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PRACTICE GUIDELINE

Consensus statement on tumour bed localization for radiation after oncoplastic breast surgery

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ABSTRACT

Background Oncoplastic surgery (OPS) is becoming the new standard of care for breast-conserving surgery, leading to some challenges with adjuvant radiation, particularly when accurate tumour bed (TBd) delineation is needed for focused radiation (that is, accelerated partial breast irradiation or boost radiation). Currently, no guidelines have been published concerning TBd localization for adjuvant targeted radiation after OPS.

Methods A modified Delphi method was used to establish consensus by a panel of 20 experts in surgical and radiation oncology at the Canadian Locally Advanced Breast Cancer National Consensus Group and in a subsequent online member survey.

Results These are the main recommendations:

- Surgical clips are necessary and should, at a minimum, be placed along the 4 side walls of the cavity, plus 1–4 clips at the posterior margin if necessary.
- Operative reports should include pertinent information to help guide the radiation oncologists.
- Breast surgeons and radiation oncologists should have a basic understanding of OPS techniques and work on "speaking a common language."
- Careful consideration is needed when determining the value of targeted radiation, such as boost, in higher-level OPS procedures with extensive tissue rearrangement.

Conclusions The panel developed a total of 6 recommendations on TBd delineation for more focused radiation therapy after OPS, with more than 80% agreement on each statement. All are summarized, together with the corresponding evidence or expert opinion.

Key Words Breast-conserving surgery, oncoplastic surgery, tumour bed, clips, radiation

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BACKGROUND

Oncoplastic surgery (OPS) is becoming the new standard of care for breast-conserving surgery (BCS). Breast-conserving surgery consists of lumpectomy or partial mastectomy and, when combined with postoperative adjuvant radiotherapy, has been shown to be comparable to mastectomy in terms of overall survival[1,2]. Oncoplastic surgery combines BCS with plastic surgery tissue displacement techniques to immediately reshape the breast, with the aim of improving cosmetic outcomes while treating the breast cancer[3–6]. Oncoplastic surgery has allowed for larger tumours or tumours in a challenging location where volume loss could affect overall cosmesis to be resected while oncologic principles and cosmetic outcomes are both maintained[5,7,8].

Although OPS has increased the ability of surgical oncologists to perform BCS, it has also led to some challenges

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with adjuvant radiation. Traditionally, radiation oncologists use various methods to define the tumour bed (TBd) and the subsequent target volumes for radiation. Accurate TBd localization is particularly important when considering partial breast irradiation (PBI). In accelerated PBI, the dose per session is higher, and the total dose is delivered over limited number of sessions (usually 5 in external-beam irradiation). In non-accelerated PBI, a standard dose per fraction is used, and the total dose is delivered in 15 fractions. Any PBI has the benefits of irradiating a lesser volume of breast tissue and a smaller skin surface, and of minimizing dose exposure to the surrounding normal tissue (lung and heart) by targeting the prescription dose of radiation over the area where the breast tumour was removed. Accurate definition of the TBd on radiation planning computed tomography (CT) images is thus critical. Localization and definition of the TBd are also very important for cases in which an additional boost of radiation dose to the TBd is indicated. The American Society for Radiation Oncology supports a TBd boost in all patients less than 50 years of age and in those more than 50 years of age at higher risk for local recurrence because of factors such as high tumour grade or positive margins[9].

Traditional methods of defining the TBd include use of the surgical incision, the postoperative seroma cavity, and implantable surgical markers or clips placed intraoperatively. Several issues arise with the use of those traditional methods of TBd delineation for radiation planning after OPS. Often, the incision is not over the lumpectomy cavity. In OPS, the lumpectomy cavity is closed, with tissue re-approximation to optimize cosmesis, and thus a seroma does not form. Glandular breast tissue flaps are often rotated from other areas of the breast into the lumpectomy cavity to fill the defect, such that the true TBd margins could be well away from the original lumpectomy site, replaced by healthy breast tissue[10,11]. And there is large variability in surgical practice in terms of clip placement, even with standard lumpectomy. Currently, no consistent practice for clip placement has been agreed upon by surgeons.

