Reports of Practical Oncology and Radiotherapy 25 (2020) 832–839

Available online at www.sciencedirect.com

Reports of Practical Oncology and Radiotherapy

journal homepage: http://www.elsevier.com/locate/rpor

Expert consensus statement

Consensus statement from the Spanish Brachytherapy Group (GEB) on accelerated partial breast irradiation using multicatheter interstitial brachytherapy

Susana Pérez-Echagüen[a,*], Camilo José Sanz-Freire[b], José Luis Guinot-Rodríguez[c], Cristina Gutiérrez-Miguélez[d], Pilar Samper-Ots[e], Víctor González-Pérez[f], Elena Villafranca-Iturre[g], Ignasi Modolell[h], Santiago Pellejero-Pellejero[i], Mauricio Cambeiro-Vázquez[j], Gustavo Ossola-Lentati[a]

[a] *Radiation Oncology Department, CIBIR – Complejo Hospitalario San Pedro La Rioja, Piqueras 98, E-26006 Logroño, Spain*
[b] *Medical Physics Department, CIBIR – Complejo Hospitalario San Pedro La Rioja, Piqueras 98, E-26006 Logroño, Spain*
[c] *Radiation Oncology Department, Fundación Instituto Valenciano de Oncología, Prof. Beltrán Báguena 8, E-46009 Valencia, Spain*
[d] *Radiation Oncology Department, Institut Català d'Oncologia, Avda. de la Granvia de l'Hospitalet 199-203, E-08908 L'Hospitalet de Llobregat, Barcelona, Spain*
[e] *Radiation Oncology Department, Hospital Universitario Rey Juan Carlos, Gladiolo s/n, E-28933 Móstoles, Madrid, Spain*
[f] *Medical Physics Department, Fundación Instituto Valenciano de Oncología, Prof. Beltrán Báguena 8, E-46009 Valencia, Spain*
[g] *Radiation Oncology Department, Complejo Hospitalario de Navarra, Irunlarrea 3, E-31008 Pamplona, Spain*
[h] *Servicio de Física Médica y Protección Radiológica, Institut Català d'Oncologia, Avda. de la Granvia de l'Hospitalet 199-203, E-08908 L'Hospitalet de Llobregat, Barcelona, Spain*
[i] *Medical Physics Department, Complejo Hospitalario de Navarra, Irunlarrea 3, E-31008 Pamplona, Spain*
[j] *Radiation Oncology Department, Clínica Universitaria de Navarra, Av de Pío XII 36, E-31008 Pamplona, Spain*

ARTICLE INFO

Article history:
Received 21 February 2020
Received in revised form 16 April 2020
Accepted 13 May 2020
Available online 25 July 2020

Keywords:
APBI
Interstitial brachytherapy
Consensus guidelines
Breast cancer

ABSTRACT

Aim: To establish consensus guidelines for a safe clinical practice of accelerated partial breast irradiation (APBI) interstitial multicatheter brachytherapy (BT).
Background: APBI with interstitial multicatheter BT has proved to be effective in the treatment of early stage breast cancer. This paradigm shift in the approach to early breast cancer conservative treatment, along with the existing controversies on the clinical practice of APBI, prompted the Spanish Brachytherapy Group (GEB) of the Spanish Societies of Radiation Oncology (SEOR) and Medical Physics (SEFM) to address BT APBI in a consensus meeting.
Materials and methods: Prior to the meeting, a survey with 27 questions on indication, inclusion criteria, BT modality, implant technique, image guidance and simulation, CTV and OAR definition, dose prescription and fractionation, dose calculation, implant quality metrics and OAR dose constrains was distributed. Items not reaching a level of agreement of 70% were discussed and voted during the meeting.
Results: 26 Institutions completed the survey, 60% of them perform APBI procedures. The analysis of the survey showed consensus reached on approximately half the questions. An expert panel discussed the remaining items; thereafter, a voting established the definite consensus.
Conclusions: This document summarizes the consensus guidelines agreed during the meeting of the Spanish Brachytherapy Group SEOR-SEFM. Institutions with BT facilities available should offer interstitial BT APBI as a treatment option to patients fulfilling the inclusion criteria. Institutions willing to implement interstitial BT APBI are encouraged to follow the consensus guidelines established herein.

