

BREAST RADIATION AFTER BREAST CONSERVING SURGERY

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The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

BACKGROUND

In the absence of radiotherapy, the risk of breast recurrence is higher for women younger than 60 years of age, with lobular carcinomas, pathologically involved axillary lymph nodes, positive excision margins, tumours larger than 1 cm diameter, or if adjuvant hormonal therapy is not used, compared to the corollary groups for each factor.^{1,2} Patients with *none* of these risk factors, have a 10-year risk of breast relapse of 5% or less after breast conservation surgery (BCS) alone. Omission of radiotherapy after BCS almost always increases the risk of local recurrence.² Vinh-Hung's meta-analysis shows that the addition of radiotherapy after breast conserving surgery for early breast cancer leads to a survival benefit (relative excess mortality of 8.6% if no radiation given).³

Women who are over 70 years of age and who have tumours 1 cm or smaller that are estrogen receptor positive and have negative axillary lymph nodes *and* who are receiving hormone therapy, likely have a 10-year recurrence risk of less than 5%.⁴ Breast radiotherapy would reduce this risk to less than 1%. According to the Lovi et al. study, only 4.8% of patients with more than three positive lymph nodes developed isolated nodal recurrence (NR) as the only site of recurrence. Having one to three positive lymph nodes was not associated with an increased risk of NR.⁵ The authors suggested that it is not necessary to prescribe nodal irradiation to patients with negative or one to three positive lymph nodes; however, in the patients with more than three positive lymph nodes, the number of isolated NR is small and does not justify node irradiation.⁵

The most common fractionation schedule used in Canada is 50 Gy in 25 fractions to the whole breast without a boost when excision margins are clear of disease.⁶ Alternative schedules that may be used range from 40 Gy in 16 fractions to the whole breast, with or without a boost, to 45 Gy in 25 fractions with a boost of 16 Gy in 8 fractions to the primary site.^{2,6} The role of boost irradiation to the primary site is unclear. Irradiation of the whole breast rather than partial irradiation is recommended.²

GUIDELINE GOAL AND OBJECTIVE

Develop consensus based recommendations for radiotherapy after breast conservation surgery.

GUIDELINE QUESTION

Can breast radiotherapy be avoided in some patients after breast conserving surgery?

DEVELOPMENT PANEL

This **guideline** was reviewed and endorsed by the Alberta Provincial Breast Tumour Team. Members of the Alberta Provincial Breast Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists. **Evidence** was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit.

SEARCH STRATEGY

The MEDLINE (1966 through July 2009), Cochrane, ASCO Abstracts and proceedings, and CANCERLIT databases were searched. The search included practice guidelines, systematic reviews, meta-analyses,

randomized controlled trials, and clinical trials. The search terms included breast, cancer*, tumour*, radiation OR radiotherapy, surgery OR conservation surgery.

TARGET POPULATION

Patients with breast cancer who have undergone breast conserving surgery

RECOMMENDATIONS

After full discussion of the benefits and risks, it is reasonable to omit breast radiotherapy after breast conserving surgery (BCS) for a woman aged 70 years or greater with a node negative breast cancer that is 1 cm or less in diameter and, ER positive provided she is receiving hormone therapy and accepts the higher risk of breast recurrence (around 5%) and the possibility of a small detriment in survival ($\leq 1\%$ at 10 years).

Such patients should discuss the pros and cons of radiation therapy with a radiation oncologist. Side-effects of hormone therapy should be considered in any decision to avoid radiotherapy. Patients who are not willing to accept hormone therapy due to concerns about side-effects, or where hormonal therapy is not recommended, should receive radiotherapy to the breast.

It was agreed that BCS followed by whole breast radiotherapy is a standard treatment for women with early-stage breast cancer. Table 1 summarizes the recommended radiotherapy for women following breast conserving surgery.

Table 1. Type and dosing of radiotherapy for ductal carcinoma in situ and invasive breast cancer treated with breast conserving surgery.

