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Impact of Radiation Wait Times on Risk of Local Recurrence of Breast Cancer: Early Stage Cancer with no Chemotherapy

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Impact of Radiation Wait Times on Risk of Local Recurrence of Breast Cancer: Early Stage Cancer with no Chemotherapy

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May 2004

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Authorship

Veronique Benk was responsible for data abstraction and completion of the written report. Andrea Fisher was the second reviewer in data abstraction. Davida Glazer was responsible for the design and execution (performance) of the literature search strategies, for the associated appendix and for the bibliographies. Lawrence Paszat assisted in the initial design of the study and made final revisions to the report.

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Pamela Slaughter and Wayne Tucker were responsible for the independent screen of abstracts.

Conflicts of Interest

None declared.

In Memoriam

In memory of Davida Glazer, who died in December 2003 from breast cancer. She was a wonderful friend and a dedicated librarian who helped to complete this work with all her enthusiasm until the end.

REPORT *IN BRIEF*

April 2004

Impact of Radiation Wait Times on Risk of Local Recurrence of Breast Cancer: Early Stage Cancer with No Chemotherapy

Technology Name

Radiation therapy; typically whole breast radiation after breast conservation surgery (BCS) with or without additional irradiation (boost radiation) localized at the surgery site.

Disease/Condition

Early stage breast cancer (stages I and II) with no chemotherapy.

Technology Description

Radiation therapy (RT) involves the use of gamma rays or high energy X-rays to damage or destroy cancer cells. While individual treatment plans (number of treatments and type of machine used) vary based on disease stage, tumour pathology and each patient's general health and preferences, patients typically undergo whole breast radiation with opposed tangential fields. When there has been axillary lymph node involvement or extracapsular growth, the axilla, the supraclavicular and the intramammary regions may be treated. Boost radiation may also be administered at the surgery site.

The Issue

While RT reduces the risk of local recurrence (LR), the optimal interval between BCS and the start of RT has not been determined. Canadian guidelines recommend that breast irradiation be started as soon as possible and not later than 12 weeks after surgery, except for patients who are receiving chemotherapy.

As patient volume and wait times have increased, patients, health care providers and government are increasingly concerned about the impact of delayed access on patient outcomes, particularly LR.

Assessment Objectives

To assess the relationship between the risk of LR of breast cancer and the waiting times for RT after BCS among women with early stage breast cancer who are not receiving chemotherapy.

Methods

A systematic review of the literature published between January 1997 and June 2003 was conducted using a standardized approach to searching, article selection, data extraction and quality assessment. Two independent reviewers selected six relevant studies out of 194 identified. Study quality was assessed using a "strength of evidence" scale. In addition, 150 web sites were examined for information on guidelines and waiting times. Requests for unpublished manuscripts were sent by letter to heads of radiation departments nationwide.

Conclusions

There was no difference between the LR rate of breast cancer among women who had earlier RT (less than eight weeks after BCS) and those who had RT up to 12 weeks after BCS. There were too few women waiting longer than 12 weeks to evaluate the risk for this group.

This summary is based on a comprehensive health technology assessment available from CCOHTA's web site (www.ccohta.ca): Benk V, Fisher A, Glazer D, Paszat L. *Impact of radiation wait times on risk of local recurrence of breast cancer: early stage cancer with no chemotherapy.*

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EXECUTIVE SUMMARY

The Issue

Breast cancer, which is the most common cancer among women, ranks second to lung cancer as the leading cause of cancer-related deaths in Canadian women. For patients with early stage breast cancer (stages I and II), breast conservation surgery (BCS) and lymph node dissection followed by radiation therapy (RT) form the recommended course of treatment. While RT reduces the risk of local recurrence (LR) of breast cancer, the optimal interval between BCS and the start of RT has not been determined. The Canadian Steering Committee on Clinical Practice Guidelines for Care and Treatment of Breast Cancer recommends that local breast irradiation should be started as soon as possible and no later than 12 weeks after surgery, except for patients who are receiving chemotherapy. Women receiving chemotherapy are excluded from our report, because intervals are distorted by the timing of chemotherapy. Over the past decade, the waiting times for RT in Canada have increased. Patients, health care providers and the government are concerned that delayed access to RT may adversely affect patient outcomes, particularly the risk of LR.

Objectives

The aim of this review is to assess the relationship between the risk of LR of breast cancer and the waiting times for RT after BCS among women with early stage breast cancer who are not receiving chemotherapy.

Methods

A systematic review was conducted using a standard approach to literature searching, article selection, data extraction and quality assessment. Electronic databases were searched for relevant literature. We did hand searching and used advice from experts. Two reviewers selected articles based on defined criteria and data were extracted using standard forms. Study quality was assessed using a “strength of evidence” scale.

Results

Among 194 potentially relevant reports, there were six retrospective, observational studies that examined the risk of LR of breast cancer among women who had undergone BCS followed by RT without chemotherapy. Waiting times in these studies varied from seven weeks, eight weeks (two studies), 12 weeks (two studies) and up to 20 weeks. Follow-up time varied from a mean of five years to a median of 8.4 years. The results were consistent between studies and revealed that there were no differences in the rate of LR of breast cancer among women who had to wait longer for RT after surgery compared to those who received earlier therapy. The impact of RT wait times on survival was not evaluated.

Conclusions

There was no difference in the LR rate of breast cancer among women who had earlier RT (less than eight weeks after BCS) and among those who had RT up to 12 weeks after BCS. As there were too few women waiting longer than 12 weeks, we could not evaluate the risk for this group.

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1 INTRODUCTION

1.1 Background

The Canadian Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer has developed a series of guidelines written by experts and reviewed by surgical, medical and radiation oncologists, radiologists, nurses, family physicians and breast cancer survivors selected from across Canada.[1] For patients with early stage breast cancer (stages I and II), breast conservation surgery (BCS) and lymph node dissection followed by radiation therapy (RT) form the recommended course of treatment. Stage I breast cancer is clinically defined as a primary tumour up to 2 cm at its greatest dimension without ipsilateral axillary node involvement. Stage II is defined clinically as a primary tumour of up to 5 cm with or without ipsilateral lymph node involvement, but without fixation of the nodes to one another or to other structures.[2] BCS (i.e., lumpectomy, partial mastectomy, wide local excision) consists of removing the tumour with a cuff of normal tissue, to try to preserve a good cosmetic appearance of the breast. Lymph node dissection involves the removal of the axillary lymph nodes to reduce the risk of recurrence in the axilla and to produce accurate staging.

Prospective, randomized controlled trials found no differences in the rates of local recurrence (LR), distant recurrence and overall survival among breast cancer patients who had BCS followed by RT compared to those who had a mastectomy.[3] There was an increased rate of LR, however, if the patient did not receive RT after BCS. Among node-negative patients who did not receive RT, the rate of LR varied between 8.8% after three years to 32% at 12 years. For node-positive patients not receiving RT, the rate of LR varied between 9.3% after five years to 41% at 12 years.[3] After 20 years of follow-up in a recent meta-analysis involving 37 randomized trials of RT for early breast cancer,[4] a significantly lower risk of LR was reported among BCS patients who had received RT (LR=7.2%) compared with those who did not (LR=22.0%, $p<0.005$).

