

Oncology Clinical Service Line  
 System-wide Consensus Guidelines:  
**Postmastectomy Radiation for Patients with 1-3 Positive Lymph Nodes**

These guidelines apply to clinical interventions that have well-documented outcomes, but whose outcomes may not be desirable for all patients.

Reference #: SYS-PC-OCSL-CG-011

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**Approved By: Allina Health Quality Council**

**System-wide Ownership Group:** Allina Health Breast Cancer Program Committee

**System-wide Information Resource:** Manager of Clinical Programs

Hospital Division Quality Council: March 2018
<b>Stakeholder Groups</b>
Virginia Piper Cancer Institute

**SCOPE:**

<b>Sites, Facilities, Business Units</b>	<b>Departments, Divisions, Operational Areas</b>	<b>People applicable to</b>
All facilities that care for breast cancer patients; Abbott Northwestern Hospital, Buffalo Hospital, Cambridge Medical Center, District One Hospital, Mercy Hospital, Mercy Hospital – Unity Campus, River Falls Area Hospital, Regina Hospital, St Francis Medical Center, United Hospital	Breast Surgery Medical Oncology Radiation Oncology	MDs Advance Practice Providers

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**PICO (TS) Framework:**

**Patient Population:** T2N1 breast cancer patients with 1-3 positive lymph nodes (LN+) after mastectomy

**Intervention:** referral to radiation oncology

**Comparison:** N/A

**Outcomes:** Patient will receive all medical information and make informed decision regarding radiation treatment after mastectomy

**Timing:** post-mastectomy surgery

**Setting:** outpatient

**CLINICAL PRACTICE GUIDELINES:**

T2N1 breast cancer patients with 1-3 positive lymph nodes (LN+) after mastectomy should be referred for Radiation Oncology consultation in order to provide patients with all medical information to make a fully informed decision.

**SUPPORTING EVIDENCE:**

**Background:**

For patients treated with mastectomy, based on the available evidence from several randomized clinical trials, chest wall and regional radiation therapy (XRT) has been shown to significantly reduce local regional recurrence) LRR and to significantly prolong overall survival for patients with positive axillary nodes.

The Danish 82b trial evaluated postoperative radiation therapy for 1708 premenopausal women with operable node positive breast cancer treated with mastectomy and methotrexate-based chemotherapy. <sup>(4)</sup>

10 year follow-up showed patients receiving radiation had lower local regional recurrence (9% versus 32%) and improved cancer specific survival rates (48% versus 34%) and overall survival rates (54% versus 45%) compared with women who did not receive radiation. This finding was present in other specific subgroups including patients with 1 to 3 involved lymph nodes.

The British Columbia trial similarly reported that the addition of radiation therapy after mastectomy and chemotherapy resulted in improved local regional control rates (87% versus 67%) and improved cancer specific survival rates (50% versus 33%) in premenopausal women with lymph node positive disease.

A separate report from the Danish breast Cancer Cooperative group (82c) demonstrated postmenopausal women with node positive breast cancer also benefited from recent therapy after mastectomy and adjuvant tamoxifen. 10-year overall survival improved from 36% to 45%,  $p=0.03$ . <sup>(6)</sup>

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Based on these studies, most clinicians would recommend adding regional nodal XRT to breast XRT for patients with 4 or more positive nodes but not in those with negative nodes. Debate exists on the need to add regional nodal XRT for patients with 1–3 positive nodes. *In particular, there is uncertainty surrounding which specific subgroups have sufficient risk of residual microscopic locoregional disease after mastectomy to warrant treatment with radiation.*

Criticisms of the above studies include concerns about the adequacy of the surgery performed including the median number of lymph nodes removed, raising concern that inadequate regional surgery may have led to the underestimation of the true extent of axillary disease in these patients and may have contributed to an increased incidence of locoregional failure. Because LRR rates after mastectomy (and without PMRT) in retrospective American series of patients with 1-3 LN+ have been lower (13% in a large series from ECOG and NSABP) than those observed in the Danish and British Columbia studies, some have questioned the role of post mastectomy radiation therapy (PMRT) for patients with only 1-3 LN involved. <sup>(4, 6)</sup>

2001 ASCO practice guidelines for the use of PMRT concluded that the evidence to support PMRT was only strong enough to sustain a recommendation for patients with 4 or more lymph nodes involved. For patients with 1-3 lymph nodes involved, the panel concluded that there was insufficient evidence to make suggestions or recommendations for the routine use of PMRT, and practice then became divided between radiation oncologists who routinely treated and those who routinely observed this subgroup of patients.

