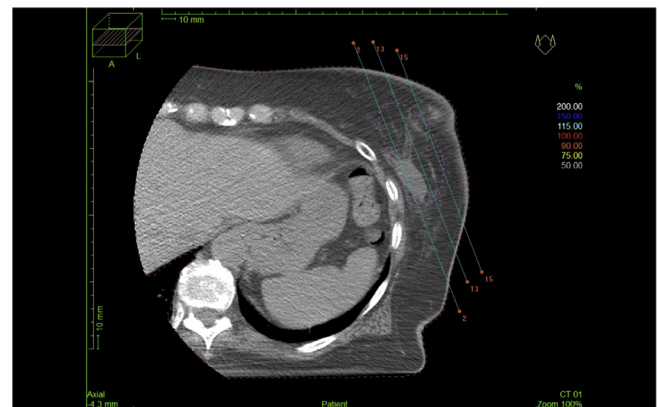
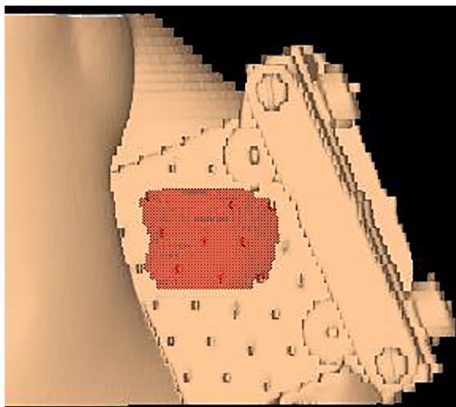


Fig. 2. Three-dimensional rendering of patient surface and template in needle's eye view showing the target volume projected to one of the plates of the template.

which is geometrically identical to the first one, is placed in the same position as the day before using the skin marks and template parameters as guides. Then, using the predefined coordinates the needles are inserted into the breast and later replaced with plastic catheters. Another CT data set is acquired for treatment planning and the target volume definition with organs at risk [14,15]. Where no appropriate target coverage is detected, a few additional catheters should be implanted by free hand – without use of a template. Obviously, in this case new CT imaging is required for planning.

#### CT-based pre-implant treatment planning and catheter insertion after closed cavity surgery

In case of closed-cavity surgery, the pre-implant CT-scanning procedure is the same as in the open cavity situation presented above. While the target volume is outlined and checked in the three main views (axial, coronal and sagittal), the physician places virtual vectors in order to cover the target volume properly leaving 12–20 mm between vectors and planes (Fig. 3). Then, the virtual implant 3D reconstructions, including sagittal and frontal views, are printed (with specific measures helping vector placement); specific breast skin marks are drawn at the entry and exit points of vector placement (Fig. 4).

#### Ultrasound based pre-implant treatment planning and catheter insertion after open cavity surgery

Before brachytherapy, all patients should undergo a CT scan to identify the surgical bed, the clips [14,15] and, in an open cavity

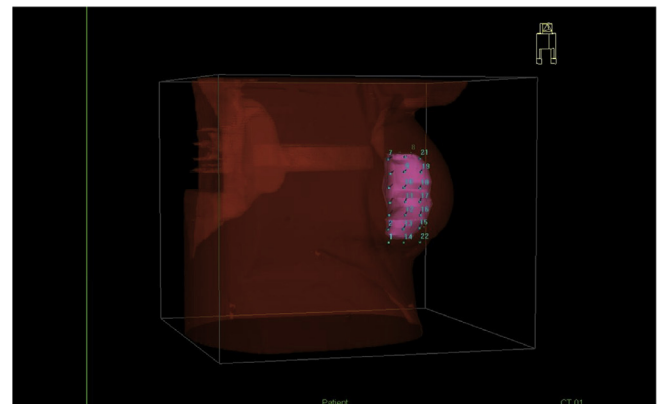


Fig. 3. Pre-implant virtual vectors in order to cover properly the PTV.

case, the seroma and the skin scar. With the aid of US, it is useful first to inject the radiological contrast agent (dilute barium) into the existing surgical cavity, so that it is easy to identify this cavity any time with US, CT or X-ray. When inserting metal implant needles, we recommend using US to check each needle position in relation to the seroma. The deepest implant plane should be dorsal the seroma and the most ventral between the skin and the seroma. Special care must be taken that the needles are positioned at a distance of at least 1 cm from the skin to avoid late skin side effects. When the seroma is completely surrounded by needles, the needles are replaced by plastic catheters and the insertion procedure is finished. Finally, the symmetry and parallelism of the implant should be checked with the US probe.