The National Surgical Adjuvant Breast and Bowel Project (NSABP) compared BCS with or without RT to mastectomy in 1,851 women with stage I or II breast cancer.[3] After an average 20 years of follow-up, disease-free survival and overall survival were identical in patients treated using BCS with or without RT and in those treated using mastectomy. When RT was omitted after BCS, LR was more frequent among women with negative nodes (36.2% versus 17.0%, $p<0.001$) and positive nodes (44.2% versus 8.8%, $p<0.001$).

One biological consideration in establishing the relative urgency of RT is the likelihood in the short term that the continued growth of tumour could result in regional spread. Radiobiological studies suggest that the massive cell depletion that occurs with surgical excision of the primary tumour is a powerful stimulus for the growth of residual tumour cells, due to the release of growth factors secondary to tissue injury or via other mechanisms.[5] As a result, shortly after primary surgery, one might expect accelerated repopulation by remaining tumour cells. One study reports that a residual tumour can be a point of origin for distant dissemination of breast

cancer.[6] It also finds that the benefits of RT seem to be greater when small tumours are involved rather than large ones. One study of head and neck cancers shows that delayed RT affects the local control of the tumour.[7]

MacKillop *et al.* developed a mathematical model to estimate the effects of delay in radiotherapy for squamous cell carcinoma of the tonsillar region.[8] This model found that the local control rate decreased by approximately 10% after a delay of 30 days. For gynecologic cancers, the focus was on total treatment time, interruption of treatment during RT and delay between external sources and internal sources of therapy. A dose-response relationship between treatment times, the rate of loss of local control and survival time was also reported.[9] Based on these findings, we anticipated that prolonged wait times between surgery and postoperative RT for patients with early stage breast cancer may also allow repopulation to occur to the extent that local control of the tumour is compromised.

Other factors that affect LR risk include tumour size,[10] age[11,12] and the likelihood of margin involvement. Grossly involved margins are associated with an increased risk of LR.[13,14] The risk of recurrence is less clear when margins are only focally involved.[15] Other microscopic features, such as poor histological grade or an extensive intraductal component, are also associated with a higher likelihood of LR.[16,17]

The impact of LR on survival is controversial. In theory, excessive waiting time to RT is associated with increased LR risk. LR may lead to further dissemination of cancer cells and to increased risk of metastasis. Thus, a decreased overall survival could be expected.[18] After 20 years follow-up, in a meta-analysis of 40 trials of RT for early breast cancer that included patients treated by mastectomy or lumpectomy followed or not by RT,[4] a LR reduction of about two-thirds was observed. The LR rate was 10.4% in the radiotherapy group versus 30.1% in the non-RT group. The mortality rate was similar in the two groups as a result of an increased number of deaths related to cardiovascular mortality in the radiated group. Whelan *et al.* reported a meta-analysis of 18 studies in which patients received systemic adjuvant therapy and RT. They showed that RT reduced the risk of LR, distant recurrence and death when RT was given within six months after surgery.[19]

The Canadian Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer (2003) recommends that local breast irradiation should be started as soon as possible after surgery and no later than 12 weeks after.[1] No optimal interval has been defined for patients who are receiving chemotherapy. In the UK, the recommended interval between BCS and RT should not exceed four weeks except for clinical reasons. In the US and in Australia, no specific recommendations have been made (Appendix 3).

Typical waiting times for RT in Canada have increased. In Ontario, waiting times for breast cancer patients after surgery increased steadily from 1982 to 1991. By 1991, breast cancer patients had median wait times of 8.3 weeks for RT (an increase of 102.7% since 1982). By 1991, few patients received care within the 12-week interval prescribed by the committee on standards of the Canadian Association of Radiation Oncologists.[20] In Quebec, waiting times were tracked between 1988 and 1995. Among 482 breast cancer patients treated between January 1988 and December 1989 at McGill University hospitals, the median time to start RT was seven weeks, with 25% of

patients waiting over 11 weeks.[21] A similar study, assessing 739 breast cancer patients treated between January 1992 and December 1993 at the same institution, reported that median time to RT increased to 9.7 weeks, with more than 50% of patients waiting over 11 weeks.[22] A Canadian study conducted from 1991 to 1995, involving 3,843 breast cancer patients receiving RT, reported median waiting times of 12.9 weeks – an increase of 5.9 weeks since 1988 to 1989.[23]

1.2 Technology Overview

In Canada, breast cancer patients who are to receive RT are referred by surgeons or medical oncologists.[20,23,24] Each province has a different system for RT services. RT delivery in all provinces, except Quebec, is organized through regional cancer centres.[21,25] During the patient's first visit to the radiation department, a radiation oncologist assesses the patient and defines the intent of treatment. The treatment plan is established according to the stage of disease, the pathologic characteristics of the tumour and the patient's preferences and general health. Further diagnostic tests may be requested. At a subsequent visit, radiation therapists simulate treatment using standard X-ray or computed tomography (CT) simulators. The technical complexity of treatment varies according to the clinical circumstances. After BCS, the recommended treatment is whole breast radiation with opposed tangential fields. In the case of axillary lymph node involvement or extracapsular growth, the axilla and the supraclavicular and intramammary regions may be treated. Measurements and radiograph films are taken for the dosimetrist and the physicist to estimate the radiation dose. RT is usually initiated during a subsequent visit to the radiation department. The number of treatments and the type of machine (low or high energy) vary according to the patient's treatment plan.

Different fractionation schedules for breast radiation have been used in Canada. Two commonly used schedules have been 50 Gy in 25 fractions (2 Gy per day, five days per week for five weeks) and 42.5 Gy in 16 fractions (2 Gy per day, five days per week for three weeks plus one day). A randomized trial in women with node-negative breast cancer has shown that the shorter schedule (42.5 Gy in 16 fractions) resulted in equivalent rates of local control and radiation morbidity at five years. Shorter schedules are often preferred because they increase convenience for the patient, resource capacity and cost-effectiveness.[1,21,26,27]

Controversies exist regarding the advantage of additional irradiation (boost radiation) that is directed at the surgery site after the completion of whole breast radiation. It is recommended in the Canadian clinical practice guidelines for the care and treatment of breast cancer that a boost of 10 Gy to 12.5 Gy be given in five fractions to the primary site for women at high risk of LR.[1] This group includes women who are less than 40 years of age and those with focally positive or close resection margins.

2 THE ISSUE

Breast cancer, which is the most common cancer among women, ranks second to lung cancer as the leading cause of cancer-related deaths in Canadian women. In 2003, 21,100 women were diagnosed with breast cancer and 5,300 women died from it.[28] The Canadian Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer recommends that all women with breast cancer who undergo breast conservation surgery (BCS) should receive post-operative radiation therapy (RT) to reduce the risk of local recurrence (LR).[1] The committee also recommends that local breast irradiation should be started as soon as possible and no later than 12 weeks after surgery, except for patients who are receiving chemotherapy (women receiving chemotherapy are not considered in this report because intervals are distorted by the timing of chemotherapy). The optimal interval between BCS surgery and the start of RT, however, has not been determined. Over the past decade, waiting times for RT in Canada have increased. Patients, health care providers and government are concerned that delayed access to RT may adversely affect patient outcomes, particularly the risk of LR.

