Radiotherapy and Oncology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery

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ARTICLE INFO

Article history:
Received 26 February 2015
Received in revised form 8 June 2015
Accepted 8 June 2015
Available online xxxx

Keywords:
Breast cancer
Target definition
Brachytherapy
APBI
Boost

ABSTRACT

Objective: The aim was to develop a delineation guideline for target definition for APBI or boost by consensus of the Breast Working Group of GEC-ESTRO.

Proposed recommendations: Appropriate delineation of CTV (PTV) with low inter- and intra-observer variability in clinical practice is complex and needs various steps as: (1) Detailed knowledge of primary surgical procedure, of all details of pathology, as well as of preoperative imaging. (2) Definition of tumour localization before breast conserving surgery inside the breast and translation of this information in the postoperative CT imaging data set. (3) Calculation of the size of total safety margins. The size should be at least 2 cm. (4) Definition of the target. (5) Delineation of the target according to defined rules.

Conclusion: Providing guidelines based on the consensus of a group of experts should make it possible to achieve a reproducible and consistent definition of CTV (PTV) for Accelerated Partial Breast Irradiation (APBI) or boost irradiation after breast conserving closed cavity surgery, and helps to define it after selected cases of oncoplastic surgery.

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Breast conserving surgery followed by whole breast radiation therapy (WBRT) is the current standard treatment for nearly all women with early breast cancer [1,3,5,14,27,50,53]. But it is well known that whole breast irradiation can be associated with some clinically significant side effects, sometimes probably even associated with an increase of mortality [7,8,17,29,31,49]. Particularly the doses on the anterior myocardial wall, more precisely on the left descending coronary artery, determine the risk of ischaemic heart disease for 20 years after radiation therapy [7,48]. It is obvious, that the larger the volume of Clinical and Planning Target Volume (CTV and PTV) the higher the risk of radiation related morbidity [28]. After surgical tumour excision, reducing CTV/PTV inside the breast around the tumour bed and using interstitial multicatheter brachytherapy (IMBT) as an outmost conformal radiation technique goes hand in hand with dose and volume reduction to the normal tissues. Same results can be observed for the skin, the heart and the lung with a dose reduction by a factor of at least 3–4 [25]. Another disadvantage of WBRT is a long treatment time of 5 to 7 weeks which can present a possible barrier for the general acceptance of this treatment method. Despite the well documented equivalence of breast conserving therapy compared to mastectomy, it has been reported that up to 30–50% of patients who are clinically eligible for breast conservation still undergo breast amputation [6,40,43]. In other series, 15–30% of women treated with breast conserving surgery failed to receive whole breast irradiation [2,13]. Reasons for the infrequent utilization of this treatment approach include patient convenience, physician preference, and logistical problems [2,13,33]. With distances between the sites of residence and radiation treatment facility of more than approximately 60–70 km the willingness of patients to accept postoperative radiation therapy decreases exponentially [2,33]. Accelerated Partial Breast Irradiation (APBI) is an attractive treatment approach not only to

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http://dx.doi.org/10.1016/j.radonc.2015.06.010
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Please cite this article in press as: Strnad V et al. Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery. Radiother Oncol (2015), http://dx.doi.org/10.1016/j.radonc.2015.06.010

reduce the volume of the irradiated breast, the radiation exposure to the skin, the lung and particularly to the heart very effectively but also to shorten the course of whole breast irradiation from 5 to 7 weeks to 4–5 days (or less). The shortening of radiation therapy duration eliminates some disadvantages of long total treatment time, especially important for elderly patients, working women, and those who live at a significant distance from the radiation treatment facility.

Furthermore, the majority of local recurrences occur in close proximity to the tumour bed [12,14,18,32,51,55]. Thus, the necessity of whole breast radiation therapy has been questioned, and several centres have evaluated the feasibility and efficacy of tumour bed irradiation alone [4,35–37,46]. In spite of the lack of specific guidelines for target volume definition of the tumour bed, the results of the EORTC 22881 phase III randomized trial [38] and a number of numerous APBI trials [4,35,36,46,54] confirmed a significant impact of local dose on local control rates. Currently, due to the new concept of APBI and the occurrence of new irradiation techniques it remains crucial to propose consensual and consistent CTV delineation rules [24,42]. Reviewing the issue of target delineation after breast conserving surgery it has to be noted that after open cavity surgery a number of analyses exist with local rules and guidelines [19,34,55,57]. But according to our knowledge no recommendations are defined for the target definition after closed cavity surgery or oncoplastic surgery.