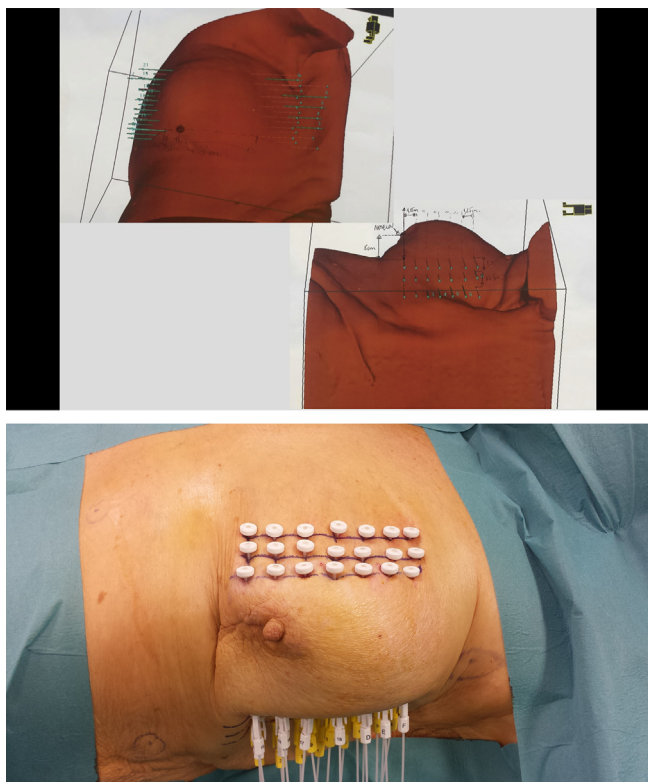


Fig. 4. 3D reconstructions of the virtual implant used before vector placement.

#### Ultrasound based pre-implant treatment planning and catheter insertion after closed cavity surgery

After closed cavity surgery it is not easy to detect the surgical bed with US. Nevertheless it is often possible to visualize some areas of the surgical scar that can be seen as white tracts instead of the dark normal lobular structure of the breast (Fig. 5). As opposed to this chest wall and ribs are easily identified. Before catheter insertion a clinical assessment of the CTV-position is

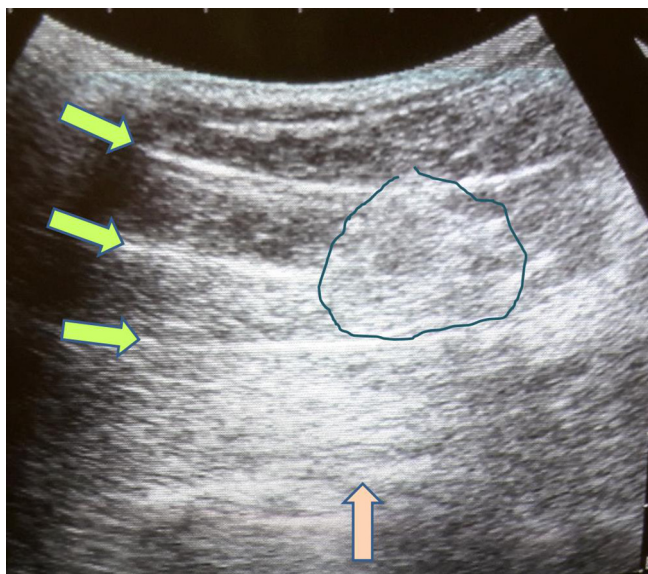


Fig. 5. US view in a closed cavity case, with three plastic tubes and a white area corresponding to the absence of lobular normal tract due to the surgical scar. The chest wall is also well defined.

required, by means of palpation (if possible), locating the quadrant with the help of cranio-caudal and oblique mammograms considering the relative distance to the nipple, and the description by the surgeon. The implant depth and plane levels should be chosen while inserting the needles. The distance of needles to the skin can be measured steadily taking care not to press too hard on the skin with the probe. Before the insertion of the first implant needle, the estimated position and area of CTV must be projected and drawn on the skin and also visualized continual with US to confirm appropriate, precise and definitive implant volume.

#### X-ray based pre-implant treatment planning and catheter insertion after closed cavity surgery

An important precondition for X-ray guided catheter insertion is, that the resection margins of the surgical bed inside the breast are labelled with surgical marker clips (at least 4, ideally 6 clips), which are easily distinguished with a C-arm X-ray-device or with CT.