<i>Breast Cancer</i>	<i>Recommendation</i>
<i>DCIS</i>	<p>Whole breast radiotherapy: 4250 cGy/16 fractions or 5000 cGy/25 fractions are standard, but other fractionation can also be used.</p> <p>Partial breast radiotherapy is considered investigational as part of a clinical trial</p> <p>For margins <3mm, re-excision is recommended (close margin at fascia is an exception)</p> <p>For margins <3mm not treated with re-excision, the role of RT boost is not well defined</p>
<i>Invasive breast cancer Node negative</i>	<p>Whole breast radiotherapy: 4250 cGy/16 fractions or 5000 cGy/25 fractions are standard, but other fractionation can also be used.</p> <p>Partial breast radiotherapy is considered investigational as part of clinical trial</p> <p>For margins <3mm, re-excision recommended (close margin at fascia is an exception)</p> <p>Radiotherapy boost recommended:</p>

	<p>In all women <40 yrs regardless of margin In women >40 yrs boost individualized based on risk assessment (grade 3 disease, <3 mm margin) 4 – 8 fractions are most common</p>
<p><i>Invasive breast cancer T1/T2 and Node positive</i></p>	<p>1-3 nodes positive: For both pre- and postmenopausal women, whole breast radiotherapy is recommended. Regional nodal radiation is not recommended. Results from MA-20 study are pending.</p> <p>4 or more nodes positive: For both pre- and postmenopausal women, breast plus regional nodal radiotherapy is recommended; IM nodes may be included at oncologist's discretion 16, 20, or 25 fractions are common, but other fractionation can also be used. If >10 nodes resected, may limit field to supraclavicular +/- IM nodes</p>
<p>For patients in whom neo-adjuvant chemotherapy recommended, pre treatment FNA of palpable node or sentinel node procedure for non-palpable node recommended to assess role of nodal RT.</p>	

DISCUSSION

Breast radiotherapy reduces the risk of breast recurrence in all subgroups of patients by 65% to 75%. The absolute benefit of radiotherapy depends on the pre-treatment risk of recurrence.⁷

There have been seven randomized clinical trials of BCS with and without radiotherapy.^{4,6,8} Two meta-analyses of these trials have shown that adding radiotherapy decreased the absolute 10-year local recurrence rate by 20%.^{3,8} This improvement in local control translated into an absolute 4% reduction in the 10 year risk of death from breast cancer.

To justify not giving radiotherapy after BCS, the anticipated 10-year breast recurrence rate should be 5% or less (annual hazard of 0.5%). Therefore, a routine recommendation that radiotherapy is unnecessary after breast conserving surgery for all women aged 70 years and older is not appropriate.

Toxicity and Side-effects of Radiotherapy

The side-effects of modern breast radiotherapy are modest including include delayed cellulitis however most of them are self limited.^{9,10} Some patients will be left with breast discomfort and firmness.^{3,11} Recent data suggests that the cardiac risks following radiotherapy for left-sided breast cancer are no greater than following radiotherapy for right-sided breast cancer.^{3,9,11,12} The risk of a second malignancy related to the treatment is approximately one per thousand women receiving radiotherapy.

In the absence of radiotherapy, the risk of breast recurrence is higher for women younger than 60 years of age, with lobular carcinomas, pathologically involved axillary lymph nodes, positive excision margins, tumours larger than 1 cm diameter or if adjuvant hormonal therapy is not used, compared to the corollary groups for each factor.⁶ Patients with *none* of these risk factors, have a 10-year risk of breast relapse of 5% or less after BCS alone.

There is a higher risk of some malignancies in women receiving radiotherapy vs. women not receiving radiotherapy.¹³ Increased relative risks (RR) was reported for lung cancer at 10-14 years and 15 or more years after initial breast cancer diagnosis (RR 1.62, 95% confidence interval [CI] 1.05-2.54 and RR 1.49, 95% CI 1.05-2.14, respectively), and for myeloid leukaemia at 1-5 years (RR 2.99, 95% CI 1.13-9.33), for second breast cancer at 5-10 years (RR 1.34, 95% CI 1.10-1.63) and 15 + years (RR 1.26, 95% CI 1.00-1.59) and oesophageal cancer at 15 + years (RR 2.19, 95% CI 1.10-4.62).¹⁰

Width of Margins Required During BCS

No consensus was reached about the width of margins required prior to breast conserving surgery without radiotherapy or breast conserving surgery with partial breast radiotherapy.