Information about the impact of wait times on the risk of LR will be important for the management of patients and waiting lists in oncology departments across Canada.

3 OBJECTIVES

The aim of this study was to conduct a systematic literature review to assess the relationship between the risk of LR and the waiting times for RT after BCS among women with early stage breast cancer who are not receiving chemotherapy.

4 METHODS

4.1 Literature Search Strategy

The search for relevant literature was conducted in several steps. Eleven electronic databases including MEDLINE®, HealthSTAR, Cochrane Library, CancerLit, CINAHL®, BioethicsLine, Dissertation Abstracts, PsycINFO®, EMBASE, ClinPSYC and Cambridge Scientific Abstracts were searched on OVID on-line and CD-ROMs. A search strategy with controlled vocabulary terms and text-words to identify published articles was used (Appendix 1). The electronic database search was limited to 1997 to 2002. The year 1997 was chosen as the start date for the literature search to provide a contemporary review of published evidence. An update was done in June 2003.

Hand searching and back referencing were performed to locate grey literature and to identify the studies that were missed in indexed sources but cited by other authors. A total of 150 web sites (Appendix 2) were examined for relevant information on guidelines and waiting times. Letters were sent to the heads of radiation departments across Canada requesting their assistance in identifying unpublished manuscripts or abstracts that focused on the topic of interest.

4.2 Selection Criteria and Methods

All electronic downloads of report abstracts were imported into a Reference Manager database. Two reviewers (PMS, WT) independently examined all abstracts for relevant papers. All pertinent reports were retrieved for further review. Reports published in languages other than English were assessed by staff at the Institute for Clinical Evaluative Sciences (ICES). Reports deemed relevant were retrieved and translated (n=4). The two reviewers screened all retrieved reports independently. Any discrepancies were discussed to ensure consensus on report selection.

Relevant reports (those examining the impact of wait times for RT after BCS on the risk of LR among women with early stage breast cancer) were selected if the study involved breast cancer patients treated with a curative intent using BCS followed by RT, but who did not receive chemotherapy (patients treated with tamoxifen were eligible); provided data on long-term outcomes such as LR and survival; and provided data on the wait times between surgery and RT initiation.

4.3 Data Extraction Strategy

Relevant studies and reports were retrieved, reviewed and classified by topic as either primary studies reporting clinical outcomes or secondary reviews, which included critical reviews of the international literature, clinical practice guidelines and reports from health technology assessment and health care agencies. The nature and extent of the evidence reviewed as a basis for these guidelines were summarized. Relevant publications were included in our report. At least two reviewers abstracted data from each study using a standard paper abstraction form.

4.4 Strategy for Quality Assessment

Study quality was estimated using a "strength of evidence" scale from the Canadian Task Force on Preventive Health Care (CTFPHC).[29] For the primary studies, evaluation was based on the nature of the study (randomized or retrospective); the number of patients participating in the study; the length of follow-up; the definition of the comparison groups (early versus late RT); the quality of the statistical analysis; and the appropriateness of the conclusions.

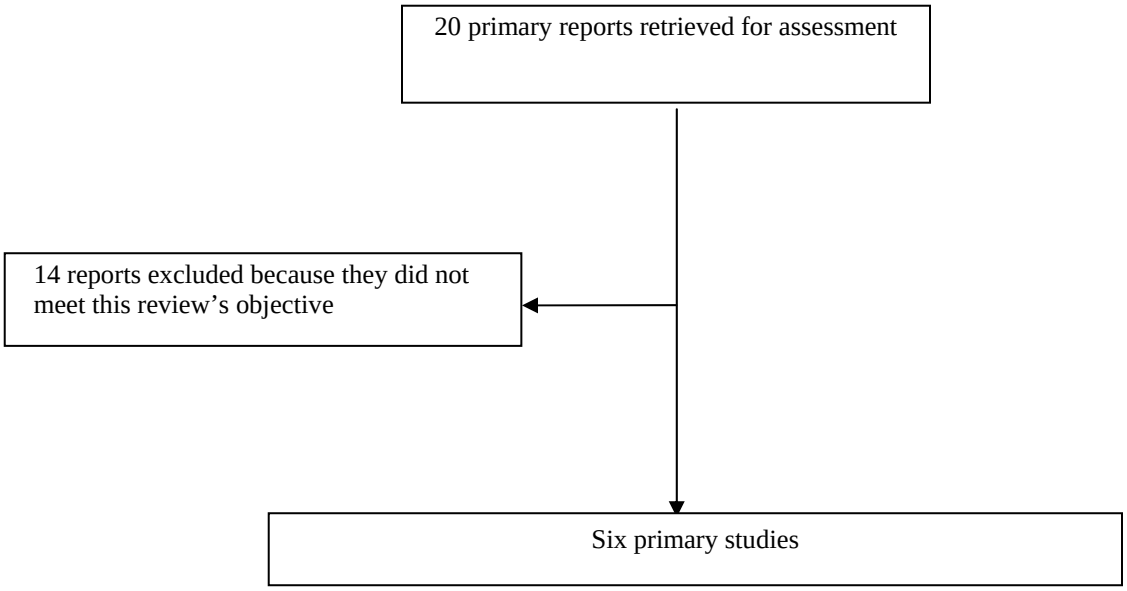
5 RESULTS

5.1 Quantity of Research Available

5.1.1 Primary reports

We found 194 reports that related to breast cancer radiation and general wait times for RT. The number of primary studies on the impact of wait times for RT on the risk of LR was limited to 20 reports (Figure 1). Of these, six examined the relationship between the risk of LR and the waiting times for RT after BCS among women with early stage breast cancer not receiving chemotherapy.

Figure 1: Selection of studies for inclusion



5.1.2 Secondary reviews

There were five secondary reviews that focused on the timing of RT in breast conserving treatment.[30-34] Relevant publications not already included in our data were added from these review articles. Conclusions were compared to our findings. Clinical guidelines were published in Australia, Canada and the UK. The level of evidence on which the guidelines were based was compared to our findings.

Relevant information from the primary studies reporting clinical outcomes included the description of the breast cancer population (period of study, number of patients, stage of disease,

proportion of positive lymph nodes, histological grade), the nature of the study (retrospective or randomized), the modalities of treatment (hospital, type of surgery, total dose of radiation, technique, length of follow-up); the outcomes (LR, mortality, definition of wait times, quality of statistics); and the evaluation of the impact of the prognostic factors for the risk of LR recurrence.

Relevant information from the five secondary studies (number of articles integrated in the systematic review, scoring of the studies, conclusion regarding local recurrence rate) was compared to that used in our analysis of the primary studies that we had identified.

Information from the clinical practice guidelines and reports from health technology assessment and health care agencies was also analyzed (Appendices 2, 3). The level of evidence was compared to that used for our conclusions.

