Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, Society of Surgical Oncology Focused Guideline Update
Introduction

• The American Society of Clinical Oncology (ASCO) guideline for the use of postmastectomy radiotherapy (PMRT) was published in 2001.

• This update of that guideline, completed in collaboration with the American Society for Radiation Oncology (ASTRO) and the Society of Surgical Oncology (SSO), focuses on key areas of ongoing controversy including:
  – Use of PMRT for patients with 1-3 positive lymph nodes
  – Use of PMRT for patients undergoing neoadjuvant systemic therapy (NAST)
  – Selected technical aspects of PMRT, particularly the extent of regional nodal irradiation (RNI)
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

• a systematic literature review by ASCO guidelines staff
• an expert panel provides critical review and evidence interpretation to inform guideline recommendations
• final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:

www.asco.org/pmrt-guideline
Clinical Questions

1. Is PMRT indicated in patients with T1-2 tumors with one to three positive axillary lymph nodes who have axillary lymph node dissection?

2. Is PMRT indicated in patients with T1-2 tumors and a positive sentinel node biopsy who do not undergo completion axillary lymph node dissection?

3. Is PMRT indicated in patients presenting with clinical Stage I or II cancers who have received neoadjuvant systemic therapy?

4. Should regional nodal irradiation include the internal mammary and/or supraclavicular-axillary apical nodes when PMRT is used in patients with T1-2 tumors with one to three positive axillary nodes?

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Target Population and Audience

Target Population
Women with breast cancer and 1-3 positive lymph nodes or undergoing neoadjuvant systemic therapy

Target Audience
Medical oncologists, pathologists, surgeons, oncology nurses, patients, and caregivers.
Summary of Recommendations

CLINICAL QUESTION 1
Is PMRT indicated in patients with T1-2 tumors with one to three positive axillary lymph nodes who have axillary lymph node dissection?

Recommendation 1a
The Panel unanimously agreed that the available evidence shows that PMRT reduces the risks of LRF, any recurrence, and breast cancer mortality for patients with T1-2 breast cancer with 1-3 positive axillary nodes (Type: Evidence-based; Evidence quality: High; Strength of recommendation: Strong).

However, some subsets of these patients are likely to have such a low risk of LRF that the absolute benefit of PMRT is outweighed by its potential toxicities (Type: Evidence-based; Evidence quality: Intermediate; Strength of recommendation: Strong).
Summary of Recommendations

In addition, the acceptable ratio of benefit to toxicity varies among patients and physicians. Thus, the decision to recommend PMRT or not requires a great deal of clinical judgement. The Panel agreed clinicians making such recommendations for an individual patient should consider factors that may decrease the risk of LRF, attenuate the benefit of reduced breast cancer-specific mortality, and/or increase the risks of complications from PMRT.

These factors include:

• Patient characteristics (age older than 40-45 years, limited life expectancy due to older age or comorbidities, coexisting conditions that might increase the risk of complications)

• Pathologic findings associated with a lower tumor burden (T1 tumor size, the absence of lymphovascular invasion, the presence of only a single positive node and/or small size of nodal metastases, or substantial response to NAST)

• Biologic characteristics of the cancer associated with better outcomes and survival and/or greater effectiveness of systemic therapy (e.g. low tumor grade, strongly hormonally sensitive)

(Type: Informal Consensus; Evidence quality: Intermediate; Strength of recommendation: Moderate)
Summary of Recommendations

There are several risk-adaptive models, which physicians may find useful in explaining the benefits of PMRT during shared decision-making with patients. However, the Panel found insufficient evidence to endorse any specific model or to unambiguously define specific patient subgroups for whom PMRT should not be given (Type: No recommendation; Evidence quality: Low; Strength of recommendation: Weak).

Further research is needed on how to accurately estimate individuals' risk of LRF and hence their potential reductions in LRF and breast cancer mortality.
Summary of Recommendations

**Recommendation 1b**
The decision to use PMRT should be made in a multidisciplinary fashion by discussion among providers from all treating disciplines early in the patient's treatment course (soon after surgery or prior to or soon after the initiation of systemic therapy), either in the context of a formal tumor board or by referral. (Type: Informal consensus; Evidence quality: Insufficient; Strength of recommendation: Strong)

**Recommendation 1c**
Decision-making must fully involve the patient, whose values as to what constitute sufficient benefits and how to weigh the risks of complications against these in light of the best information the treating physicians can provide as to those of PMRT in their situation must be respected and incorporated into the final treatment choice. (Type: Informal consensus; Evidence quality: Insufficient; Strength of recommendation: Strong)
Summary of Recommendations

CLINICAL QUESTION 2
Is PMRT indicated in patients with T1-2 tumors and a positive sentinel node biopsy who do not undergo completion axillary lymph node dissection?

Recommendation 2
For patients with clinical T1-2 tumors with clinically negative nodes sentinel node biopsy (SNB) is now generally performed at the time of mastectomy with omission of ALND if the nodes are negative. ALND has generally been performed if the nodes are positive, but there is increasing controversy about whether this is always necessary, especially if there is limited disease in the affected nodes. The Panel recognizes that some clinicians omit axillary dissection with 1 or 2 positive sentinel nodes in patients treated by mastectomy. This practice is primarily based on extrapolation of data from randomized trials of patients treated exclusively or predominantly with breast-conserving surgery and whole breast irradiation or breast plus axillary irradiation. In such cases where clinicians and patients elect to omit axillary dissection, the Panel recommends that these patients receive PMRT only if there is already sufficient information to justify its use without needing to know that additional axillary nodes are involved. (Type: Informal consensus; Evidence quality: Weak; Strength of recommendation: Moderate.)
Summary of Recommendations

CLINICAL QUESTION 3
Is PMRT indicated in patients with clinical Stage I or II cancers who have received neoadjuvant systemic therapy?

Recommendation 3
Patients with axillary nodal involvement that persists following NAST (e.g. less that a complete pathological response) should receive PMRT. Observational data suggest a low risk of local-regional recurrence for patients who have clinically negative nodes and receive NAST or who have a complete pathological response in the lymph nodes with NAST. However, there is currently insufficient evidence to recommend whether PMRT should be given or can be routinely omitted in these groups. The Panel recommends entering eligible patients into clinical trials that examine this question. (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Weak.)
Summary of Recommendations

CLINICAL QUESTION 4
Should RNI include both the internal mammary and supraclavicular-axillary apical nodes when PMRT is used in patients with T1-2 tumors with one to three positive axillary nodes?

Recommendation 4
The Panel recommends treatment generally be given to both the internal mammary nodes and the supraclavicular-axillary apical nodes in addition to the chest wall or reconstructed breast when PMRT is used for patients with positive axillary lymph nodes. There may be subgroups that will have limited, if any, benefits from treating both these nodal areas compared to treating only one of them or, perhaps, treating only the chest wall or reconstructed breast. There is insufficient evidence at this time to define such subgroups in detail. Additional research is needed to identify them. (Type: Informal consensus; Evidence quality: Intermediate; Strength of recommendation: Moderate)
Discussion

• The Panel recommends strongly that input from all clinicians as well as the patient is needed to yield the best results from PMRT.

• This is best done by discussion among providers early in the patient's treatment course (before or soon after surgery and prior to or soon after the initiation of systemic therapy), either in the context of a formal tumor board or by referral to the surgical, medical, and radiation oncologists caring for the patient.

• Patients vary in how much they wish to participate in decision-making, but ultimately their values determine whether the potential long-term benefits of PMRT are sufficient to outweigh potential short- and long-term risks of side effects.
Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/pmrt-guideline

Patient information is available at www.cancer.net
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