* Corresponding author.
E-mail addresses: spechaguen@riojasalud.es (S. Pérez-Echagüen), csanz@riojasalud.es (C.J. Sanz-Freire), jguinot@fivo.org (J.L. Guinot-Rodríguez), cgutierrezm@iconcologia.net (C. Gutiérrez-Miguélez), pisamot@gmail.com (P. Samper-Ots), vgonzalezper@hotmail.com (V. González-Pérez), elena.villafranca.iturre@navarra.es (E. Villafranca-Iturre), imodolell@iconcologia.net (I. Modolell), santiago.pellejero.pellejero@navarra.es (S. Pellejero-Pellejero), mcambeiro@unav.es (M. Cambeiro-Vázquez).

https://doi.org/10.1016/j.rpor.2020.05.004
1507-1367/

1. Introduction

The publication of the non-inferiority results of the randomized, multicenter study carried out by the GEC-ESTRO Group on interstitial BT APBI versus whole breast irradiation (WBI) after breast-conservative surgery brings about a paradigm shift in the approach to early stage breast cancer and ductal carcinoma in situ.[1] The adoption of BT APBI as a standard of treatment, alternative to WBI, makes it necessary to establish common working guidelines that can be assumed by the scientific community. There is a need to standardize criteria and to establish common, accepted guidelines for a safe clinical practice of BT APBI.[2–5] These consensus guidelines should help the clinicians to develop protocols to ensure this safe clinical practice. Consensus guidelines should cover the indications and inclusion criteria, as well as practical issues of the procedure, which should include but shall not be restricted to implant technique and geometry, image guidance, simulation procedure, CTV and OAR definition, fractionation, dose calculation and implant quality evaluation. Common practice criteria will ultimately facilitate the comparison of results between institutions.

To satisfy the need to establish standardized practice criteria the Spanish Brachytherapy Group (GEB) of the Spanish Societies of Radiation Oncology (SEOR) and Medical Physics (SEFM) brought together a group of Radiation Oncologists and Medical Physics experts. The meeting was held in La Rioja (Spain) and focused exclusively on BT APBI. The findings and conclusions of the meeting are summarized in this consensus statement document which is purposely designed to achieve a three-fold goal: to support the safe practice of this technique, to set the basis for intergroup comparison of clinical results and to guide practitioners through the implementation process of interstitial BT APBI.

2. Materials and methods

This consensus document is based on the results of an institutional experience survey distributed nationwide in Spain and on the conclusions agreed during the meeting. Previously a reduced group of experts identified the main topics to be discussed, those that provide an adequate and complete description of the technique, as well as other more controversial hot topics. An extensive literature review was also carried out during this phase, including recent results of large trials.

The list of analyzed items comprises description of the technique, clinical indications and risk groups, practical aspects of the implant, prescription and fractionation, simulation process, clinical target volume and organ at risk definition, dose calculation and optimization, metrics for dose evaluation. The survey was elaborated with the aim of acquiring a detailed knowledge of the current routine practice of APBI in Spain, and so included some points that allowed the respondents to describe the availability of APBI in their institutions, and accumulated experience. The above-mentioned list of topics was developed into an extensive questionnaire consisting of 27 multiple choice questions. The questionnaire was sent to 33 Institutions with Brachytherapy facilities in Spain and one Institution in Portugal. 26 Institutions filled out the questionnaire.

The analysis of the questionnaires served as a starting point to classify the topics regarding the degree of controversy, and so to identify those that might deserve a comprehensive discussion. The method followed consisted in sorting the questions into two groups depending on the level of agreement reached. A threshold of 70% agreement was established. Questions with agreement level below or equal to the threshold were classified as having "*little consensus*". Questions with agreement above the threshold were classified as having "*broad consensus*". From this classification it was decided that:

1. *Broad consensus* topics are presented at the experts meeting, but only discussed and voted if explicitly requested during the meeting. Otherwise, consensus is assumed.
2. *Little consensus* topics are brought up for discussion and then voted in all cases.