5.2 Study Characteristics

5.2.1 Primary studies

The six studies that qualified for this review were classified as level III evidence on the basis of Sackett's criteria[35] and on the basis of the CTFPHC criteria.[29] They were all retrospective, observational studies. Two of these studies were reported as abstracts.[36,37] The number of breast cancer patients ranged from 400 to over 1,800 and the median follow-up of these patients ranged from five to eight years. The LR rates for breast cancer ranged from 2.9% to 18%. The local failures were usually observed within 30 months after the initial diagnosis. The radiation schedules ranged from 40 Gy in 16 fractions to 50 Gy in 25 fractions, which may have been followed by a boost of 10 Gy to 16 Gy, reflecting variations in clinical practice. Waiting times for RT varied from five weeks to 20 weeks. For the statistical analysis, the delay was defined with a cutoff that varied among studies. In most studies, no information on standard error was provided.

5.3 Data Analysis and Synthesis

5.3.1 Primary studies

Six studies[36-41] examined the impact of RT wait times after BCS on the rate of LR among breast cancer patients (Table 1). None of the studies reported a significant increase in LR rate among those women who had to wait longer for RT after BCS compared to those who received RT earlier. The studies did not use similar definitions of delay. The wait time varied among the studies from a median of five weeks to eight weeks.

Table 1: Retrospective studies examining relationship between local recurrence (LR) rate of breast cancer and interval between breast conserving surgery (BCS) and radiation therapy (RT) among women with early stage breast cancer

Study	Number of Patients	Length of Follow-up (years)	Level of Radiation Treatment (Boost)	Interval between BCS and RT	% of Local Recurrence	Significance Level
Clarke *et al.* 1985[38]	N=436	5 (mean)	45 Gy (15 Gy)	≤7 weeks=378 >7 weeks=58	<7 weeks=4.5 >7 weeks=12.1	NS
Nixon *et al.* 1994[39]	N=591	8.3 (median)	50 Gy (10 Gy)	① ≤4 weeks=283 ② 5 to 8 weeks=308 ③ 9 to 12 weeks=54	≤4 weeks=13 5 to 8 weeks=7	① versus ② p=0.34 NS
Fourquet 1995[36]	N=1,839	6.5 (median)	65 Gy	① ≤5 weeks=1,200 ② 5 to 8 weeks=578 ③ ≥8 weeks=61	≤5 weeks=12 5 to 8 weeks=9 >8 weeks=18	① versus ② p<0.04 ① versus ③ NS
Whelan *et al.* 1996[37]	N=400	8.4 (median)	40 Gy (12.5 Gy)	≤8 weeks=215 >8 weeks=185	≤8 weeks=8.4 >8 weeks=12.4	p=0.10 NS
Vujovic *et al.* 1998[40]	N=568	5.3 (median)	50 Gy (10 Gy)	≤12 weeks=436 >12 weeks=132	<12 weeks=7.8 >12 weeks=3.8	p=0.19 NS
Froud *et al.* 2000[41]	N=1,274	5.9 (median)	44 Gy (10 Gy)	① ≤5 weeks=172 ② 6 to 8 weeks=532 ③ 9 to 12 weeks=409 ④ ≥13 weeks=161	<5 weeks=3.6 6 to 8 weeks=2.9 9 to 12 weeks=3.1 >13 weeks=4.1	① versus ② p=0.58 ① versus ③ p=0.25 ① versus ④ p=0.41 NS

NS=not significant.

Clarke *et al.* examined the LR rate in 436 women (30% with positive lymph nodes) from France with early stage breast cancer who underwent BCS and RT (45 Gy followed by a 15 Gy boost to the tumour bed).[38] No adjuvant treatment was given. After five years of follow-up, investigators reported a higher LR among women who had a RT delay greater than seven weeks. When the tumour grade was taken into account, however, the rate of LR among those who had to wait longer than seven weeks for RT did not differ significantly from that among women who had received RT within seven weeks of BCS.

Nixon *et al.* found that a delay of up to eight weeks was not associated with an increase in the risk of LR.[39] They examined 653 patients with early stage breast cancer who underwent BCS and then received RT (45 Gy to the whole breast followed by a boost of 15 Gy; the minimum dose to the tumour bed was 60 Gy). No adjuvant systemic treatment was given. They found that the LR rate among patients who received RT five to eight weeks after surgery did not differ significantly from that in patients treated with RT within four weeks after surgery. Women were followed-up for 8.3 years.

In the largest study (1,839 women treated with wide excision, axillary node dissection, radiation and no adjuvant chemotherapy), which was published as an abstract, Fourquet *et al.* found that women experiencing shorter RT delays after BCS (less than five weeks) had a significantly higher rate of LR compared with women who waited five to eight weeks for RT ($p<0.04$).[36] A selection bias was suggested. LR rates for women waiting longer than eight weeks for RT did not differ significantly from those in women with the shortest waiting times. Women were followed-up for 6.5 years.

After over eight years of follow-up, Whelan *et al.* reported that there was no difference in the LR rate among Ontario women waiting less than eight weeks for RT and those waiting longer (n=400).[37] They were all node-negative and did not receive any adjuvant treatment. As in an earlier study,[38] there was a trend towards an increase in LR with increasing wait times, but these differences were not statistically significant.

Vujovic *et al.* examined the LR rate among 568 early stage breast cancer patients from Ontario who received RT (50 Gy, 10 Gy boost) within 12 weeks of BCS and among those receiving RT 12 weeks or more after BCS.[40] They were all node-negative and did not receive adjuvant treatment (tamoxifen). There was no significant difference in LR among the two groups of patients. A subset of patients with a RT delay of up to 16 weeks did not have a higher risk of LR. This may be due to the fact that 54% of these patients received a boost to the tumour bed after conventional RT. Romestaing *et al.*[42] have shown that this technique reduces the LR risk.

Froud *et al.*[41] examined LR among 1,274 women treated in British Colombia who underwent BCS and RT (44 Gy, 10 Gy boost) for stages I to III breast cancer (24% had positive lymph nodes and 51% received tamoxifen). They concluded that a delay up to 20 weeks did not increase the LR risk. Only 23 patients (1%) were waiting more than 20 weeks. In the Cox analysis, a comparison of the shortest interval group (zero to five weeks, n=244) and the longer interval group (>13 weeks, n=269) bordered on statistical difference (p=0.055). There was a low LR incidence in these two groups (3.6% in the zero to five weeks group versus 4.1% in the >13

weeks group) and a lack of statistical significance. These results showed no increased risk of LR up to 13 weeks, but they remained inconclusive after 20 weeks. Follow-up was 5.9 years.

5.3.2 Secondary review articles

Critical reviews of the literature on delay in adjuvant RT and outcome of breast cancer have been published. The material used for the reviews is similar to that in our analysis, but some reviews also include studies in which some patients had received chemotherapy. The reports come to different conclusions.

