Ann Surg Oncol (2024) 31:5483–5486
https://doi.org/10.1245/s10434-024-15639-5

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL – BREAST ONCOLOGY

Surgical Perspectives on the Updated ASTRO Guideline on Partial Breast Irradiation for Breast Cancer

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ABSTRACT This is an executive summary of the most recent American Society for Radiation Oncology (ASTRO) guidelines on use of partial breast irradiation in early-stage breast cancer.

In the conscientious pursuit of "right-sizing" the management of patients with early-stage breast cancer, there has been an emphasis on judicious de-escalation of therapy. A component of this paradigm shift is partial breast irradiation (PBI), an approach characterized by targeted radiation therapy (RT) to lumpectomy cavity margins rather than to the whole breast (i.e., whole breast irradiation [WBI]) after breast conservation surgery (BCS). The American Society for Radiation Oncology (ASTRO) recently completed a revision of its evidence-based guidelines for the application of PBI.[1]

To accomplish this, recent PBI data were reviewed by panel members, including representatives of the American Society for Radiation Oncology (ASTRO), in collaboration with the American Society of Clinical Oncology (ASCO), and the Society of Surgical Oncology (SSO), which provided representatives and peer reviewers. The guideline was approved by the ASTRO Board of Directors and endorsed by the Canadian Association of Radiation Oncology, European Society for Radiotherapy and Oncology, Royal Australian and New Zealand College of Radiologists, and the Society of Surgical Oncology.

First Received: 20 May 2024
Accepted: 5 June 2024
Published online: 13 July 2024

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The recommendations focused on indications for PBI as an alternative to WBI and technical considerations specific to PBI. This editorial provides a summary and comments on the updated ASTRO PBI guidelines, offering insights into the implications of these findings for clinical practice and multidisciplinary decision-making while underscoring technical considerations for optimal incorporation of PBI into patient care.

KEY FINDINGS FOR PATIENT SELECTION AND PBI DELIVERY

The ASTRO PBI guideline is summarized below (Table 1).[1] The role of PBI in the setting of neoadjuvant systemic therapy, recurrent or second breast cancers, and locally advanced cancers is not addressed in the guideline.

SURGICAL MANAGEMENT CHALLENGES FOR APPLICATION OF PBI

The ASTRO guideline has important implications from a practical standpoint for surgeons counseling patients regarding PBI with respect to both the SSO Choosing Wisely guideline, created initially in conjunction with the American Board of Internal Medicine's (ABIM) Choosing Wisely Campaign (https://choosingwisely.org/), and the recently published SOUND trial results.[2,3]

The SSO Choosing Wisely Campaign for sentinel lymph node (SLN) surgery was introduced in 2016 largely based on results of the CALGB 9343 trial. In this trial, which included women with low risk, hormone receptor-positive breast cancer ≥70 years of age, routine axillary surgery was omitted in a subset of patients. Long-term results demonstrated an axillary recurrence rate of only

TABLE 1 Summary of ASTRO guidelines on PBI as safe and recommended alternative to WBI

	Recommendation		
	Recommended	Conditionally recommended	Not recommended
Condition	40 years or older with all of the following: • Tumors ≤2 cm • Grade 1–2 ductal carcinoma in situ (DCIS) or invasive ductal carcinoma • Estrogen receptor (ER)-positive	• Tumors 2–3 cm • Grade 3 disease • ER negative	• BRCA1/2 mutation • Positive lymph node(s) • Positive surgical margins without planned re-excision (or expanded RT fields)
PBI technique	External beam: • 3-dimensional conformal RT • Intensity modulated RT (IMRT) Multi-catheter brachytherapy	Single-entry brachytherapy	Unless part of clinical trial or multi-institutional registry: intraoperative radiation therapy (IORT), such as electron intraoperative radiation therapy (ELIOT) and kilovoltage (kV) IORT

3% in patients who received endocrine therapy and no radiotherapy. The SSO Choosing Wisely Campaign recommends against routine use of SLN surgery in clinically node-negative women ≥70 years with early-stage hormone receptor positive, HER2-negative invasive breast cancer and has subsequently been endorsed by several other professional societies.[4,5]

The recent SOUND trial demonstrates the oncologic safety of minimizing use of SLN surgery in patients who are clinically node negative with low risk cancers and negative axillary ultrasound. In patients with tumors ≤2 cm undergoing lumpectomy and RT there was no difference in recurrence, distant disease-free survival, or overall survival at 5 years when SLN surgery was omitted after a negative axillary US and/or negative core biopsy of a suspicious node.[2] The majority of the patients had grade 1–2, ER-positive, and invasive ductal histology. Because the SOUND trial was designed originally for patients who underwent BCS and WBI, only approximately 10% of patients in each arm underwent PBI (ELIOT), and there was no specification of treatment fields for WBI. As the ASTRO PBI guideline *specifically endorses PBI only if there is no nodal involvement*, the use of PBI in the absence of surgical axillary staging will be an important area of discussion with patients and the multidisciplinary team to ensure shared decision making.

Another population wherein PBI can be challenging is for patients who opt for oncoplastic surgery, such as BCS with concurrent reduction and/or mastopexy. PBI is an excellent option for women with macromastia as it can minimize the radiation dose to the uninvolved, large volume of breast tissue. However, localizing the original tumor bed is imperative for PBI, which may be difficult after oncoplastic surgery and tissue rearrangement. While surgical clips may be placed around the tumor bed to delineate the original tumor location, the oncoplastic tissue rearrangement can distort the lumpectomy cavity and clips, making it challenging to reliably delineate a precise tumor bed location for RT planning.[6]

Because omission of surgical axillary staging or use of oncoplastic surgery may preclude a patient from PBI, an upfront multidisciplinary discussion addressing PBI eligibility is recommended before finalizing local-regional therapy decisions. These clinical challenges again require a patient-centered approach to counseling regarding adjuvant therapy decisions.