As a result of the voting during the experts meeting, topics were in turn compiled under two headings:

1. "*There is consensus*" if the voting showed agreement above 70%
2. "*There is no consensus*" if the voting showed agreement equal to or below 70%

3. Results

3.1. Literature review

Breast cancer is the most frequently diagnosed cancer among women in Europe. Studies showing equivalent results after 20 years follow-up of mastectomy versus conservative treatment consisting of tumour removal with a safety margin and sentinel node selective biopsy or lymphadenectomy, followed by WBI in early stage breast cancer have been published in the past.[6,7]

These results support conservative treatment as standard practice in early stage breast cancer, reducing surgical morbidity and improving the aesthetic results. Conservative treatment includes whole breast irradiation, which is completed in 5 weeks if conventional fractionation is considered (50 Gy, 2 Gy per fraction) or 3–4 weeks if hypofractionation is considered (40 Gy, 2.67 Gy per fraction). Both fractionation schemes are considered equivalent.[8,9] Randomized studies show the benefit of a tumour bed dose boost after WBI, specifically in young patients with histological risk factors for local relapse.[10,11] If indicated, dose boost can be performed with external beam radiotherapy (EBRT) or BT. BT boost was indeed the main topic of a consensus meeting of GEB held in 2003.[12] The results of the phase III randomized trial with 20-year follow-up and 5318 patients, comparing WBI versus WBI plus 16 Gy added to the tumour bed, showed a benefit in terms of local control but no improvement on overall survival, which allows to guide the indication of dose boosting the tumour bed.[13]

On the other hand, some specific factors are associated with a low risk of local relapse. A dose boost to the tumour bed might not be necessary in these cases, the indicated treatment being conventional or hypofractionated WBI alone.[8]

Reference works such as Holland's and colleagues[14] studied surgical specimens from mastectomy, finding that the proportion of tumour cells reduces as the distance to the primary tumour increases. Viable tumour cells could be found at 2 cm from the primary tumour in 39% of cases, whilst at 3 cm in 22%. Faverly et al.[15] showed that the proportion of tumour cells is 12–18% for pT1 tumours, hence, for selected cases, the resection of the tumour with a 2 cm margin will be associated with a very low local relapse probability.

It follows that it is in the proximity of the primary tumour where local relapses occur, while the risk of relapse for the remaining ipsilateral breast is similar to the risk of relapse for the contralateral breast. Radiation treatment should only be administered to the breast area surrounding the primary tumour for low risk breast cancer cases.[16,17]

A new approach emerges which consists in a partial irradiation of the breast area at the highest risk.[18] This involves a reduction of the treatment volume and dose to the organs at risk, which allows a higher dose per fraction and shortens the treatment course. Following this approach, similar TCP with lower toxicity treatment

schemes could be designed, giving rise to the concept of accelerated partial breast irradiation (APBI).

A vast initial experience exists in the field of low dose rate (LDR) Ir-192 interstitial BT with plastic catheters. HDR BT complements this experience at a later stage. Pioneers in this area were Institutions with an extensive BT experience. Martinez and Vicini from William Beaumont Hospital, Michigan[19–22] presented the results of the first experiences initiated in the 1980s. They did not, however, make an exhaustive patient selection, which led to inconsistent results.

It was thus necessary to determine the risk factors for low risk of local relapse in order to have an adequate selection of candidate patients to APBI. While results of phase III randomized trials were not yet available, ASTRO in 2009[3] and GEC-ESTRO in 2010[23] proposed classifications into risk groups with similar characteristics. The defined categories consider unifocal small tumours with no affected lymph nodes, no vascular or lymphatic invasion, tumour free surgical margins and no associated extensive intraductal component in postmenopausal women. Similarly, intermediate risk groups and contraindication characteristics for APBI were described.

In the late 1990s and early 2000s and due to technological innovations, different APBI techniques were developed and applied to patients fulfilling the selection criteria. The common rationale behind these approaches was to irradiate less than 25% of the breast in less time, reducing the associated toxicities. Both BT (interstitial, balloon, electronic) and EBRT (3DCRT, IMRT, IORT) APBI techniques were considered.[16] Regardless of the applied technique, the idea is that the irradiation of the tumour bed with 1–2 cm margin after conservative surgery as an alternative to the standard treatment.