In the absence of any current guidelines for delineating the TBd after OPS, the main objective of the present work was to use a modified Delphi consensus process to establish a national clinical practice guideline. Here, we summarize the existing literature and expert opinion on TBd localization, from which a national consensus statement has been created. The target audience for this guideline is surgical oncologists who perform OPS, radiation oncologists and radiation technologists who treat women who have undergone OPS, and provincial or jurisdictional cancer agencies and funding bodies, with the aim of facilitating implementation of the guideline in all major cancer centres across Canada.

METHODS

A modified Delphi process, which took place between April and July 2018, was used to reach the consensus[12]. The present study follows the methodologic strategy described by the AGREE II instrument (https://www.agreetrust.org/).

The expert panel consisted of participants in the Canadian Locally Advanced Breast Cancer National Consensus (LABCNC) Group on intraoperative and postoperative strategies for TBd identification in oncoplastic BCS. The group met in Toronto, Ontario, 29–30 April 2018. The 20 Canadian participants had been identified as peer leaders in the area of locally advanced breast cancer within the fields of radiation oncology (9 participants) and breast surgical oncology (11 participants). The participants in the consensus panel and their disclosure of any relationships that could be seen as a potential conflict of interest are listed in supplementary Table 1.

Before the LABCNC meeting, a comprehensive search of the literature about OPS and radiation was conducted. Two independent reviewers examined each study for relevance, identifying articles that were used as the basis for the guideline recommendations. Based on the literature search, three main topics were identified. Within each main topic, questions were developed:

- Intraoperative clip placement
  - Is intraoperative clip placement for TBd identification necessary?
  - What is the optimal number and location of clips for TBd identification?
- Speaking the same language: the surgical oncologist and the radiation oncologist
  - Is standardization of operative reports necessary?
  - What should be included in operative reports to make communication more clear?
  - What should radiation oncologists know about OPS?
  - Should there be surgeon involvement in radiation planning?
- Issues with OPS and targeted radiation
  - In patients who have had advanced OPS (level II or III), can the TBd be accurately located to facilitate PBI or boosting?
  - Should PBI or boost be used after level II or III OPS?

At the LABCNC meeting, the first step was to present the main issues as identified beforehand and to give participants a chance to identify new issues. The issues were then summarized as a final set of statements presented to all participants. A chance for further discussion ensued. The statements were then sent to the group in an online survey, giving them a final chance to review the statements. All statements are graded using the 1–4 Levels of Evidence system, as is standard practice for consensus statements and routinely used by the American Society of Clinical Oncology and the European Society for Medical Oncology. Any statement without a grade is considered standard clinical practice or expert opinion[13].

RESULTS

The online survey had a response rate of 75% (15 of the 20 participants from the conference).

The final consensus statements are presented in the next section, with the associated evidence and expert opinion. Table I summarizes the statements and presents the percentage agreement for each one.

TABLE I The final consensus statements as recommended by the expert panel

Clinical domain		Recommendation	Level of evidence	Agreement [% (*n* of 15)]
Intraoperative clip placement				
	1	In breast-conserving surgery, surgical clips should be placed intraoperatively to assist in tumour bed delineation and postoperative radiation planning.	3	100 (15)
	2	The optimal number of surgical clips to be placed is at least 4, with 1 clip placed on each of the cavity side walls (medial, lateral, superior, inferior) at the level where the tumour was originally situated. Additionally, 1–4 clips can be placed on the posterior margin, which might or might not be the chest wall.	3	93.3 (14)
	3	Surgeons should avoid the use of clips anywhere else in the breast or axilla except for the purposes of tumour bed delineation. If clips are necessary beyond those required for tumour bed delineation, then the surgeon should clearly document, within the operative report, where and why the clips were used.	4	80 (12)
Speaking the same language: the surgical oncologist and the radiation oncologist				
	4	Operative reports should ideally include the tumour size and location, defect size, an accurate description of the surgical procedure (including oncoplastic procedure level, incision, tissue that has been rotated), explanation of clip placement (including how each margin is marked and whether clips were used for other reasons), and closure technique (that is, deep tissue, superficial tissue, or both).	4	93.3 (14)
	5	Breast surgeons, radiation oncologists, and radiation technologists should have a basic knowledge of the various oncologic and oncoplastic techniques commonly performed by the surgeons at their institution. Radiation oncologists and surgeons should attempt to establish "a common language" for their local institution.	4	100 (15)
Issues with oncoplastic surgery and targeted radiation techniques				
	6	Given the extensive rearrangements of breast tissue with level II and III oncoplastic procedures, the resultant difficulty in tumour bed delineation, and the large volume that might be included in a boost, the radiation oncologist might have to carefully consider the value of boost and the eligibility of such patients for partial breast irradiation.	3	100 (15)

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Recommendation 1

- In breast-conserving surgery, surgical clips should be placed intraoperatively to assist in TBd delineation and postoperative radiation planning.