With simultaneous consideration of the surgical scar on the skin and of the deepest part of the surgical scar inside the breast (surgical clips), the radiation oncologist can project the surgical bed on to the skin and define the target volume inside the breast. The first step in the insertion of plastic catheters is the insertion of the guide needle (Fig. 6). The insertion point of the first (guide) needle and desired direction of the insertion should first be marked on the skin (CT- or C-arm guided) and should guarantee that the position of the guide needle corresponds to the deepest point dorsal the centre of the surgical bed. The guide needle usually represents the centre of the deepest plane of the whole implant. In addition, during this first step as well as during the whole insertion procedure, it is important to take into account not only the position of the clips the surgical scar inside the breast and the skin scar but also the location of the tumour inside the breast as shown in the preoperative imaging. After insertion of the guide needle, we recommend that a template of appropriate size is taken over the guide needle in order to guarantee that all the following needles will be inserted parallel and equidistant to the guide needle, which makes it easier to meet quality parameters. The appropriate size of the template also allows the tumour bed and the surgical scar inside the breast to be encompassed with an adequate safety margin [14] in all directions. An acceptable alternative is free-hand insertion of catheters (without template) which is safe in experienced hands. Thus, the corresponding number of needles will be implanted, the position of needles in relation to the surgical scar verified with CT or C-arm and as a final step the needles are replaced by plastic catheters (Fig. 1).

#### Intraoperative insertion of catheters

Here the surgical bed is well defined, because the cavity is at time of catheter insertion still open and the surgeon or the radiation oncologist can point to the exact former position of the removed tumour to insert the first catheter. The catheters are inserted immediately as the lumpectomy is performed. Metal clips (cranial, caudal, ventral, dorsal, medial, lateral) mark the surgical bed, that is, the area of the tissue removed by the surgeon. Although the tumour location inside of surgical bed can be eccentric, the perioperative procedure allows consider exactly this fact. As consequence the central needle should be considered as the reference needle to define the position of the tumour bed ("guide needle"). All needles can be inserted using a template or free-hand as the surgical cavity is still open, or the surgeon can close the cavity and skin after inserting the "guide needle". The next parallel needles are inserted to create the 2-3 planes around the guide-needle. As soon as the insertion of all needles is finished, the needles are replaced by plastic catheters, and secured on both sides with buttons.

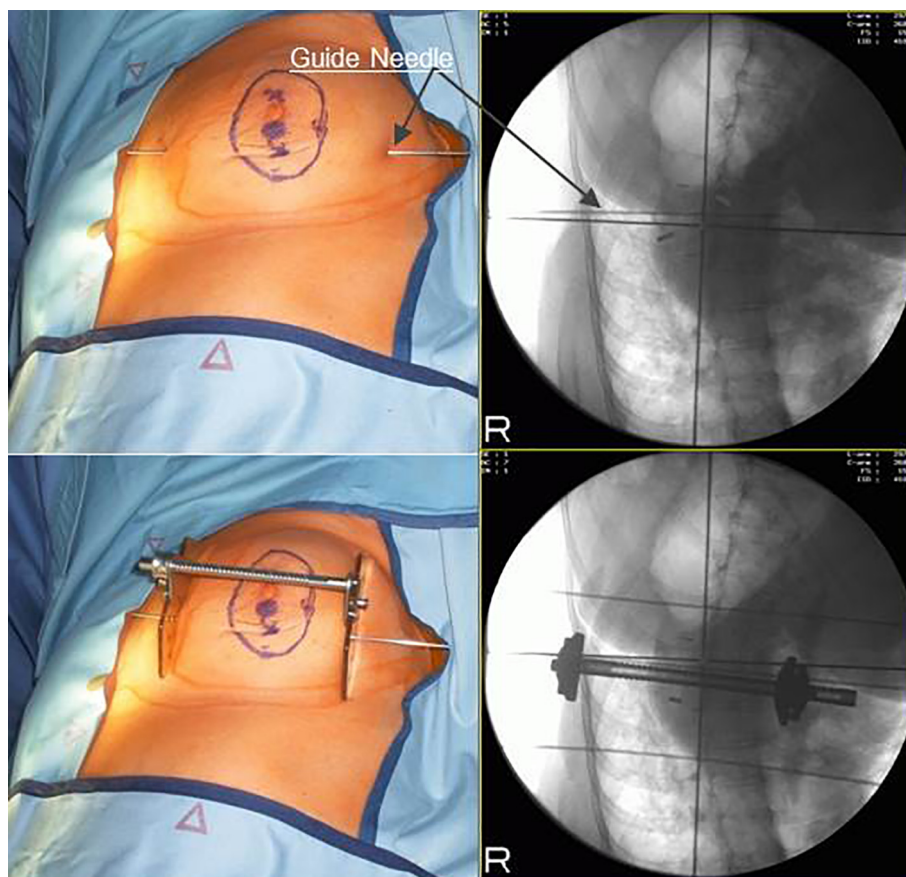


Fig. 6. X-ray based insertion of guide needle.