Several studies compared the results of WBI versus APBI. The phase III NASBP B39/RTOG 0413 trial recruiting 4126 patients compared 3 different APBI techniques delivering 34 Gy (21% intracavitary BT, 6% interstitial BT, 73% 3DCRT) versus 50 Gy WBI, optionally followed by a 10–16 Gy boost. Long term primary results were recently published,[24] showing 10-year local control non-equivalence of APBI and WBI for the considered pool of patients (4.6% vs. 3.9%). The authors recognize, however, that the trial was not designed to detect differences between subgroups of patients, and the enrolment had broad eligibility criteria. The small tumour recurrence rates differences between both approaches leaves the door open to APBI as an acceptable treatment option for selected groups of patients.

The objective of the RAPID trial was to determine whether 3DCRT APBI is not inferior to 3DCRT WBI.[25,26] 2135 patients were randomly allocated, 1065 to the WBI arm and 1070 to the APBI arm. The delivered dose was 42.5 Gy in 16 daily fractions or 50 Gy in 25 daily fractions in the WBI arm and 38.5 Gy administered in 5 days, twice a day, in the APBI arm. Adverse cosmetic results at 3- and 5-year follow-up were found in the APBI arm which may be related to an excessively high dose per fraction, suggesting that 3DCRT APBI should only be used in the context of a clinical trial.[25]

The Florence phase III trial compared standard WBI versus IMRT APBI.[27,28] 520 patients were 1:1 randomly assigned to both arms. Patients in the WBI arm received 50–60 Gy, 2 Gy per fraction. Patients allocated in the APBI arm received 30 Gy in 5 fractions over 2 weeks. No significant differences were found in terms of local relapse rates and overall survival at 5 years. Acute and late toxicity and cosmesis were better in the IMRT APBI arm. A study with a greater number of patients and a more extensive follow-up is necessary to confirm results.

The intraoperative (IORT) approach has been considered in two large trials: ELIOT and TARGIT. The ELIOT trial is a prospective 1:1 randomized phase III trial with 1305 patients enrolled, sponsored by the European Institute of Oncology, Milan.[29] The trial compared intraoperative partial irradiation of the breast with a single electron dose of 21 Gy (EIORT) versus WBI followed by a boost. The 5-year recurrence rates for the EIORT arm and the WBI arm patients were 4.4% and 0.4%, respectively, concluding a significant difference in local control. An ELIOT subset of low risk patients could be identified with recurrence rate of only 1.5%, suggesting that preoperative criteria based on tumour size, age and pathological and biological examination of the biopsy specimen should have been taken into consideration for a proper patient selection.[30]

The TARGIT trial considered IORT with a 50 kV X-rays beam generated by an Intrabeam® device (CARL ZEISS MEDITEC AG).[31] The TARGIT trial is a multicenter randomized study with 3451 patients enrolled from 33 institutions in 11 countries. The experimental arm (1721 patients) consisted of a single 20 Gy IORT fraction. The control arm considered 1730 patients undergoing standard 50 Gy WBI in 25 daily fractions. Addition of WBI is permitted for those patients in the IORT arm at high risk of recurrence because of risk factors – surgical margins less than 1 mm, invasive lobular carcinoma, extensive intraductal component, histological grade G3, lymph vascular infiltration or positive lymph nodes – determined at the time of surgery or when final pathology is available. The 5-year risk of local recurrence rates were 3.3% in the TARGIT arm versus 1.3% in the EBRT arm. A detailed analysis showed that the difference becomes apparent only for the "post-pathology" subset of patients undergoing TARGIT IORT after results of final pathology are available and determined no risk factors. The "pre-pathology" subgroup of patients had overall recurrence results compared to EBRT within the pre-set noninferiority margin.[32]

Although the first publications of APBI versus WBI were based on interstitial brachytherapy, updated trials with properly selected patients, using the advances in high dose rate interstitial brachytherapy were needed. In this regard, the first phase III study with very promising results in efficacy and aesthetic outcome for the APBI approach with HDR interstitial brachytherapy versus WBI up to 50 Gy and direct electron beam boost, corresponds to the Hungarian group, though with a very limited number of patients.[33]

The first level-1 evidence results come from the publication of the large multicenter randomized trial of the European GEC-ESTRO Brachytherapy Group, involving 1184 patients with low-risk invasive carcinoma and ductal carcinoma in situ treated with conservative surgery.[1] This study includes 551 patients treated with WBI up to 50 Gy, 2 Gy per fraction, versus 633 patients treated with multi-catheter interstitial HDR brachytherapy in 8 fractions, 4 Gy per fraction, or 7 fractions, 4.3 Gy per fraction, twice a day, or PDR brachytherapy up to 50 Gy. At 5 years, the authors found no significant differences in terms of local control, with a relapse rate of 0.92% in the WBI group versus 1.44% with brachytherapy, reporting fewer G2–G3 adverse effects in the brachytherapy group (3.2% versus 5.7%).[34] The results after 5 years of follow-up show no inferiority in local control, disease-free survival and overall survival. The authors conclude that APBI with multicatheter brachytherapy is as effective as WBI after conservative surgery for early-stage breast cancer in appropriately selected patients and should therefore be considered and offered as a standard treatment to patients.