Trovo[34] concluded that without an indication for chemotherapy, postoperative radiation must be delivered within eight weeks, but this conclusion was based on one article.[39] Fietkau[30] reports no clear relationship between delay and local control. His report was based on seven articles[37-40,43-45] of which three included patients receiving chemotherapy.[43-45] Redda[33]concluded that RT should be given as soon as possible after surgery to maintain the lowest possible rate of breast cancer recurrence. His conclusion was based on seven articles[37-41,43,45] of which two included patients receiving chemotherapy.[43,45] Hébert-Croteau[31] reports that RT delay has no impact on either local or distant control or survival. His conclusion was based on four articles.[38-41] Huang conducted a recent systematic review[32] of eight studies.[38 36,37,40,41,45-47]While this review was designed to study the relationship between RT delay and local control after lumpectomy without chemotherapy, two studies included patients who received chemotherapy.[45,46] The five-year LR rate was significantly higher in patients treated with adjuvant RT more than eight weeks after surgery than in those treated within eight weeks of surgery (odds ratio=1.62, CI=1.21; 2.16). However, there was no impact caused by a delay in RT on the risk of metastases or the probability of long-term survival. It was recommended that the wait times in starting RT be kept as short as could be achieved.

5.3.3 Guidelines and reports (Appendix 3)

The treatment guidelines from Australia, Canada, UK and US were reviewed. In Canada, the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer recommends that local breast irradiation should be started as soon as possible after surgery and not later than 12 weeks after.[1] This recommendation was based on the Ontario Clinical Oncology Group trial, where the maximum interval between surgery and radiation was 12 weeks (level 3 evidence) and on expert opinion developed through an iterative process during external review of the original guidelines published in 1998.[37] In the UK, the recommended interval between BCS and postoperative RT should not exceed 20 working days except for clinical reasons. In the US and Australia, no specific recommendations have been made. ICES (Institute for Clinical Evaluative Sciences) published an article about the waiting lists for RT in Ontario.[48] No recommendation was made to adopt a target waiting time that would be significantly shorter than those recommended by the Canadian Association of Radiation Oncologists.[1]

6 DISCUSSION

6.1 Primary Studies

One study out of the six showed that a delay of more than seven weeks increased the LR risk but only in the univariate analysis.[38] Once the effect of tumour grade was considered, there was no difference between the LR rate of breast cancer among women who had earlier RT (less than eight weeks after surgery) and those who had RT after this time. From these studies, "acceptable" waiting times were up to 12 weeks. Beyond 12 weeks, the number of patients dropped and the risk became difficult to evaluate.

6.2 Limitations

While most of the women studied had early stage breast cancer with negative nodes, some had positive lymph nodes, which are associated with poor prognostic factors and an increased risk of LR. Tamoxifen was prescribed in Froud's study for half of the patients. This adjuvant hormonal treatment has an impact on LR that is independent from the impact of RT.[49] This variation in the nature of cancer and treatment may influence the conclusions.

The quality of the study designs might influence the results. All studies in this review are retrospective. Despite adjustments for significant covariates and multivariate analysis, unperceived medical selection bias might exist. Some patients who are seen as being at high risk of LR (e.g., younger age, nodal involvement and negative hormonal receptors) are more likely to receive RT sooner. In several studies, the women with the lowest waiting times had higher LR rates, suggesting that women with higher risk may have received RT before those at low risk. This could explain why there is little difference in the LR rates among women who have short and long wait times for RT.

Two studies were reported as abstracts. While this is a rapid method to communicate findings to physicians, the lack of peer review and the unavailability of detail are shortcomings.

6.3 Secondary Review Reports

Even though the secondary reviews evaluated some of the same reports as did this systematic review, their conclusions differed. Some included comparisons of two groups of patients: those receiving chemotherapy who were delayed and those treated by RT alone.[43,45] Two reviews reported no relationship between delay and LR[30,31] and two concluded that RT must be delivered as soon as possible after surgery.[33,34] Huang *et al.*[32] suggested that a delay longer than eight weeks could be detrimental for breast cancer patients. Most of the studies, however, were observational. Thus, the main problem was the lack of adequate control for confounding factors, as few clinical variables were available for this purpose. Furthermore, certain components of the analysis were questionable. Heterogeneity was evaluated using Bayes factors, but the results

were reported using p values, which were not generally associated with Bayes factors. Also, it was unclear whether the random effect model was used when no heterogeneity was found. Finally, the eight-week "cutoff" used by Huang *et al.* was arbitrary. The use of continuous times would have provided more information on what constituted an "acceptable waiting time." This was important given the current guidelines, which use a 12-week cutoff.

6.4 Guidelines and Reports

Clinical guidelines and health technology assessment agencies based their recommendations on the same secondary review literature. Some endorsed the concept that patients should be treated as soon as possible after surgery and that waiting lists must be shorter. Some thought that targets should be defined by treatment centres and pertinent associations of medical professionals. Canadian guidelines recommend that radiation treatment start as soon as possible or no later than 12 weeks after surgery. The evidence in our review supports wait times up to 12 weeks post surgery, but there is insufficient data to evaluate the risk of LR beyond 12 weeks.

6.5 Future Research

More research is needed to address the psychological impact of waiting for RT. Studies to date have included small numbers of patients and the instruments used to measure the impact on women varied between studies. Keyes[50] suggested that there was an improvement of the fatigue, cognitive functioning and financial difficulties that occurred during the waiting period, while Miller[51] reported that many patients expressed trust that their doctor would not have them wait if waiting was potentially harmful.

7 CONCLUSION

There was no difference between the LR rate of breast cancer among women who had earlier RT (less than eight weeks after BCS) and those who had RT up to 12 weeks after BCS. There were too few women waiting longer than 12 weeks to evaluate the risk for this group.

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Appendix 1: Literature Search Strategies

Relevant published literature was searched in MEDLINE®, HealthSTAR, CancerLit, CINAHL®, ClinPSYC, EMBASE, BioethicsLine, Dissertation Abstracts, Cochrane Library, PsycINFO® and Cambridge Scientific Abstracts databases on OVID on-line and CD-ROMs. The Internet was searched for grey literature. The headings used reflect the main areas relevant to the topic and to the particular database.

1. MEDLINE AND HealthSTAR (OVID 1997 to December 2000)

These searches were performed on the above databases from 1997 to December 2000. The search was not limited to English language articles. MeSH and text-words were used. Most, though not all MeSH were "exploded" to include the narrower terms. Duplication was removed between MEDLINE and HealthSTAR.

An asterisk indicates that the term was "exploded" to include more specific headings. TW indicates text-word, PT indicates publication type, $ indicates truncation. The first two sets were changed according to the various cancer sites. The subheadings used were ra=radiography, ri=radionuclide imaging, rt=radiotherapy. The MeSH for these cancer sites is:

1. exp colorectal neoplasms/
2. colorectal neoplasms/ra,ri,rt
3. waiting lists/ or (wait$ or delay or interval$).tw.
4. time factors/ or workload/
5. (queue$ or ("best practice" or "best practise")).tw.
6. exp survival analysis/ or survival rate/ or neoplasm recurrence, local/ or recurrence/
7. "referral and consultation"/ or exp health services research/
8. small-area analysis/ or "regional variation". tw. or comparative study/
9. exp health services accessibility/ or rural population/
10. physician's practice patterns/ or physician role/
11. disease management/ or disease progression/
12. cost of illness/ or adaptation, psychological/
13. patient participation/ or physician-patient relations/
14. exp "outcome and process assessment (health care)"/
15. exp socioeconomic factors/
16. neoplasm staging/
17. preoperative care/
18. exp decision making/
19. or/3-18
20. exp radiotherapy/ or radiation oncology/
21. 19 and 1 and 20
22. 21 or 2
23. l/22
24. 23 not animal/
25. 24 not letter.pt.
26. exp guidelines/ or guideline.pt.
27. exp consensus development conferences/
28. consensus development conference.pt.