The CT planning is done the next day. Treatment can be initiated once the pathology report (usually the same day or 2–3 days after surgery) is available. A good collaboration with the pathologist allows keeping the total number of days the catheters remain implanted to a minimum. If multi-catheter brachytherapy is used as a boost with this perioperative method, the treatment can start on the same day.

#### Treatment with rigid needles

The interstitial multi-catheter technique was used for many years in selected cases of breast carcinoma to deliver a boost dose by means of rigid needles with LDR Iridium-192 wires [43–45]. The calculation of the dose and dosimetry was based on isodose curves according to the Paris system, without an image-related target volume [39]. Clinical assessment of the tumour bed and location of clips and needles using only an X-ray C-arm is now standard. The use of needles instead of plastic tubes is a matter of tolerance by the patient during a treatment that lasts at least four days. In these cases, the homogeneity that can be achieved with parallel needles is very high and this allows increasing the total dose and dose per fraction (HDR-brachytherapy).

#### Catheter reconstruction

Since the dose distribution depends on the source dwell positions in the catheters, their 3D arrangement must be known. As a first step, the catheters have to be reconstructed in space using cross-sectional imaging. CT is the recommended imaging method for treatment planning including catheter reconstruction. Using a slice thickness of 3 mm or less is recommended. As dwell times inside the catheters will vary, clear and unequivocal catheter numbering (on the CT data set) and labelling (of the real catheters) is

very important during the reconstruction, especially when the planning data are transferred to the control unit of the afterloading machine. For better visualization, special markers can be inserted into the catheters before imaging, but in most cases the internal air in the catheters can be a surrogate for the markers, and with proper windowing, the reconstruction can be properly performed. The CT-marker can show the first possible dwell position in the catheter, but the equivalence of the planned and real source positions must be known and has to be verified – at least once or periodically – by measurement. When markers are not used, the fixation button at the distal end of each catheter must be visible on the CT images, because the first possible dwell position has to be related to it. The catheter reconstruction can be performed in any of the main orthogonal planes (axial, sagittal, and coronal). Furthermore, oblique planes parallel with, or orthogonal to, the catheters can be created in many TPSs by defining an extra coordinate system (ECS) which helps in the reconstruction process. Having reconstructed all possible source dwell positions, the actual active source length must be determined. This is done taking into account the expansion of the PTV and OAR structures. In the first step, active source positions could be set within the PTV (from surface to surface). The final arrangement of active source positions depends on the type of optimization and ultimately the resulting dose distribution and DVH values. If needed, the active lengths can extend beyond the PTV by a few mms.

#### Normalization of dose distribution, dose specification and prescription

In order to select an appropriate isodose for which a certain absolute dose value should be prescribed, the dose distribution has to be uniquely normalized. For a reproducible normalization procedure, we recommend distributing four to ten dose reference



points in the central implant plane midway between the active source positions in the regions where the dose gradient has a local minimum. As the gradient varies with the source dwell time during the optimization process, the actual positions of individual reference points can be corrected slightly during the planning process. The initial dose distribution is normalized to the mean dose in the reference points (corresponding approximately to the mean central dose (MCD) in ICRU 58 [48]). After specification of the prescribed dose on an isodose line between 80 to 90% of the mean dose at the reference points, the dose distribution is renormalized, and as a consequence the 100% isodose corresponds to the prescribed dose (PD).

Alternatively, in case of an inverse optimization the prescribed absolute dose by default is set to the 100% isodose. The dwell times are calculated on the basis of volumetric dosimetric constraints, with preset goals defined in the objectives like target coverage, dose homogeneity and dose to OAR-s.