3.2. Institutional experience survey

The analysis of the questionnaire initially distributed to hospitals throughout Spain provides a clear picture of the reality of the technique of BT APBI. A summary of this analysis is shown in Table 1.

3.3. Expert panel discussion

From the analysis above, items classified as "little consensus" could be identified and discussed during the meeting. These items were simplified and grouped into 11 discussion points. The possible answers were then drafted according to results and comments of

Table 1
Questionnaire analysis summary. The given percentage values refer to the total number of hospitals that replied each question, unless otherwise stated.

Technical expertise	
1. Availability of BT APBI	60% of RT departments perform APBI. 22% of RT departments do not perform APBI but have interest and/or intention of implementing the technique, 18% of RT departments have no interest in the technique
2. BT APBI technique	87% use flexible catheters. 13% use electronic brachytherapy (EBT). 3 hospitals use rigid needles.
3. Workload	The median number of patients treated per year is 12, with a maximum of up to 150 patients per year and a minimum of 2 patients per year.
4. Experience	Most hospitals have 3 to 6 years experience of APBI. There are hospitals having more than 25 years experience.
Indications	
1. Indications considered	94% include initial stage cases fulfilling the inclusion criteria. 63% consider local relapses after EBRT cases. 25% include large breasts cases not suitable for EBRT. 31% include as indication social or family circumstances of the patient. Other indications explicitly indicated are: "previous RT treatment including part of the breast, thyroid carcinoma, mediastinal lymphomas", or "Physical impossibility for EBRT (frozen shoulder, severe arthrosis, etc. that prevents correct positioning), previous thoracic RTE".
2. Inclusion criteria	38% use GEC-ESTRO inclusion criteria exclusively. 12% consider ABS-ASTRO inclusion criteria exclusively. 50% consider different combined inclusion criteria (GEC-ESTRO, ABS-ASTRO and inclusion criteria described in the Spanish Consensus of Madrid). 2 hospitals with EBT use TARGIT criteria.
Implant	
1. Surgery and implant timing	44% perform both peri- and post-operative procedures. 12% perform only perioperative procedures and 31% perform only post-operative HDR procedures. There are 13% of hospitals with intra-operative EBT.
2. Number of implanted planes and catheters	Most hospitals use 3 planes (79%). 45% of them occasionally use 2 planes. Only 2 hospitals perform *always* 2-planes implants. The number of catheters implanted varies greatly, ranging from 21 to only 5, with a median of 12.
3. Catheter spacing	Gap between catheters ranges from 18 to 10 mm, the most common value being 16 mm (6 hospitals). 3 hospitals use 10 mm gap and 3 hospitals 15 mm gap.
4. Pre-insertion image	80% perform image before implantation. 100% of these use CT imaging. 1 hospital adds MRI imaging. 1 hospital adds ultrasound imaging. 1 hospital adds mammographic image.
5. Image guidance of the implant	40% image guide the insertion. All hospitals that image-guide the insertion use ultrasound image. 1 hospital performing peri-operative APBI also uses fluoroscopy.
6. Implant and treatment administration timing	In post-operative procedures, 85% perform the first fraction the same day of the implant. 15% delay 1–3 days the delivery. In peri-operative procedures, the first fraction is delivered with a delay of 1–6 days, with a median of 3.5 days.
CTV and OAR definition	
1. Simulation	All hospitals perform CT-based simulation.
2. Tumour bed definition	Almost all hospitals (93%) consider as information for tumour bed definition the "number and position of the surgical clips" and preoperative image information, (mammography and MRI). Most of them (73%) also consider information obtained from "scar on skin" and "preoperative ultrasound image".
3. CTV delineation	Almost all hospitals (87%) follow GEC-ESTRO recommendations for the definition and delineation of CTV. 2 hospitals do not follow GEC-ESTRO recommendations, they instead define the CTV guided by "clips and preoperative image" or "clips + added margin".