The recommendation of the GEC ESTRO Breast Cancer Working Group is focused on reproducible target definition and target delineation for partial breast irradiation (PBI) after closed cavity or oncoplastic breast conserving surgery using interstitial multicatheter brachytherapy, irrespectively whether PBI is intended for sole APBI or for a boost after external beam WBRT. The objective is to define tissue structures inside the post-operative breast in CT images after a breast conserving surgery in order to be able not only to propose a consensual and reproducible definition of what the target is but also to provide consistent rules for delineation of Clinical Target Volume (CTV) and Planning Target Volume (PTV).

The results of the deliberations of the Working Group Breast of GEC-ESTRO and corresponding proposal for recommendations for the target definition for APBI using multicatheter interstitial brachytherapy are presented in the following sections.

Method

Appropriate delineation of CTV (PTV) with low inter- and intra-observer variability in clinical practice is complex and needs various steps:

1. DETAILED KNOWLEDGE is obligatory of the primary surgical procedure (type of surgery, /number and location of surgical clips position of the skin scar), of all details of the pathology report including size of resection margins in 6 directions, as well as of preoperative imaging (mammography and/or MRI and/or ultrasound).
2. TUMOUR LOCALIZATION before breast conserving surgery inside the breast and translation of this information into current CT imaging data set.
3. Calculation of the size of SAFETY MARGINS needed to cover CTV in all 6 directions.
4. DEFINITION OF TARGET – CTV/PTV.
5. DELINEATION OF THE TARGET – CTV/PTV according to defined rules.

Tumour bed localization

For appropriate localization of the tumour bed the following information is needed: Preoperative clinical examination, preoperative imaging (preoperative mammograms, preoperative ultrasound; MRI if available), the surgical report including detailed information about the surgical technique (closed cavity, open cavity, oncoplastic technique, eventual skin resection in regard to the tumour), position of the skin scar (as gateway towards the tumour bed), number and positioning of the surgical clips. Breast surgery history could be important to know in case of multiple skin scars in the ipsilateral breast. The decision on what belongs to the tumour bed/CTV is taken based on a critical evaluation of ALL this information.

The skin scar is the gateway of the surgeons for tumour resection, but its relevance for the tumour bed localization should be evaluated cautiously. The distance between the scar on the skin and the surgical clips is on average 4 cm and reaches up to 9 cm [16]. Consequently the scar of the skin represents important information about the onset of the "tumour resection scar inside the breast" but has no or only limited value about the localization of the tumour bed [22].

Surgical clips can help the radiation oncologist to delineate the tumour bed. Well placed clips can help the radiation oncologist to indicate which part of the scar belongs to the tumour bed and which part to the access scar. Sometimes clips are placed in the cavity but so far from the initial tumour location that they are showing the surgical bed, not the tumour bed. For instance some clips on the thoracic wall can be excluded from the tumour bed, if they do not correspond to the localization of tumour. The corresponding correct information, and as far as possible a mutually accepted protocol between radiation oncologist and surgeon can help to decide the degree of the relevance of the clips for the tumour bed localization. Taking into account the surgical clips the first information we need is to know "how and to which structures inside the breast the surgeon clamps the clips" and the number of clips. In principle, we are faced with two situations: either the clips can be fixed to the thoracic wall (here 4 clips should be a minimum to be able to visualize the position of resection margins in medial, lateral, cranial and caudal directions) or the clips have been clamped into the breast parenchyma or fat tissue inside the breast – especially in elderly women due to the risk of clips migration (here 6 surgical clips should be a minimum to be able to visualize the resection margins in all body axes). The surgical clips should always represent the deepest end of surgical scar inside the breast. In this situation, the surgical clips correlate not necessarily exactly with the surgical margins of the tumour bed. Clips in the breast parenchyma on the other hand can provide more adequate information about positions of all surgical margins and if done correctly the clips correspond with surgical margins in this parenchymal area [11,20,39].

The surgical clips make it possible to visualize the deepest part of the surgical scar, during the insertion of brachytherapy catheters. When the first needle is put in the middle of this posterior plane, it can serve to define the base plane for the implant. When the clips are inside the breast parenchyma their use significantly improves the ability to visualize the tumour bed with up to approx. 70% rate between physicians regardless of the breast tissue density [10,11].

The accuracy of surgical clips placement is essential. Generally, we are confronted with two kinds of inaccuracy: first with variability – change of position of the clips – during the time after breast conserving surgery – and second with random inaccuracy – inaccuracy of position of clips due the surgical hand. It is a well-known fact that variability of surgical clips with time leads to movement of clips of about 3 mm after breast conserving surgery [9,56]. From our point of view, it is not necessary to take this into consideration because typically these clips move together with the tumour bed (with the resection margins) or with scar retraction within the breast tissue. Other important question is

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