#### Dose optimization methods

Dose optimization means the determination of individual dwell time in each dwell position in order to get an optimal dose distribution regarding target coverage, sparing of OARs and dose homogeneity. Dose optimization methods help to improve dose distribution, but it has to be stressed that no optimization can compensate for poor implant geometry. The aims of any optimization method can be summarized as follow:

- to get an appropriate dose coverage of the PTV with a conformal dose distribution,
- to achieve to some extent a homogeneous dose distribution inside the implant,
- to keep the dose to OARs as low as possible, or at least below the corresponding tolerance doses,
- to keep high-dose volumes below certain absolute values.

Optimization methods can be categorized to forward and inverse techniques. The simplest forward optimization is the *manual editing of the dwell times*. Since this is rather time consuming, it is recommended only for small local adjustments. A very popular method is called *geometrical optimization (GO)* which results in a homogeneous dose distribution. Provided that the catheters geometrically cover the target volume properly, the target coverage by the reference dose will also be acceptable. To change the shape of isodoses locally or globally, *graphical optimization (GRO)* can be used during which a selected isodose line can be shifted into the desired position with the “drag and drop” function using a computer mouse. The target coverage and conformity can be improved with GRO but it must not be forgotten that at the same time the homogeneity may deteriorate. In many clinical cases the GO followed by GRO results in an acceptable dose distribution. After usage of GRO the dwell times should be checked so as to avoid high gradients in the dwell time distributions. Another forward optimization method is the so-called *polynomial optimization using pre-defined dose points*. However, dose homogeneity is not taken into account during this optimization, therefore its use is not recommended. As all of these optimization methods are part of forward planning, the influence on DVH parameters of target volume and OAR-s has to be verified. Recently, *inverse optimization (IO)* algorithms have become available with commercial BT planning systems. The great advantage of inverse optimization is that all dosimetric requirements (dose coverage, dose homogeneity and protection of organs at risk) are simultaneously and automatically taken into account during the optimization. Before its use, volume and surface based clinical objectives have to be defined. However, the requirements for target coverage, dose homogeneity and sparing of OARs are often conflicting, therefore finding the

proper dose parameters and weighting factors is not easy and needs some planning experience. Another benefit of inverse IO is that it is user-independent and typically faster than a manual approach.

#### Dose recommendation for multicatheter HDR-/PDR-brachytherapy

The radiobiology of HDR/PDR-brachytherapy and the use of the linear-quadratic model to convert HDR to LDR doses were previously described and discussed in detail particularly for HDR/PDR-brachytherapy of cervical carcinoma and prostate carcinoma [46–50] and as a result, can be used in a similar way for breast brachytherapy. It should be emphasized that because of the complexity of all biological processes, these radiobiological calculations are approximations only, but can be used as a tool to make comparisons between different fractionations, for example in HDR brachytherapy where dose per fraction can deviate a lot from the conventional 2 Gy.

#### The recommended schedules for APBI/APBrI with HDR-Brachytherapy

The schedules for HDR-brachytherapy based APBI, validated in a randomized trial [1,4] are  $8 \times 4$  Gy and  $7 \times 4.3$  Gy scheduled 2 times per day, with an interval between fractions of at least 6 h, and with a total treatment time of 4–5 days.

Other fractionations can be used. Nonetheless we recommend that the chosen fractionation corresponds to a biologically equivalent total dose EQD2 ( $\alpha/\beta = 4-5$  Gy) in the range of 42–45 Gy.

#### The recommended schedules for boost with HDR-Brachytherapy

A biologically equivalent total dose (EQD2 for  $\alpha/\beta = 4-5$  Gy) in the range of 10–20 Gy in 1 to 4 fractions should be selected according to current recommendations [37].

The panel of experts recommends preferably  $2 \times 4-6$  Gy, or  $3 \times 3-5$  Gy scheduled 2 times per day, with an interval between fractions of at least 6 h, and a total treatment time of 1–2 days, or a single fraction of 7–10 Gy, depending on the desired total EQD2.

#### The recommended schedules for APBI/APBrI with PDR-Brachytherapy

Pulsed-dose 0.5–0.8 Gy/pulse, total dose 50 Gy, scheduled every hour, 24 h per day, total treatment time 4–5 days.

#### The recommended schedules for boost with PDR-Brachytherapy are

Pulsed-dose 0.5–0.8 Gy/pulse, total dose 10–20 Gy [37], scheduled every hour, 24 h per day, total treatment time 1–2 days.