Table 1 (*Continued*)

4. Additional extension to CTV	Almost all hospitals (92%) do not use any added margin to CTV in order to consider additional uncertainties. 2 hospitals occasionally consider adding a margin to the CTV if: "there is a poor definition of Estimated Tumour Bed and the CTV margin is unclear, then a margin is added only if there is availability of implanted catheters" and "if CTV definition protocol cannot be easily applied and T > 2.2 cm, a margin of 2 to 5 mm is added". Only 1 hospital routinely adds 5 mm margin to the CTV.
5. OAR definition	Almost all hospitals (93%) contour skin, normally as an internal margin of 3–5 mm of the external contour of the body. 67% contour the ribs. 47% contour lung and 40% heart in left breast cases. Few hospitals delineate the ipsilateral breast (27%). 2 hospitals define the scar on skin, 1 hospital delineate the areola and 1 hospital contours the vascular structure under the skin (2 mm internal margin to the skin). 1 hospital contours no OARs unless "dosimetry is compromised".
Fractionation	
1. Standard fractionation	60% prescribe 8 fractions of 4 Gy/fx as standard fractionation. 78% of them use *bis in die* schemes in some or all fractions. 13% use 7 fractions of 4.3 Gy/fx, or 10 fractions of 3.4 Gy/fx. 1 hospital prescribe 12 fractions of 2.5 Gy/fx and 1 hospital uses a single fraction of 18 Gy. All hospitals using EBT prescribe 1 single fraction of 20 Gy.
Optimization and dose calculation	
1. Active length	71% use active dwell positions within CTV plus a margin. Most of them indicate a margin of 5 mm, although some add up to 10 mm if calculated dose distribution fulfils the constrains.
2. Source dwell positions close to skin	All hospitals avoid active dwell positions close to skin. The median safety margin to skin is 5 mm, generally adjusted depending on dose distribution.
3. Source dwell times	54% do not consider any source dwell time restrictions. If considered, source dwell time restriction is always based on dosimetry limitations (V150, V200, DHI, etc.).
4. Optimization	64% use sequential optimization methods, initially a geometrical or sometimes inverse optimization, followed by graphical optimization. 21% use *only* geometrical optimization. 14% use *only* graphical or inverse optimization.
Dosimetry evaluation	
1. Implant dosimetry metrics	There is a great disparity in metrics selection to evaluate the quality of dosimetry, and an even greater disparity in tolerance values to apply to these parameters. – 75% evaluate D90. 20% of them require D90 > 90%, 60% require D90 > 100% and 20% require D90 > 110%. – 50% evaluate V100, 83% of them require V100 > 95%. – 50% evaluate V150 50% of them require V150 < 70 cc and 50% V150 < 20–35 cc. – 58% evaluate V200. 50% of them require V200 < 20 cc. For the rest of participants, a wide range of more restrictive values is considered. – 42% calculate the dose non-uniformity ratio (DNR). All of them require DNR < 0.35. – 84% use some sort of metrics to evaluate implant homogeneity, mainly DNR and DHI. – Only few hospitals routinely evaluate the Conformity Index (CI) (8%), COIN (17%) or V90 (17%).
2. Normal tissue constraints	– Skin: 73% evaluate $D_{max}/D_{0.1\,cc}$ as skin dose metric. Most of them (88%) require $D_{max}/D_{0.1\,cc}$ < 70%. – Vascular structure under skin: Nearly all participants do not contour it. – Ribs: Hospitals that consider ribs dose evaluate $D_{max}/D_{0.1\,cc}$. 33% require D_{max} < 80%, 33% require D_{max} < 90% and 33% require D_{max} < 100%. – Heart: Several hospitals delineate it, but no tolerance values are indicated. – Lung: Several hospitals delineate it, but no tolerance values are indicated.