29. consensus development conference,nih.pt.
30. exp practice guidelines/ or practice guideline.pt.
31. (guideline$ or recommend$ or consensus or standard$ or parameter$).tw.
32. or/26-31
33. (1 and 20) or 2
34. 33 and 32
35. 34 not 22
36. l/35
37. 36 or 25

2. Cochrane Library (Issue 1, 2001)

The Cochrane database was searched using a general strategy. ME indicates MeSH.

1. radiotherapy ME
2. waiting and list
3. 1 and 2
4. breast neoplasms ME
5. 2 and 4
6. waiting lists ME
7. radiation and wait
8. radiation and (delay or interval)

3. CancerLit (OVID 1997 to November 2000)

The MEDLINE strategy was run on CancerLit. Duplication removal between the database subsets resulted in no hits. A general text-word search was then performed. Most of the retrieved hits were meeting abstracts.

1. wait$.tw.
2. (radiotherapy or radiat$).tw.
3. (referral or consult$).tw. and 2
4. (survival or stag$ or recurrence).tw.and 2
5. (breast).tw.
6. (5) and (3 or 4)
7. 1 or 6
8. limit 7 to (nonMEDLINE and yr=1997-2000)

4. CINAHL (OVID 1997 to December 2000)

As in MEDLINE, the following terms were applied separately to breast cancer.

1. waiting lists/ or (wait$ or delay).tw.
2. time factors/ or workload/
3. exp Radiotherapy or Radiation Oncology/
4. queue$.tw. or exp survival analysis

5. neoplasm recurrence, local or Recurrence/
6. or/1-5
7. (6) or 7

5. BIOETHICSLINE (OVID 1997 to October 2000)

This database was searched in general terms. MP denotes that the title, abstract, MeSH and keyword fields were searched.

1. wait$.tw. or interval.tw.or delay. or surgery.tw.
2. radiation therapy.mp. or radiotherapy.mp.
3. cancer.tw or neoplasm$.tw.

6. Dissertation Abstracts (OVID 1997 to February 2000)

As the most relevant information seems to be found in the breast cancer literature, this was searched separately. The other sites were incorporated into a general cancer search.

1. ("breast neoplasms" or breast cancer").tw.
2. 1 and wait$.tw.
3. radiation therapy.mp. or radiotherapy.mp.
4. 4 and (wait$ or delay or interval or surgery).tw.
5. "waitlist$".tw.
6. (cancer or neoplasm).tw.
7. 7 and (wait$ or delay or interval or surgery).tw.

7. PsycINFO (OVID 1997 to November Week 4, 2000)

(perrformed on Dec. 21/00)

1. Exp Radiation Therapy/
2. "wait$ list$".tw. and exp Neoplasms
3. Emotional Stress/ or Stress Management/
4. 3 and exp Neoplasms
5. ("burden of disease" or "burden of illness").tw.
6. queue.tw.
7. Exp Socioeconomic Status/ or exp Cross Cultural Differences/
8. Exp Family Socioeconomic Level/ or exp Health Care Delivery/
9. Exp Health Care Utilization/ or exp At Risk Populations/
10. 7 or 8 or 9
11. Exp Breast Neoplasms and 10
12. Exp Breast Neoplasms and delay.tw.
13. 1 and delay.tw.
14. Exp Adjustment and Exp Breast Neoplasms
15. Exp Epidemiology or Exp Canada or Exp Client Characteristics
16. 15 and Exp Breast Neoplasms

8. PSYCHLIT (Cambridge Scientific Abstracts 1984 to January 10, 2001)

PsycINFO on OVID was no longer available when a second attempt was made to search the literature. DE denotes descriptor, AB=abstracts

1. neoplasms (DE)
2. list or queue or wait or delay or referral or radiation (AB)
3. 1 and 2

9. ClinPSYC (OVID 1997 to September 2000)

1. Exp Breast Neoplasms/ and wait$.tw.
2. Exp Radiation Therapy
3. 1 and 2

Appendix 2: Web Sites

Web Site Searches	Web Site
Agency for Health Research & Quality	http://www.ahrq.gov
Alberta Association of Medical Radiation Technologists	http://www.aamrt.org/
Alberta Cancer Board	http://www.cancerboard.ab.ca/
American Association for Cancer Research (AACR)	http://www.aacr.org/
American Association of Physicists in Medicine	http://www.aapm.org/
American Board of Radiology	http://www.theabr.org/
American Brachytherapy Society	http://www.brachytherapy.net/
American Cancer Society	http://www.cancer.org/
American College of Obstetricians and Gynecologists	http://www.acog.org/
American College of Radiation Oncology	http://www.acro.org/
American College of Radiology (ACR)	http://www.acr.org/
American College of Radiology Imaging Network	http://www.acrin.org/
American College of Surgeons Oncology Group (ACOSOG)	http://www.acosog.org
American Gastroenterological Association (AGA)	http://www.gastro.org/
American Institute for Cancer Research	http://www.aicr.org/
American Medical Association	http://www.ama-assn.org/
American Registry of Radiologic Technologists	http://www.arrt.org
American Society for Therapeutic Radiology and Oncology	http://www.asrt.org
American Society of Clinical Oncology	http://www.asco.org/
American Society of Radiologic Technologists	http://www.asrt.org
Association of Oncology Social Work (AOSW)	http://www.aosw.org
Association of Residents in Radiation Oncology	http://www.arro.org/
Australian Department of Health and Aged Care	http://www.health.gov.au/hfs/pubhlth/
BC Cancer Agency	http://www.bccancer.bc.ca
BC Cancer Agency, Communities Oncology Network	http://www.bccancer.com/
BC Ministry of Health	http://www.gov.bc.ca/hlth/
British Association for Cancer Research	http://www.icr.ac.uk/bacr/home.htm
British Columbia Association of Medical Radiation Technologists	http://www.bcamrt.bc.ca
British Institute of Radiology	http://www.bir.org.uk/
British Medical Journal	http://www.bmj.com
British Society of Interventional Radiology (BSIR)	http://www.bsir.org/new/html/bsir.asp
Canadian Association of Medical Radiation Technologists	http://www.camrt.ca/
Canadian Association of Radiologists	http://www.caro-acro.ca/
Canadian Breast Cancer Foundation (CBCF)	http://www.cbcf.org/
Canadian Breast Cancer Network (CBCN)	http://www.cbcn.ca
Canadian Breast Cancer Research Initiative	http://www.breast.cancer.ca
Canadian Cancer Society	http://www.cancer.ca
Canadian Coalition on Cancer Surveillance	http://www.hc-sc.gc.ca/main/lcdc/web/bc/ccocs/index.html
Canadian Health Care Network (CHN)	http://www.canadian-health-network.ca
Canadian Institute for Health Information (CIHI)	http://www.cihi.ca
Canadian Medical Association	http://www.cma.ca
Canadian Oncology Societies	http://www.cos.ca/
Canadian Society for Surgical Oncology	http://www.cos.ca/csso/csso.htm
Canadian Strategy for Cancer Control	http://www.cancercontrol.org/
Cancer Advocacy Coalition of Canada (CACC)	http://www.canceradvocacycoalition.com/