More recently, however, increasing evidence has accumulated in support of a role for PMRT even among patients with 1-3 lymph nodes involved. The Danish studies were pooled and reanalyzed to include only the 1152 node positive patients with 8 or more lymph nodes removed. A survival benefit of the same absolute magnitude (9%) was observed in patients with 1-3 lymph nodes positive even though LRR rates were lower. In this situation, the survival benefit of PMRT was thought to be related to the ability of systemic therapy to eliminate any existing metastatic deposits at the time of diagnosis. Therefore, PMRT may be particularly important in the subset of patients with less extensive nodal involvement in whom the burden of distant disease at diagnosis is likely to be less substantial (and potentially amenable to elimination by systemic therapies). It is understood, however, that not all patients have the same risk of harboring residual locoregional disease after mastectomy and systemic therapy, nor of that reservoir being an isolated one. <sup>(4, 6)</sup>

Further compelling findings have emerged from the Oxford Early Breast Cancer Trialists Collaborative Group's meta-analysis. Published in 2005, the landmark Early Breast Cancer Trialist's Cooperative Group (EBCTCG) reported on 8450 postmastectomy patients (from 20 randomized trials) with 1-3+ lymph nodes who randomly were assigned

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to receive radiation therapy or not (generally given to chest wall and regional LN's). The majority received systemic therapy. <sup>(1)</sup>

The addition of radiation was associated with an absolute reduction and local recurrence of 16.1% at five years (22.8% to 5.8%) and 15-year breast cancer mortality risks of 54.7% versus 60.1% (reduction 5.4%, 2P=0.0002) and overall mortality reduction of 4.4% (64.2% versus 59.8%, 2P=0.0009). This led the EBCTCG to conclude that there was a 4:1 ratio, such that for every four local recurrences prevented at five years, one life was saved. <sup>(1)</sup>

There was no apparent evidence of a differential effect between groups of patients by number of positive lymph nodes (1, 2 or 3). When the investigators restricted the data to be more consistent with contemporary treatment regimens and surgical techniques, benefits and local regional recurrence and breast cancer survival were maintained, albeit at more modest levels (10.1% at five years and 3.3% at 15 years, respectively). <sup>(1)</sup>

The most recent EBCTCG meta-analysis published in 2014 looked at the role of PMRT in women with 1-3 lymph nodes involved. PMRT reduced locoregional recurrence, overall recurrence and breast cancer mortality even when systemic therapy was given. In the 1133 women who had 1-3 involved lymph nodes involved after mastectomy, axillary dissection and systemic therapy, the 10 year LRR was 21% without RT and 4.3% with RT. The 20-year breast cancer mortality was 49.4% with no RT vs. 41.5% with RT. <sup>(2)</sup>

Results from the NCIC MA.20 trial demonstrated that in lumpectomy patients with 1–3 positive nodes (some high-risk node-negative patients were also included), the addition of regional nodal XRT to breast XRT significantly reduced locoregional recurrence and significantly prolonged disease-free survival (DFS) and distant disease-free survival (DDFS). On the basis of the above results, chest wall and regional nodal XRT are commonly prescribed for mastectomy patients with positive axillary nodes. By showing that there are substantial benefits with the addition of regional nodal radiation in women with one to three positive lymph nodes, this trial indirectly validates the findings of three modern post mastectomy radiation therapy trials. <sup>(14)</sup>

Multiple single institution data in the era of modern chemo has identified the following risk factors as having an increased risk of LRR in this subset of patients including young age, LVSI, extracapsular extension, triple negative disease and grade 3 disease.

### **Conclusions:**

When taking all of this data together, the most recent set of consensus guidelines from the National Comprehensive Cancer Institute (NCCN) states that patients with one to three involved lymph nodes who undergo mastectomy should “strongly consider”

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radiation therapy. This is a Category 2B recommendation - i.e. "Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate." <sup>(3)</sup>

With data showing both local control and survival gained by adding post mastectomy radiation therapy to patients with positive lymph nodes – while we wait for further research to best define the subgroups – it is inappropriate to not give the information we currently have, in a multidisciplinary fashion, to any patient in this category so that they can participate in the decision-making process.

Patients with stage II disease who have 1-3 lymph nodes involved after mastectomy should be counseled by a radiation oncologist regarding their estimated risk of LRR in the absence of radiotherapy, the estimated benefit in terms of locoregional control expected from radiotherapy and the estimated impact on overall survival associated with this treatment weighed against potential side effects of treatment so that they can determine whether or not they wish to receive postmastectomy radiation.

**DEFINITIONS:** N/A

**SPECIAL ENTITIES:** N/A

**FORMS:** N/A

**ALGORITHM:** N/A

**ADDENDUM:**

**Plan for monitoring adherence:**

**Who** will be measured for guideline adherence?

- Metro Sites

**Where** is the data located?

- EDW/ERS

**How** will the guideline adherence be monitored?

- It will be monitored through the Breast Program Committee

**What** will be measured?

- % patients seen by radiation oncologist for radiation treatment after mastectomy with 1-3 positive lymph nodes

**When** will adherence data be collected?

- Program committee will continue to monitor yearly at minimum

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**Alternate Search Terms:** N/A

**Related Guidelines/Documents**

Name	Content ID	Business Unit where Originated
N/A		

**Guidelines/Documents Replacing**

Name	Content ID	Business Unit where Originated
N/A		

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