Table 2
Summary of GEC-ESTRO recommendations on patient selection criteria for APBI.[23]

Characteristics	Low-risk group – good candidates for APBI	Intermediate-risk group – possible candidates for APBI	High-risk group – contraindication for APBI
Age	>50 y	40–50 y	<40 y
Histology	IDC, mucinous, tubular, medullary, and colloid cc	IDC, ILC, mucinous, tubular, medullary, and colloid cc	–
Invasive lobular carcinoma	Not allowed	Not allowed	–
Associated lobular carcinoma in situ	Allowed	Allowed	–
Ductal carcinoma in situ	Not allowed	Allowed	–
Histologic grade	Any	Any	–
Tumour size	pT1-2 (<30 mm)	pT1-2 (<30 mm)	pT2 (>30 mm), pT3, T4
Surgical margin	Negative (>2 mm)	Negative, but close (<2 mm)	Positive
Multicentrity	Unicentric	Unicentric	Multicentric
Multifocality	Unifocal	Multifocal (limited within 2 cm of the index lesion)	Multifocal (>2 cm from the index lesion)
Extensive intraductal carcinoma	Not allowed	Not allowed	Present
Lympho-vascular invasion	Not allowed	Not allowed	Present
Oestrogen/progesterone receptors status	Any	Any	–
Nodal status	pN0 (Sentinel lymph node biopsy or axillary lymph node dissection)	pN1mi, pN1a (Axillary lymph node dissection)	pNx; PpN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

the survey, as well as the input of the attendees. Once the possible options were clarified, a voting established the definite consensus, which is summarized in the next section.

3.4. Consensus statement

1. BT technique.
   a. BT APBI must be performed interstitially, with either plastic or rigid catheters. Intraoperative APBI can be performed with electronic BT, although is not considered a standard of treatment. Patients must be properly selected, and an informed consent must be obtained.
2. Indications.
   a. BT APBI indication is low risk, early stage breast cancer, fulfilling GEC-ESTRO criteria (Table 2).
   b. There is no consensus on the adoption of other inclusion criteria, although some institutions consider different well-established standards in practice (ABS-ASTRO or ABS-ASTRO/GEC-ESTRO combined, inclusion criteria).
   c. There is a consensus that BT APBI can be offered to patients under particular circumstances, different from those indicated in paragraph 2.a:
      1. Local relapses after EBRT or BT.[36,37]
      2. Large breast patients not suitable for EBRT.
      3. Patients not suitable for the EBRT procedure.
   d. There is no consensus on the indication of BT APBI motivated on social or family circumstances of the patient, such as: distance to hospital, occupational situation, family situation, etc.
3. Implant.
   a. Maximum recommended time for BT APBI after surgery is 6–8 weeks. It is agreed that up to 12 weeks after surgery is acceptable under certain circumstances.
   b. Decision on peri- or post-operative implant is not based on oncologic criteria but depends only on the logistics of the hospital.[38]
   c. There is a consensus that a pre-insertion image for CTV localization and definition purposes is recommended.
   d. CT image modality is the choice of pre-insertion image, not excluding other complementary modalities if available.
   e. It is recommended to image guide the needles insertion, if image guidance is available. Image guidance for needle insertion can be skipped if a tumour bed is well defined.
   f. A 3-plane implant geometry is recommended, although 2-plane implant geometry may be acceptable depending on the CTV size. 1-plane implants are highly discouraged.
   g. There is no particular recommendation on the number of catheters to use, which will depend on the CTV size.
   h. Parallel catheters should be placed from 10 to 18 mm apart, 16 mm being a reasonable distance.
4. CTV and OAR definition.
   a. Post-implant clinical target volume and organs at risk definition, as well as the dose planning process must be mandatorily based on CT image modality.
   b. There is a consensus that the following information will be considered for CTV definition purposes:
      1. Number and position of surgical clips.
      2. Pre-operative image information (mammography, MRI image, echography).
      3. Scar on skin.
   c. CTV definition procedure will follow GEC-ESTRO Breast Cancer WG recommended procedure,[39,40] which is briefly summarized:
      1. Whole visible surgical bed (WS) including visible scar tissue inside the breast and all surgical clips; in case there are no clips and the scar tissue is not visible, the WS will not be delimited.
      2. Tumour volume defined on pre-operative image (ImTV).
      3. Estimated tumour bed (ETB) defined by encompassing surgical clips (all surgical clips but those in chest wall), WS and ImTV.
      4. CTV, defined as ETB plus safety margins.
   d. It is recommended not to add any extra margin to the CTV. It is agreed that only in case of poor ETB definition and availability of implanted catheters, an additional extension to the CTV is added. This will define the "*extended CTV*".
   e. Skin and ribs must be contoured
   f. Contouring of other organs at risk such as the lung, ipsilateral breast, heart is not mandatory, although advisable.
5. Fractionation.
   a. Fractionation schemes such as 8×4 Gy/fx, 7×4.3 Gy/fx, 10×3.4 Gy/fx are accepted as standard.
   b. Other different fractionation schemes described, including one-fraction treatments, are not considered standard and must remain investigational.
6. Optimization and dose calculation.
   a. Active dwell positions are allowed outside the CTV boundaries. The margin ranges from 5 to 10 mm and should be adjusted depending on the final dose distribution.