Partial Breast Radiotherapy

The use of accelerated partial breast radiotherapy was discussed. It was felt to be an acceptable treatment option only within the context of a prospective, institutional Ethics Review Board approved clinical trial. There was consensus that patients with pathologically positive axillary lymph nodes were not good candidates for partial breast radiotherapy.

GLOSSARY OF ABBREVIATIONS

Acronym	Description
BCS	breast conservation surgery
ER	estrogen receptor
NR	nodal recurrence

IMPLEMENTATION STRATEGY

- Present the guideline in the tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.

EVALUATION STRATEGY

A formal review will be conducted in 2011, however if new evidence is brought forward before that time, the guideline will be changed accordingly.

DECLARATION OF CONFLICT OF INTEREST

None of the authors of this guideline had any conflict of interest related to evidence or recommendations in this guideline.

REFERENCES

- ¹ Coles CE, Moody AM, Wilson CB, Burnet NG. Reduction of radiotherapy-induced late complications in early breast cancer: The role of intensity-modulated radiation therapy and partial breast irradiation. Part II - Radiotherapy strategies to reduce radiation-induced late effects. *Clinical Oncology*. 2005;17(2):98-110.
- ² Canadian Association of Radiation Oncologists. Breast radiotherapy after breast-conserving surgery. The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. *CMAJ*. 1998;158 (Suppl 3):35-42.
- ³ Vinh-Hung V, Verschraegen C. For the breast-conserving surgery project. Breast-conserving surgery with or without radiotherapy: pooled-analysis for risks of ipsilateral Breast tumour recurrence and mortality. *J Natl Cancer Inst*. 2004; 96:115–121.
- ⁴ Kunkler IH, King CC, Williams IJ, Jack W. What is the evidence for a reduced risk of local recurrence with age among older patients treated by breast conserving therapy? *Breast*. 2001;10(6):464-469.
- ⁵ Lovi L, Paiar F, Simontacchi G, Barca R, Detti B, Fondelli S, et al. Loco regional failure pattern after lumpectomy and breast irradiation in 4,185 patients with T1 and T2 breast cancer. Implications for nodal irradiation. *ACTA Oncol*. 2006;45(5):564-570.
- ⁶ Whelan T, Olivetto I, Levine M. Clinical practice guidelines for the care and treatment of breast cancer: Breast radiotherapy after breast-conserving surgery (summary of the 2003 update). *CMAJ*. 2003;168(4):437-439.
- ⁷ Dodwell DJ, Dyker k, Brown J, Hawkins K, Cohen D, Stead M, Ash D. A randomised study of whole-breast vs. tumour-bed irradiation after local excision and axillary dissection for early breast cancer. *Clinical Oncology*. 2005;17(8):618-622.
- ⁸ Jatoi I, Proschan MA. Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: A pooled analysis of updated results. *AM J Clin Oncol*. 2005;28(3)289-294.
- ⁹ Miller SR, Mondry T, Reed JS, Findley A, Johnstone PA. Delayed cellulites associated with conservative therapy for breast cancer. *J Surg Oncol*. 1998;67(4):242-245.
- ¹⁰ Tho LM, McIntvre A, Ross A, Gallagher C, Yap C, Ritchie DM, Canney PA. Acute supraclavicular skin toxicity in patients undergoing radiotherapy for breast cancer: An evaluation of the 'T'-grip method of patient positioning. *Clinical Oncology*. 2006;18(2):133-138.
- ¹¹ Delaney G. Recent advances in the use of radiotherapy to treat early breast cancer. *Curr Opin Obstet Gynecol*. 2005;17(1):27-33.
- ¹² Korreman SS, Pedersen AN, Joispovi M, Aarup LR, Juhler-Nottrup T, Specht L, Nystrom H. Cardiac and pulmonary complication probabilities for breast cancer patients after routine end-inspiration gated radiotherapy. *Radiotherapy & Oncology*. 2006;80(2):257-262.
- ¹³ Roychoudhri R, Evans H, Robinson D, Moller H. Radiation-induced malignancies following radiotherapy for breast cancer. *Br J Cancer*. 2004;91(5):868-872.