Web Site Searches	Web Site
Cancer Association of South Africa	http://www.cansa.org.za/
Cancer Bureau - Health Canada	http://www.hc-sc.gc.ca/main/lcdc/web/bc/index.html
Cancer Care Ontario (CCO)	http://www.cancercare.on.ca/
Cancer Care Ontario Practice Guidelines Initiative	http://hiru.mcmaster.ca/ccopgi
Cancer Care, Inc	http://www.cancercare.org/
Cancer Research Foundation of America	http://www.preventcancer.org/
Cancer Research Unit - University of Newcastle	http://www.ncl.ac.uk/cancer.research/
Cancer Society of New Zealand	http://www.cancernz.org.nz/
Cancer Therapy Evaluation Program (CTEP)	http://ctep.info.nih.gov
Cancer Treatment News	http://www.cancerconsultants.com
CancerBACUP	http://www.bacup.org.uk/
CancerCare Manitoba	http://www.mctrf.mb.ca/
CancerNet - National Cancer Institute	http://www.cancernet.nci.nih.gov/
Centers for Disease Control and Prevention	http://www.cdc.gov/
Centre for Behavioural Research and Program Evaluation (CBRPE)	http://www.cbrpe.uwaterloo.ca/
Centre for Evaluation of Medicines	http://www.thecem.net
Coalition of National Cancer Cooperative Groups, Inc	http://www.ca-coalition.org/
College of Medical Radiation Technologists of Ontario	http://www.cmrto.org/
Department of Radiation Oncology - University of Chicago	http://www.radonc.uchicago.edu
Eastern Cooperative Oncology Group (ECOG)	http://ecog.dfci.harvard.edu/
European Association for Cancer Research	http://www.eacr.org/
European Organization for Research and Treatment of Cancer (EORTC)	http://www.eortc.be/
European Society for Therapeutic Radiology and Oncology	http://www.estro.be
European Society of Surgical Oncology (ESSO)	http://www.esso-surgeonline.be/
Federation of European Cancer Societies	http://www.fecs.be/
Fraser Institute	http://www.fraserinstitute.ca
Fraser Valley Cancer Centre	http://www.fvcc.org/
Grand River Regional Cancer Centre	http://www.grrcc.on.ca/
Hamilton Regional Cancer Centre	http://www.hrcc.on.ca/
Health Canada	http://www.hc-sc.gc.ca
Hong Kong College of Radiologists	http://www.hkcr.org/
Icelandic Cancer Society	http://www.krabb.is/cancer/
Institute of Cancer Research	http://www.icr.ac.uk
International Agency for Research on Cancer (IARC)	http://www.iarc.fr/
International Oncology Study Group (IOSG)	http://www.iosg.org/
International Union Against Cancer (UICC)	http://www.uicc.org/
Journal of Clinical Oncology	http://www.jco.org/
Kingston Regional Cancer Centre	http://www.krcc.on.ca/
London Regional Cancer Centre	http://www.lrcc.on.ca/

Web Site Searches	Web Site
Mayo Clinic	http://www.mayohealth.org/
Ministry of Health and Long-Term Care	http://www.gov.on.ca/health
National Alliance of Breast Cancer Organizations	http://www.nabco.org/
National Board for Certified Counselors	http://www.nbcc.org
National Breast Cancer Centre	http://www.nbcc.org.au/
National Breast Cancer Coalition	http://www.natlbcc.org/
National Cancer Institute	http://www.nci.nih.gov
National Cancer Institute of Canada - Clinical Trials Group	http://www.ctg.queensu.ca/
National Cancer Institute of Canada	http://www.ncic.cancer.ca/
National Cancer Services Analysis Team	http://www.cancerNW.org.uk/
National Coalition for Cancer Research	http://www.cancercoalition.org/
National Comprehensive Cancer Network (NCCN)	http://www.cancernetwork.com/
National Guideline Clearinghouse	http://www.ngc.gov
National Institutes of Health (NIH)	http://www.nih.gov
New South Wales Cancer Council	http://www.nswcc.org.au
New South Wales Public Health Division	http://www.health.nsw.gov.au
New Zealand Guidelines Group	http://www.nzgg.org
Newfoundland Cancer Treatment and Research Foundation (NCTRF)	http://www.nctrf.nf.ca/
NHS Cancer Reform Plan (Calman-Hine Report)	http://www.doh.gov.uk/cancer
NHS Centre for Reviews and Dissemination	http://www.york.ac.uk/inst/crd
NHS National Patients' Access Team	http://www.health-secure.net/channels/npat
NIH Consensus Statements	http://www.odp.od.nih.gov
North American Association of Central Cancer Registries	http://www.naaccr.org/
Northeastern Ontario Regional Cancer Centre	http://216.223.67.50/eindex.htm
Northwestern Ontario Regional Cancer Centre	http://www.nworcc.on.ca/
Norwegian Cancer Society (NCS)	http://www.kreft.no/english/
Office of Disease Prevention	http://odp.od.nih.gov/
OncoLink, The University of Pennsylvania Cancer Resource	http://cancer.med.upenn.edu/
Oncology Nursing Society (ONS)	http://www.ons.org
Oncology.com	http://www.oncology.com
Ontario Association of Medical Radiation Technologists	http://www.oamrt.on.ca/
Organization of European Cancer Institutes (OECI)	http://www.uicc.org/others/oeci/
Ottawa Regional Cancer Centre	http://www.orcc.on.ca/
Pan American Health Organization	http://www.paho.org/
Prince Philip Hospital	http://www.holtsd.demon.co.uk/
Princess Margaret Hospital	http://www.uhealthnet.on.ca/
Radiation Oncology Research Unit (RORU) at Queen's University	http://www.krcc.on.ca/roru/
Radiation Research Society	http://www.radres.org/
Radiation Therapy Oncology Group	http://www.rtog.org/
Radiological Society of North America (RSNA)	http://www.rsna.org/
Radiotherapy Guideline Site	www.radiotherapy.com/Guidelines
Royal Australian and New Zealand College of Radiologists	http://www.racr.edu.au/
Royal College of Physicians	http://www.rcplondon.ac.uk/
Royal College of Physicians and Surgeons of Canada	http://rcpsc.medical.org/
Royal College of Radiologists	http://www.rcr.ac.uk/