b. Active dwell positions close to the skin must be avoided. A safety margin must be applied, its value depending on the final dose distribution.
c. Optimization comprises a global optimization method available to the user (geometrical, conformal, inverse) sequentially followed by local graphical optimization.

7. Implant dosimetry metrics
   a. CTV D90 and V100, and one or several indexes directly or indirectly describing dose homogeneity such as V150, V200, DNR or DHI, will be mandatorily evaluated and reported.
   b. There is a consensus that target values to achieve are:
      1. CTV D90 > 100% of prescribed dose.
      2. CTV V100 > 95% of prescribed dose.
      3. DNR < 0.35.
   c. Tolerance values described in literature[2] for V150 and V200 will be accepted, although strict fulfilment of these limitations will not be required as the CTV size must be taken into consideration.
8. Normal tissue constrains.
   a. D_{max} or alternatively $D_{0.1\,cc}$ of the skin will be evaluated and reported. This maximum dose to the skin should be kept below 70% of the prescribed dose.
   b. D_{max} or alternatively $D_{0.1\,cc}$ of ribs will be evaluated and reported. There is no consensus on the ribs dose constrain to apply, but it is recommended that it should not exceed the prescription dose.

4. Discussion

In the context of conservative treatment of early-stage breast cancer, conservative surgery has been associated with a significant improvement in the quality of life of patients from all perspectives, due to lower surgical morbidity, and improvement in social, family and work aspects.[34,41] Radiation therapy of the entire breast after conservative surgery involves 3–6 weeks of treatment, depending on the fractionation, as well as a non-negligible probability of adverse effects to surrounding organs at risk.

If those patients with early stage breast cancer and low risk of local relapse are adequately identified, there is no need to irradiate the whole breast, thus reducing the treatment volume and therefore the toxicity to organs at risk, allowing an increase in dose per fraction and reducing the treatment time to 2–5 days compared to the standard 3–5 weeks. It has been the pursuit of the radiation treatment technique which allows partial irradiation of the breast with equivalent results in local control, disease-free survival and toxicity compared with WBI,[1,42] which has led to the implementation of multiple phase III randomized trials.[18]

The implementation of any new technique requires the establishment of well-defined criteria, clear and unambiguous working procedures, and a basis for comparative analysis of clinical results. This objective can be achieved through consensus meetings the results of which are reflected in consensus guidelines documents.[2,3,5,35] During the elaboration of the Spanish interstitial BT APBI Consensus document, a sufficient number of aspects of the technique were shared and agreed upon to allow a complete description. The document thus elaborated constitutes a valuable practical guide for the implementation of the technique.

5. Conclusions

Consistently with the results of the GEC-ESTRO phase III study, which demonstrated the non-inferiority of APBI versus WBI in adequately selected early-stage breast cancer patients, all institutions with Brachytherapy facilities available should offer interstitial BT APBI to patients fulfilling the inclusion criteria as a favourable alternative to external beam radiotherapy.

Institutions willing to implement interstitial BT APBI are encouraged to follow the consensus guidelines set out in this document.

Conflict of interest

None declared.

Financial disclosure

None declared.

Acknowledgements

We would like to acknowledge the remarkable job of the Radiation Oncology and Medical Physics staff of CIBIR for the brilliant organization of the consensus meeting. We would also like to extend a warm thank to the moderators of the different sessions for the smooth conduct of the meeting and to participants in the institutional experience session.

Finally, we are profoundly grateful to all attendees, radiation oncologists, medical physicists, oncology nurses, for their active contribution to the success of the meeting.

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