Compared with traditional clinical methods using the surgical scar or postoperative seroma cavity, implanted surgical markers or clips are widely recognized as the most common and accurate method of TBd localization[4]. Several studies have demonstrated that traditional clinical planning techniques tend to underdose the TBd, to increase radiation to normal surrounding tissue, and to result in low interobserver reliability in target delineation[1,4–6].

A 2016 U.K. Royal College of Radiologists consensus statement unanimously supports the use of TBd clips as the standard of care in BCS to improve the planning and administration of adjuvant boost radiation[3]. The U.K. Association of Breast Surgery agreed that the use of surgical clips improves the quality of whole-breast radiotherapy and supported clip use as a national standard of care[4]. In an audit of 30 patient cases and 2 consultant radiation oncologists on behalf of the IMPORT trial management group, the Association demonstrated the benefit of surgical clips for TBd localization. The physicians were able to identify the TBd using CT images of the seroma cavity in 8 of 30 patients. Localization of the TBd was improved using surgical clips in the remaining 22 patients, resulting in border modifications to the radiotherapy field and contributing to improved inter- and intra-observer variability in target definition.

Despite the known benefit of clipping, further review of the literature suggests that clip placement is still inconsistent and often varies between centres[1]. A commonly cited reason for poor compliance is that surgeons are forgetting to place the clips during the procedure[1,4].

Recommendation 2

- The optimal number of surgical clips to be placed is at least 4: 1 clip on each of the cavity side walls (medial, lateral, superior, inferior) at the level where the tumour was originally situated. Additionally, 1–4 clips can be placed on the posterior margin, which might or might not be the chest wall.

Among surgeons who consistently place clips during BCS to delineate the TBd, the number and location of clips used varies. Published guidelines supporting clip placement do not indicate exactly how many clips should be used nor where they should be placed within the lumpectomy cavity. Thus, no international consensus has been reached with respect to those practices. The literature was reviewed to assist in deriving a consensus about the optimal number of clips[2,4,14].

The IMPORT trial management group used 6 pairs of clips to mark the boundaries of the TBd in the 6 main directions: medial, lateral, superficial (anterior), deep (posterior), superior (cranial), inferior (caudal)[2]. The Groupe Européen de Curiethérapie and the European Society for Radiotherapy and Oncology, an amalgamation of two radiation oncology expert groups in Europe, published consensus guidelines in 2016 about target delineation for

accelerated or boost PBI after BCS, recommending that 6 single clips be placed on the boundaries of the TBd for its optimal definition[14].

Kirby *et al.* used 4 common methods of clip placement to perform a within-patient comparison of TBd volume delineation after lumpectomy cavity closure: insertion of 6 clips (4 radial, 1 deep, 1 superficial); 5 clips (4 radial, 1 deep); 1 clip at the chest wall; and no clips. Target definition for accelerated PBI or boost radiation based on no clips or only 1 clip was not recommended because large additional margins (median 8 mm and 5 mm respectively) would be required to compensate for uncertainty about the true TBd location. The study concluded that 5 clips—1 deep (posterior), and 4 radial—are adequate for TBd delineation when PBI or boost is indicated[2].

The consensus panel recommends the intraoperative placement of a minimum of 4 clips in the breast parenchyma on the superior, inferior, medial, and lateral walls of the lumpectomy cavity at the depth of the tumour in the plane between skin and chest wall (anterior to posterior). The clips should be placed before any breast tissue rotation or movement is performed[1,7,15]. If the tumour cavity extends to the chest wall, the panel suggests that 1–4 additional clips be placed on the chest wall to indicate the most posterior aspect of the tumour resection.