#### Dose-volume parameters and dose constraints

For an objective assessment of any treatment plan, quantitative parameters have to be employed. Without taking into account any outlined volumes, implant related dose volume parameters like the volume that is irradiated by the prescribed dose (PD) ( $V_{PD}$ ) or 1.5 times the PD ( $V_{1.5 \times PD}$ ) can be calculated. The homogeneity of the dose distribution is characterized with the ratio of the  $V_{1.5 \times PD}$  to  $V_{PD}$  which is called the dose-non-uniformity ratio (DNR). The lower the DNR, the more homogeneous dose distribution is. As a complementary index to DNR, dose homogeneity index (DHI) can also be formulated. By definition,  $DHI = (V_{PD} - V_{1.5 \times PD})/V_{PD}$  that is  $DHI = 1 - DNR$ .

For outlined structures, additional parameters can be calculated. The percentage of the PTV receiving a given percentage of the PD is generally used and denoted as  $V_{xx}$ . For example,  $V_{100}$  means percentage volume of the PTV receiving 100% dose of the PD or more. To characterize high-dose volumes  $V_{150}$  and  $V_{200}$  are calculated. The overdose volume index (OI) characterizes the dose homogeneity using the volume irradiated by  $2 \times PD$ , related to volume of the PTV. The coverage index (CI) is the fraction of the PTV receiving at least the PD, and it is equal to  $V_{100}/100$ . The conformal index (COIN) takes into account the coverage of the PTV by the PD

( $PTV_{PD}/V_{PTV}$ ) and also the unwanted irradiation of normal tissues outside the PTV ( $PTV_{PD}/V_{PD}$ ) [51].  $PTV_{PD}$  is the volume inside the PTV irradiated by the PD and the  $V_{PD}$  is the volume receiving at least the PD. The dose distribution is at its most conformal when the COIN is maximal and is as close to 1 as possible. Dose irradiating a certain part of the PTV is also used.  $D_{xx}$  means the relative dose that irradiates xx% of the PTV. Depending on the type of the OARs, mean dose, volume irradiated by a given relative dose (eg. V5), absolute dose (eg.  $V_{5Gy}$ ), or dose irradiating a small volume (eg.  $D_{0.1cm^3}$ ,  $D_{2cm^3}$ ) are generally reported. Regarding the skin, in addition to the maximum surface point dose, reporting  $D_{0.2cm^3}$  or  $D_{1cm^3}$  [52] is recommended. Table 1 lists the most common dose–volume parameters used in interstitial breast brachytherapy. In addition, on the post-implant CT-scan, the dose distribution must be analysed in the 3 different views (axial, coronal and sagittal) in order to verify the main dose constraints but also to avoid the confluence of two consecutive  $V_{200}$  isodoses and a  $V_{200}$  isodose diameter >10 mm [14,53–55].

#### Dose–volume limits for PTV and OARs

To date, no generally accepted criteria for a “good” breast implant exist. In the GEC-ESTRO randomized trial the coverage index (CI) had to be larger than 0.90, i.e., at least 90% of the PTV had to receive the PD [56]. The NSABP B-39/RTOG protocol is more lenient, since it requires that only 90% of the PD must cover 90% of the PTV [19]. In the GEC-ESTRO study there was only one requirement for dose uniformity, namely the  $DNR < 0.35$ . According to the experience of the centres participating in the GEC-ESTRO study and respecting current available data [19,52,56,57] the recommended dose–volume constraints for the implant, PTV and organs at risk are presented in Tables 2 and 3. Since the dose to contralateral breast and lung is low in interstitial brachytherapy, no threshold is given for these organs, only a few parameters are recommended for reporting.

#### Recommended parameters for reporting

The following data and parameters are recommended for treatment reporting when using APBI, boost or APBrI with multi-catheter brachytherapy:

**Table 1**  
The most common dose–volume parameters used for reporting in interstitial breast brachytherapy.

Parameter	Definition/calculation
<b>Implant related</b>	
$V_{PD}$	Absolute volume irradiated by the prescribed dose
$V_{1.5xPD}$	Absolute volume irradiated by 1.5 x the prescribed dose
DNR – dose non-uniformity ratio	$V_{1.5xPD}/V_{PD}$
DHI – dose homogeneity index	$(V_{PD} - V_{1.5xPD})/V_{PD}$
<b>Target related</b>	
$V_{PTV}$	Volume of the PTV
$V_{xx}$	Percentage of PTV receiving xx% of the PD
OI – overdose volume index	$V_{2xPD}/V_{PTV}$
CI – coverage index	$V_{100}/100$
COIN – conformal index	$PTV_{PD}/V_{PTV} \times PTV_{PD}/V_{PD}$
$D_{xx}$	Percentage dose that covers xx% of the PTV
<b>OAR related</b>	
$D_{mean}$	Mean dose in organ
$V_{xGy}$	Relative volume receiving x Gy
$V_{xx}$	Percentage of organ receiving xx% of the PD
$D_{xcm^3}$	Relative dose given to most exposed x cm <sup>3</sup> of organ

PD: prescribed dose,  $PTV_{PD}$ : volume in PTV received at least the PD.