OMISSION OF RT

As PBI is a way of de-escalating RT in early-stage breast cancer, growing evidence through completed and ongoing clinical trials is leading to a decrease in the use of RT in appropriately selected, low-risk patient populations. For women older than 70 years with small, ER-positive breast cancer and clinically negative nodes, guidelines recommend not only against routine SLN surgery as discussed above, but also against the routine use of post-lumpectomy irradiation.[7] The National Comprehensive Cancer Network (NCCN) guidelines cite the CALBG 9343 study in encouraging shared decision making regarding the use or omission of RT after lumpectomy in patients who are willing to commit to using adjuvant endocrine therapy. At 12.6 years median follow-up in the CALGB study, there was no significant difference in breast cancer-specific survival in women who received or did not receive post-lumpectomy radiotherapy.[8,9] The prospective cohort LUMINA trial in patients ≥55 years and tumors with low risk biological features (T1N0, grade 1 or 2, luminal A) demonstrated a low 2.3% risk of in-breast recurrence after a median follow-up of 5 years with omission of radiotherapy and use of endocrine therapy alone.[10]

The ongoing randomized NRG BR007 DEBRA trial is also addressing the oncologic safety of omitting post-lumpectomy RT in patients by identifying biologically low risk tumors through use of genomic assays.[11] Patients with low 21-gene recurrence scores (Oncotype DX ≤ 18) with stage I, ER-positive, Her-2-negative breast cancer are

randomized post lumpectomy to breast RT (whole breast or PBI) with endocrine therapy versus endocrine therapy alone.

Taken together, these studies emphasize the need to have informed discussions with patients regarding the overall benefit of post-lumpectomy RT, whether WBI or PBI.

INTRAOPERATIVE RADIATION THERAPY

Based on current data, the ASTRO guideline does not endorse IORT alone unless performed in the setting of a prospective clinical trial or multi-institutional registry. The randomized controlled ELIOT trial is repeatedly cited as a reason single fraction electron-based IORT (IOERT) is considered unacceptable; however, the inclusion/exclusion criteria that were applied in the ELIOT trial are incompatible with any current PBI recommendations.[12] For example, 51% of the patients were <60 years, 26% of patients had involved nodes (5% had 4 or more positive nodes), and only 21% received chemotherapy or combined chemotherapy and endocrine therapy despite high-risk biology. A number of recent studies evaluated IOERT, two of which were considered in the current ASTRO guideline.[13,14] Importantly, none of the IOERT studies have shown worse survival.

The relative merits of kV IORT, as in the TARGIT trial, are less clear.[15] Studies have shown that acceptable results can be achieved if appropriate selection criteria are applied; local control was 97.1% at 53 months[16] with a local relapse rate of 1.7% at 40 months[17] using the Intrabeam® technique. While assessing single fraction TARGIT results on an intent-to-treat basis has caused debate, the *risk adaptive* approach, defined as adding WBI when treating higher-risk patients, was sensible and safer in reducing in-breast recurrence. Given patient reported outcomes (PROs) and cosmetic data increasingly support IORT as a patient-centric option, continued review of mature clinical data is warranted as suggested in the ASTRO guideline.[18,19] Future studies with IORT should provide single fraction IORT results for IORT alone, rather than on an intent-to-treat basis, to more clearly elucidate the benefits of single fraction IORT. As none of the kV IORT studies to date have shown worse overall or disease-specific survival, additional IORT data are needed and when available should be considered in future recommendation updates.

FUTURE DIRECTIONS

As de-escalation of locoregional therapy continues to evolve, understanding how the different trials fit into the context of an individual patient will become increasingly complex. For instance, the FAST-Forward trial has made significant advances in WBI by delivering five fractions of RT in 1 week; this matches the speed of the most common, current approaches to PBI which uses 3-D conformal RT in 1 week.[20] Now that both WBI and PBI of comparable duration are available, future studies and guidelines will need to determine whether the slightly lower in-breast recurrence rates associated with WBI are offset by the tissue sparing effects associated with PBI and whether PBI remains a standard alternative to WBI or should it be reserved for special situations, such as prior chest wall RT, lower risk pathology, or repeat breast conservation.

CONCLUSIONS

These updated ASTRO guidelines provide an important, refreshed evaluation of the indications and technical considerations for use of PBI in patients with early-stage breast cancer and DCIS. Familiarity with the updated ASTRO guidelines will help ensure appropriate shared decision making for patients.

ACKNOWLEDGMENT Collaborators: Society of Surgical Oncology Breast Disease Site Work Group: Christine Laronga, MD, Judy C. Boughey, MD, Doreen Agnese, MD, Miral Amin, MD, Andrea V. Barrio, MD, Astrid Botty Van Den Bruele, MD, Erin Burke, MD, Frederick M. Dirbas, MD, Oluwadamilola M. Fayanju, MD, MA, MPHS, Olga Kantor, MD, Shicha Kumar, MD, Toan T. Nguyen, MD, Ko Un Park, MD, Jennifer K. Plichta, MD, MS, Shayna L. Showalter, MD, Puneet Singh, MD, MS, Nicholas Tranakas, MD, Anna Weiss, MD, Ashlee A. Woodfin, MD.

DISCLOSURES Dr. Andrea V. Barrio reports speaker honorarium, Novartis; Dr. Oluwadamilola M. Fayanju reports research support outside the current work from Gilead Sciences, Inc.; Dr. Anna Weiss, MD, reports advisory board member/consult payments, Merck, Myriad, Abbvie. There are no other disclosures to report.

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