The Groupe Européen de Curiethérapie and the European Society for Radiotherapy and Oncology guideline published in 2015 for target definition and delineation after closed-cavity breast surgery states that the estimated TBd will be a combination of the surgical clips, the visible surgical changes on planning CT, and the original tumour location on preoperative imaging[7].

Recommendation 3

- Surgeons should avoid the use of clips anywhere in the breast or axilla except for the purposes of TBd delineation. If clips are necessary beyond those required for TBd delineation, then within the operative report, the surgeon should clearly document where and why the additional clips were used.

Additional clips placed outside of the true TBd—for hemostatic purposes, for example—could lead to overestimation of the target volume if all clips visualized are encircled[8]. If clips are necessary for hemostasis or during the reconstruction phase of the procedure, the consensus panel strongly suggests that, within the operative report, the surgeon clearly document where, relative to the true TBd, the additional clips were placed and indicate why they were used (for example, for hemostasis, axilla surgery, etc.) so that the additional clips are not misinterpreted as localization clips by the radiation oncologist.

Recommendation 4

- Operative reports should ideally include the tumour size and location, defect size, accurate description of the surgical procedure (including OPS level, incision, tissue that has been rotated), explanation of clip placement (including how each margin is marked and if clips were used for other reasons), and closure technique (that is, deep tissue, superficial tissue, or both).

Management of breast cancer requires the orchestrated involvement of a multidisciplinary team. Clear communication between specialties is therefore crucial throughout the care of patients with breast cancer. An editorial published in the *European Journal of Surgical Oncology* acknowledged advances in breast radiation techniques, including PBI, but emphasized that the success of such targeted radiation strategies "may be jeopardised unless surgeons and radiation oncologists work closely together to ensure that the tumour bed can be reliably identified"[15].

The consensus panel recommends that surgeons and radiation oncologists establish a standardized method of operative procedure reporting. Currently, no guidelines for operative reports have been published, and no single format is widely used. Minimum requirements should include the tumour size and location, defect size, accurate description of the surgical procedure (including OPS techniques, skin incision placement, boundaries of anterior and posterior margins, tissue relocation), explanation of clip placement (that is, number of clips placed and their exact location on the margins, whether clips were used for other purposes), closure technique (that is, deep tissue closure, superficial tissue closure only, or both)[15]. The Groupe Européen de Curiethérapie and the European Society for Radiotherapy and Oncology Breast Cancer Working Group guideline states that those details are important for proper target delineation[7]. The consensus panel did not develop a report template to be followed, but instead recommends that surgeons and radiation oncologists within a single institution collaborate to develop their own preferred standard reporting tool.

Recommendation 5

- Breast surgeons, radiation oncologists, and radiation technologists should have a basic knowledge of the various oncologic and OPS techniques commonly performed by the surgeons at their institution. Radiation oncologists and surgeons should attempt to establish "a common language" for their local institution.

Although surgeons might strive to create detailed operative reports for conveying all the information necessary for radiation, each clinician involved in the planning and delivery of radiation must be able to understand and clinically apply that information. Radiation oncologists must have knowledge of the procedure and anatomy being described, including a basic understanding of various higher-level OPS techniques. Thus, surgeons and radiation oncologists must establish and speak "a common language."

The consensus panel recommends that physicians and clinicians involved in radiation therapy have a basic knowledge of the oncologic and OPS techniques commonly performed by the surgeons at their institution. Everyone involved in the treatment of the patient during surgery and radiation therapy should have a unified understanding of what is involved in the various levels of OPS. As previously discussed, an understanding of the surgical steps is especially important with procedures in which the skin scar provides little information about the previous location of the tumour. Classification systems for OPS have been well described[10,11].

The authors of an editorial published in the *European Journal of Surgical Oncology* recommended that, for optimal multidisciplinary collaboration, radiation oncologists should participate in or observe various types of lumpectomy procedures as part of their ongoing education, including level I and II OPS procedures[15]. Other authors have also strongly suggested that surgeons arrange a preoperative referral to radiation oncology whenever the use of complex OPS techniques is anticipated[16]. Similarly, the surgeons must also have a working knowledge of the techniques involved in the planning and delivery of radiation therapy. The consensus panel suggests that surgeons attempt to be present with the radiation oncologists during target contouring and radiation boost planning. Through such partnerships, the challenge of translating geometric information from one medical specialty to another for the optimal treatment of the patient can be overcome.