**Table 2**  
Recommended dose–volume limits for implant and PTV.

	Constraints
Implant	$V_{PD} \leq 300 \text{ cm}^3$ $DNR \leq 0.35$
PTV	$V_{100} \geq 90\%$ $V_{150} < 65 \text{ cm}^3$ $V_{200} < 15 \text{ cm}^3$ $COIN \geq 0.65$

**Table 3**  
Recommended dose–volume limits for OAR-s.

Organ	Constraints
Ipsilateral non-target breast	$V_{90} < 10\%$ $V_{50} < 40\%$
Skin*	$D_{1cm^3} < 90\%$ $D_{0.2cm^3} < 100\%$
Rib	$D_{0.1cm^3} < 90\%$ $D_{1cm^3} < 80\%$
Heart**	$MHD < 8\%$ $D_{0.1cm^3} < 50\%$
Ipsilateral lung	$MLD < 8\%$ $D_{0.1cm^3} < 60\%$

\* Skin volume is defined as a 5 mm shell below the body contour.

\*\* Left sided lesion only, MHD: mean heart dose, MLD: mean lung dose

1. Type (nuclide) of the radioactive source and technique (HDR/PDR).
2. Number of catheters used and number of implanted planes.
3. Method of dose optimization (manual, geometric, graphical, inverse) and normalization (description of positions of the reference points).
4. Method of dose prescription (on isodose line, volumetric), dose per fraction (pulse), total dose, and fractionation scheme with time pattern.
5. Reference air *kerma* rate/source activity at the time of first fraction.
6. Total reference air *kerma* (TRAK).
7. Implant related volume parameters:  $V_{PD}$ , DNR.
8. Target related parameters:  $V_{PTV}(\text{cm}^3)$ ,  $V_{100}$ ,  $V_{150}$ ,  $V_{200}$ , D90.
9. Optional OARs related parameters:
  - ipsilateral non-target breast:  $V_{90}$ ,  $V_{50}$
  - skin:  $D_{0.2cm^3}$ ,  $D_{1cm^3}$
  - rib:  $D_{0.1cm^3}$ ,  $D_{1cm^3}$
  - heart: MHD (mean heart dose),  $D_{0.1cm^3}$
  - ipsilateral lung: MLD (mean lung dose),  $D_{0.1cm^3}$
  - contralateral breast:  $D_{1cm^3}$
  - contralateral lung:  $D_{1cm^3}$

#### Quality management issues for HDR-/PDR-brachytherapy

The use of HDR-/PDR-brachytherapy requires careful monitoring and quality management (QM), given the potential for toxicity and misadministration [58]. Protocol consistency within an institution will help to avoid errors. Institutions should document the insertion procedure, the planning parameters including normal-tissue dose, the method of treatment, and follow-up. QM issues common to all brachytherapy modalities, including treatment planning systems, treatment delivery systems, applicator commissioning, and periodic checks, will not be addressed in this document. With the objective of preventing errors in treatment

planning and dose delivery, prior to the start of a treatment, the following quality assurance procedures are recommended:

1. *Check of treatment plan (before export to control unit)*
  - a. Plan parameters
    - Patient information (name, ID number, date of birth, cancer type),
    - Dose prescription including fraction- (pulse-) dose and number of fractions (pulses),
    - Correspondence of first source dwell position to distal catheter reconstruction point,
    - Correct drive-out lengths depending on the type and length of catheters (depends on afterloading system),
    - Total reference air kerma (TRAK).
  - b. Plan results
    - A rough estimation of the calculated treatment time. This could be done by comparing with the results of similar plans or by creating a set of implant specific “indicators of reasonableness” like the “total time index”  $T_i = (\text{sum of dwell time} \times \text{source strength}) / (\text{PD} \times \text{number of dwell positions})$  [59] that should be of the same order for implants of comparable geometry.
    - If possible, a recalculation with a second independent verification system is favored.
2. *Plan data transfer*
  - After export of the treatment plan to the control unit of the afterloader, the correctness of the transferred parameters including patient data, prescribed dose, fractionation, source drive-out length, total and individual source dwell times should be verified.
3. *Connection of catheters with transfer tubes*
  - Correct labelling and numbering of the catheters must be verified.
  - A photograph of the connecting end of the catheters taken before the start of treatment planning is recommended to verify the numbering. The correct labelling of the individual catheters should be checked by a second person.
  - If the catheters are cut individually to a specific internal length, prior to starting treatment, the length should be checked by a second person.
  - Connecting the catheters to transfer tubes: Even if the tubes themselves are numbered, they might get mixed up. Therefore, it is recommended not to rely on the tube number only but to follow the course of each transfer tube from the afterloader’s indexer to the corresponding catheter.
  - Make sure that the catheters are in the correct position in the breast and the fixation buttons are in contact with the skin surface.
  - Make sure that during imaging and treatment identical patient positioning is guaranteed, to ensure the same anatomical positions of the organs.
4. *Final control before initiation of irradiation*
  - The total length (transfer tube with catheter) should be checked (with a marked wire or special manufacturer’s tools like “source position simulator”).
  - A test run with a check cable should be performed for all catheters prior to drive-out of the source to verify the proper connection and to eliminate catheter obstruction.

not impair already inserted plastic catheters so that no liquid or blood can enter the catheters.

Post-implantation care: While the patient is receiving radiation therapy check that the buttons are not pressing on the skin too hard while not being too loose to avoid ulceration and the development of chronic skin marks, such as acromia or skin necrosis, in the future. Although use of antibiotics is not mandatory in some centres, a pre-implantation single-shot antibiotics, for example with Ampicillin/Sulbactam iv  $1 \times 3$  g, is standard in others. Here, adequate rules according to the corresponding surgical discipline of each centre should be adhered to.

It goes without saying that a responsible physician will perform a daily ward round to rule out signs of breast infection and to detect possible changes in breast volume (may indicate development of haematoma). In case of apparent or suspected changes in the breast volume or the position of plastic catheters a verification of these findings by CT must be done and if necessary planning issues taken into consideration.

## Conclusion

Early breast carcinoma after BCT can be treated with radiation therapy with a very limited volume of irradiated tissue and APBI has become a standard postoperative treatment modality. Postoperative APBI with multi-catheter-brachytherapy for selected patients with early breast cancer to date is the only radio-oncological treatment method with duration of only 4–5 days for which there is level 1 evidence [1,4,60]. In addition to appropriate patient selection [13] and target definition [14,15,61], we consider that practical issues like the method of catheter insertion, dose optimization and quality assurance are of great importance and need to be standardized. The technical aspects and QA have until now been discussed only marginally in some US guidelines [17,62] and no European guidelines are available at the moment. The current guideline finally fills this gap and is intended to promote the safe and efficient delivery of APBI with image-guided multi-catheter brachytherapy. It is based on the current practice of APBI in Europe as reviewed from clinical trials, published literature, and prior clinical experience of panel experts. This guideline was developed as a consensus-based statement and has been reviewed and approved by the board of the GEC-ESTRO and ACROP. The aim is to assure a standard quality level during the procedure of implantation, definition of the CTV and treatment with multi-catheter brachytherapy in breast carcinoma.

We hope that the present guideline can be viewed as an important aid to radiation oncologists in managing patients with early breast cancer. Interstitial multi-catheter brachytherapy has been used for many years, therefore diverse techniques have been developed, and outcome data prove that they are adequate to offer an improved breast cancer control without severe acute and late effects. The practitioner’s experience is useful, but only if there is a recording of data and an appraisal of long-term results.

The panel of experts also recommends that the radiation oncologists and the medical physicists at a facility introducing APBI with multi-catheter image-guided brachytherapy for the treatment of patients with early breast cancer attend courses designed to review APBI practice and QM and spend an adequate amount of time learning the procedure at a facility with extensive experience in APBI using brachytherapy.

In summary it can be stated that the presented guidelines make it possible to assure the best possible quality and accuracy of image-guided breast brachytherapy as well as adequate dose coverage of the target volume inside the breast with appropriate quality of the dosimetry, in order to achieve optimum long-term

## Perioperative and post-implantation care

Perioperative care: The insertion of catheters should be performed under sterile conditions. Special care should be taken to



results. The same rules should be used for the boost with multicatheter brachytherapy after WBI and for APBRI.

### Conflict of interest statement

None declared.

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