Web Site Searches	Web Site
Saskatchewan Cancer Agency	http://www.scf.sk.ca/
Saskatoon Cancer Centre	http://www.sdh.sk.ca/cancercentre/
SBU – Statens beredning för medicinsk utvärdering	http://www.sbu.se/
Scottish Health on the Web	http://www.show.scot.nhs.uk/
Scottish Radiological Society	http://www.radiology.co.uk/
Society for Radiation Oncology Administrators	http://www.sroa.org/
Society of Surgical Oncology	http://www.surgonc.org/
Southwest Oncology Group	http://www.swog.org
Statistics Canada	http://www.statcan.ca/
Supportive Cancer Care Research (SCCR) Unit	http://www.fhs.mcmaster.ca/slru/sccru
Toronto-Sunnybrook Regional Cancer Centre	http://www.tsrcc.on.ca
UK Department of Health	http://www.doh.gov.uk/
University of Michigan Comprehensive Cancer Centre	http://www.cancer.med.umich.edu/
Vancouver Cancer Centre - BC Cancer Agency	http://www.bccancer.bc.ca/vcc/
Vancouver Island Cancer Centre	http://www.islandnet.com/~vicc/homepage.html
Varian Medical Systems, Inc.	http://www.varian.com
Western Australia Central Wait List Bureau	http://www.health.wa.gov.au/
Western Canada Waiting List Project	http://www.wcwl.org/
Windsor Regional Cancer Centre	http://www.wrcc.on.ca/
World Health Organization	http://www.who.int

Appendix 3: International Findings and Recommendations

Breast Cancer			
Country	**Report or Article Title**	**Findings**	**Comments**
Australia	Radiotherapy and Breast Cancer, 1999[52]		Updated in 2000
Australia	Clinical Practice Guidelines for the Management of Early Breast Cancer, 2000[53]	Radiotherapy after complete local excision is recommended as it significantly reduces risk of LR in the breast and need for further surgery. It should not be omitted even in selected patients	Effects of radiotherapy and surgery in early breast cancer. An overview of the randomized trials. Early Breast Cancer Trialists' Collaborative Group. *N Engl J Med* 1995;333(22):1444-55. Liljegren G, Holmberg L, Adami HO, Westman G, Graffman S, Bergh J. Sector resection with or without postoperative radiotherapy for stage I breast cancer: five-year results of a randomized trial. Uppsala-Orebro Breast Cancer Study Group. *J Natl Cancer Inst* 1994;86(9):717-22
Canada	Radiotherapy after breast-conserving surgery, 1998[26]	Recommendation: local breast irradiation should be started as soon as possible after surgery and not later than 12 weeks after, except for patients in whom radiotherapy is preceded by chemotherapy. **Optimal interval between BCS and start of irradiation has not been defined**	In a 1985 study from the Institut Gustave-Roussy, patients who began radiotherapy more than 7 weeks after BCS seemed to be at greater risk of recurrence (14%) than patients receiving treatment earlier (5%). Interval between radiotherapy and surgery was not significant when other relevant factors were considered in multivariate analysis (level III evidence). In a 1994 study by Nixon of node-negative patients who received a dose of 60 Gy or greater to the primary tumour site, when risk factors were controlled, there was no difference in recurrence rates associated with intervals ranging from 4 to 8 weeks between surgery and radiotherapy (level III evidence). Studies by Fisher, Levine and Wallgren showed that delaying radiotherapy until chemotherapy was complete did not show any apparent increases in local recurrence.

Breast Cancer			
Country	**Report or Article Title**	**Findings**	**Comments**
Canada (BC)	Provincial Wait List Trends, 2000[54] (last revision 29 May 2003)	Cancer radiotherapy section reports that nearly 65% of BC residents start radiotherapy within 4 weeks of consultation with a radiation oncologist at BC Cancer Agency. At end of fiscal 1999, 505 patients were waiting, with a median wait of 1.6 weeks (In March 2003, 307 patients were waiting, with a median wait of 1.1 weeks)	Trended numbers of patients waiting between fiscal 1993 to 1994 and 1998 to 1999. Increase of 9.5% in number of patients waiting. Most importantly, number dropped until fiscal 1997, so increase between fiscal 1997 to 1999 is 26% (using numbers provided). New site, new machinery and expanded services planned in 3 centres.
Scotland	Breast Cancer in Women, 1998[55]	It is accepted that any delay in being seen at a breast clinic is associated with anxiety, although delays of onset of treatment of less than three months are unlikely to be associated with a measurable difference in survival. Urgency should be assigned on basis of the general practitioner (GP) referral. Breast cancer units must develop with GPs details of how patients can be referred for rapid access. They should collaborate with GPs to find method of achieving targets to ensure that more than 80% of urgent referrals are seen within five working days and remainder within 10 working days (after receipt of referral). 70% of all new referrals should be seen within 20 working days.	Richards MA *et al.* Provision of breast services in the UK: the advantages of specialist breast units. Report of a working party of the British Breast Group. British Breast Group; 1994.
UK	A Policy Framework for Commissioning Cancer Services, 1995[56]	Equity of: • access to cancer services • quality of cancer services • clinical outcomes	Considered baseline planning document in UK
UK	A Survey of Radiotherapy Services in England, 1999[57]	Algorithm and report found at www.doh.gov.uk	Report and algorithm for health authorities to plan future services
UK	Reducing delays in cancer treatment, 1993[58]	Interval between BCS and postoperative radiotherapy should not exceed 20 working days except for clinical reasons. For patients requiring palliative radiotherapy, interval should not exceed a maximum of 10 working days for non-severe symptoms and should not exceed 48 hours	Example of local hospital adoption of UK guideline. Building on the report. Dr. Peter Barrett-Lee, Consultant Oncologist, Cardiff Quality Standards for Breast Services.

Breast Cancer			
Country	**Report or Article Title**	**Findings**	**Comments**
		for urgent symptom control.	
UK (Scotland, with sourcing to Royal College of Physicians)	Reducing delays in cancer treatment: some targets, 1993[58]	Recommended waiting time targets from date of first oncology consultation to start of radiotherapy or chemotherapy: urgent radiotherapy or chemotherapy: good practice=24 hours; maximum acceptable=48 hours palliative radiotherapy (according to symptom severity): good practice=48 hours; maximum acceptable=2 weeks (non-severe symptoms) radical radiotherapy involving complex treatment planning: good practice=2 weeks; maximum acceptable=4 weeks	Joint Council for Clinical Oncology. Reducing delays in cancer treatment: some targets. London: Royal College of Physicians; 1993
US	Treatment of early stage breast cancer, 1990[59]	In patients receiving adjuvant chemotherapy, no precise recommendations regarding sequence and timing of radiation therapy and chemotherapy can be given	

Joint Council for Clinical Oncology Target Waiting Times	
Recommended waiting time targets from date of first oncology consultation to start of radiotherapy or chemotherapy are:	
For urgent radiotherapy or chemotherapy	Good practice=24 hours Maximum acceptable=48 hours
For palliative radiotherapy (according to severity of symptoms)	Good practice=48 hours Maximum acceptable=2 weeks (for non-severe symptoms)
For radical radiotherapy involving complex treatment planning	Good practice=2 weeks Maximum acceptable=4 weeks*

* Where additional specialist staging procedures are necessary

Source: Adapted from Joint Council for Clinical Oncology. Reducing delays in cancer treatment: some targets. London: Royal College of Physicians; 1993. Annex 4 Recommended waiting time targets. http://www.show.scot.nhs.uk/sign/html/htmtxt29.htm#5