Recommendation 6

- Given the extensive rearrangements of breast tissue that occur with level II and III OPS procedures, the resultant difficulty in TBd delineation, and the large tissue volume that might be included in a boost, the radiation oncologist may have to carefully consider the value of boost and the eligibility of such patients for PBI.

The increasing use of OPS techniques for BCS necessitates the ongoing modification of targeted radiation planning and application. The consensus panel recognizes that higher-level OPS procedures pose a greater challenge for accurate TBd delineation and can even preclude a patient from receiving a more focused radiation treatment plan. In addition, boost radiation can diminish cosmetic results, potentially compromising the primary goal of OPS[16]. Those considerations present a major challenge, because patients deemed candidates for OPS tend to be younger and to present with cancers that are more advanced; they would therefore derive greater benefit from boost for lowering the risk of local recurrence[16,17].

A retrospective review by Pezner *et al.*[8] highlighted the challenges of TBd delineation for boost radiation after OPS and also concluded that the research into this issue has been minimal. Despite clips being placed intraoperatively to mark the lumpectomy margins, the TBd was frequently located in a larger region of the breast or in a region completely different from the preoperative location identified based on physical exam and radiologic images. In some cases, clips were scattered in 2 or 3 regions of the breast, suggesting that the TBd might have been separated into portions and relocated to adjacent areas[8]. Other studies have found that, in 43%–73% of patients who had undergone OPS with clip placement, clips on postoperative CT imaging were visualized outside the original tumour quadrant[1]. The authors of the paper suggested that, although the usefulness of boost after whole-breast radiotherapy for lowering the risk of local recurrence has been well demonstrated in conventional BCS, its benefit in patients receiving oncoplastic BCS remains unclear. Although the boost might provide additional local control, delivery of radiation to a poorly localized target can result in unnecessary exposure of healthy tissue and in diminishment of cosmetic outcomes[8].

A systematic review by Yoon *et al.*[16] aimed to evaluate the evidence for various adjuvant radiation methods after OPS compared with conventional BCS. The authors suggested that the limited number of studies prevented drawing any statistically significant conclusions, further emphasizing the need for additional research into these topics.

The consensus panel thoroughly discussed the utility of boost radiation after OPS. The aim of boost is to apply additional doses to the tissue directly surrounding the TBd to minimize the risk of local recurrence, given that most in-breast recurrences develop in that region[4]. The American Society for Radiation Oncology recommends boost in patients at high risk for local recurrence (young age, close or positive margins, and high tumour grade)[9]. The success of BCS requires complete resection of the cancer, with adequate clear margins. Although no panel consensus was reached about whether patients treated with oncoplastic BCS are good candidates for boost, the panel members endorsed the view that OPS techniques allow surgeons to resect large volumes of tissue and achieve wider margins, potentially negating the need for boost[10,11,17–22].

A meta-analysis published in 2014 reported that OPS was performed on larger tumours and yet, compared with the lumpectomy-alone group, was associated with significantly lower positive margin rates (12% vs. 21%) and lower local recurrence rates (4% vs. 7%)[20]. A single-centre study of 222 breast procedures reported that patients undergoing BCS via oncoplastic reduction had wider free margins and lower incidences of positive margins, re-excision, and completion mastectomy[17]. Oncoplastic surgery holds the potential to negate the need for boost, given its ability to achieve wider resection margins and, possibly, lower rates of margin positivity. Future work is needed to clarify the degree of benefit gleaned from boost radiation in patients receiving OPS.

The consensus panel has no recommendations to make about the management of positive margins (re-excision vs. mastectomy vs. boost radiation therapy) after OPS, but the members acknowledge that further research and standardization of treatment in such cases is necessary.

CONCLUSIONS

The Canadian Consortium for LABC 2018 has developed 6 recommendations for optimal TBd delineation to increase accurate and effective delivery of adjuvant focused radiation in patients receiving OPS. Table I summarizes the panel's recommendations. Further work is needed to evaluate any incremental benefit of boost or accelerated PBI in terms of recurrence reduction for OPS patients, considering their higher dosimetry volumes and risk of toxicity to normal tissue.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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