

Waiting Time for Radiation Therapy in Breast Cancer Patients in Quebec from 1992 to 1998

Temps d'attente pour la radiothérapie chez les femmes atteintes de cancer du sein au Québec de 1992 à 1998

A study of surgically treated breast cancer patients in Quebec documents and helps to explain increased waiting times for radiation therapy.



by BERNARD FORTIN, MD, FRCPC

*Department of Epidemiology, Biostatistics, and Occupational Health, McGill University
Department of Radiation Oncology, Centre Hospitalier de l'Université de Montréal*

MARK S. GOLDBERG, PHD

*Department of Epidemiology, Biostatistics, and Occupational Health, McGill University
Division of Clinical Epidemiology, McGill University Health Centre
Department of Medicine, McGill University
Department of Oncology, McGill University*

NANCY E. MAYO, PHD

*Department of Epidemiology, Biostatistics, and Occupational Health, McGill University
Division of Clinical Epidemiology, McGill University Health Centre
Department of Medicine, McGill University*

Waiting Time for Radiation Therapy in Breast Cancer Patients in Quebec from 1992 to 1998

MARIE-FRANCE VALOIS, MSC
Department of Medicine, McGill University

SUSAN C. SCOTT, MSC
Division of Clinical Epidemiology, McGill University Health Centre

JAMES HANLEY, PHD
Department of Epidemiology, Biostatistics, and Occupational Health, McGill University
Division of Clinical Epidemiology, McGill University Health Centre
Department of Medicine, McGill University

Abstract

Background : This study was conducted among surgically treated breast cancer patients in Quebec to determine waiting time between surgery and post-operative radiation therapy and factors influencing it.

Methods : Records of fee-for-service claims and hospitalizations were obtained for all women who, between 1992 and 1998, underwent an invasive procedure for non-metastatic breast cancer. Waiting time was defined as the time between either the last surgical procedure or the last cycle of chemotherapy and the initiation of radiation therapy. Hierarchical linear regression models were used to identify predictors of waiting time.

Results : Over seven years, 29,072 episodes of breast cancer treatments were identified, of which 17,684 included radiation therapy. The number of cases increased by 5.5% per year, but concurrent broadening of indications for radiation therapy led to an increase in the number of breast cancer patients receiving radiation therapy of 9% per year. In hierarchical linear modelling, comparing 1998 to 1992, median waiting time increased by 63% (95% confidence interval [CI] 35%–97%) in patients not receiving chemotherapy and by 35% (95% CI 3%–88%) in patients receiving chemotherapy. Other predictors of shorter waiting times were localized cancer stage, breast-conserving surgery, early consultation with a radiation oncologist, having surgery in a centre with a radiation therapy facility, living close to a radiation therapy facility and living in a higher socio-economic area.

Interpretation : Using administrative databases to evaluate waiting times is feasible. Explanations of the increased waiting time include increased demand, insufficient resources and changes in the indications for breast-conserving surgery and radiation therapy.

Résumé

Contexte: Cette étude a été menée auprès de femmes atteintes du cancer du sein et qui ont reçu un traitement chirurgical au Québec en vue de déterminer le temps d'attente entre la chirurgie et la radiothérapie postchirurgicale, ainsi que les facteurs influençant le temps d'attente.

Méthodes: Nous avons obtenu les données sur les demandes de paiement d'honoraires à l'acte et les hospitalisations pour toutes les femmes qui ont subi une intervention chirurgicale invasive pour un cancer du sein sans métastase entre 1992 et 1998. Le temps d'attente a été défini comme étant le délai entre la dernière intervention chirurgicale ou le dernier cycle de chimiothérapie et le début du traitement de radiothérapie. Des modèles de régression linéaire hiérarchique ont été utilisés pour déterminer les facteurs de prédiction du temps d'attente.

Résultats: Sur une période de sept ans, 29,072 épisodes de traitement contre le cancer du sein ont été répertoriés, dont 17,684 comportaient une radiothérapie. Le nombre de cas a augmenté de 5,5 % par an, mais une hausse concomitante des recommandations de traitement de radiothérapie a entraîné une augmentation de 9 % du nombre de femmes atteintes du cancer du sein qui reçoivent un tel traitement. Lorsqu'on compare 1998 à 1992, le temps d'attente moyen a augmenté de 63 % (intervalle de confiance [IC] de 95 % : 35 à 97 %) chez les patientes n'ayant pas besoin de chimiothérapie et de 35 % (IC de 95 % : 3 à 88 %) chez celles qui reçoivent des traitements systémiques. Parmi les autres facteurs permettant de prédire un temps d'attente plus court, citons le cancer localisé, le traitement chirurgical conservateur, la consultation précoce d'un oncoradiologiste, la chirurgie dans un centre offrant des traitements de radiothérapie, le fait de résider à proximité d'un centre de radiothérapie et l'appartenance à un milieu socio-économique plus favorisé.

Interprétation: Il est possible d'utiliser des bases de données administratives pour évaluer le temps d'attente. Parmi les raisons pouvant expliquer l'augmentation du temps d'attente, citons la demande accrue, les ressources insuffisantes et les changements dans les recommandations de traitement chirurgical conservateur et de radiothérapie.

DURING THE LAST 20 YEARS, THE MANAGEMENT OF BREAST CANCER HAS changed dramatically. With screening, tumours are smaller, and randomized controlled trials have shown equivalence between mastectomy and breast-conserving surgery followed by radiation therapy (Verkonesi et al. 1990; Sarrazin et al. 1989; van Dongen et al. 1992; Blichert-Toft et al. 1992; Jacobson et al. 1995; Fisher et al. 2002). This, combined with the aging of the population (Wiener and Tilly 2002; Gouvernement du Québec 2001), has generated a continually increasing demand for

radiation therapy in treating breast cancer. There are concerns that this increasing demand will reduce the availability of radiation treatments (Mackillop et al. 1995; Benk et al. 1998; Mackillop et al. 1994; Mayo et al. 2001).

Increased waiting times may be important, as the local recurrence rate after conservative surgery and radiation therapy appears to be about 5% but is 20% to 50% after conservative surgery alone (Fisher et al. 2002). However, there is no consensus as to the optimal time to offer radiation.

... researchers surveyed major radiation centres in the United States and in Canada ... the median waiting time before radiation therapy was 40 days in the United States and 73 days in Canada.

We knew from a recently published study (Mayo et al. 2001) that waiting times for the surgical component of breast cancer treatment were increasing in Quebec. An earlier report from Ontario on wait times for radiotherapy also depicted a situation that was deteriorating over time (Mackillop et al. 1994). In 1991, the median time between the

completion of surgery and initiation of post-operative radiation for breast cancer was 57.8 days – an increase of 102.7% compared to 1982. In 1994, the same researchers surveyed major radiation centres in the United States and in Canada (Mackillop et al. 1995). Their study showed that the median waiting time before radiation therapy was 40 days in the United States and 73 days in Canada. A report from a single centre in Quebec in 1992 showed a median waiting time of 68 days (Benk et al. 1998). Some literature from Europe suggests that waiting times are comparable to those seen in the United States, with a Spanish report showing an overall maximum waiting time of only 60 days for all cancer types and centres in that country (Esco et al. 2003).

Because of the concerns about availability of services, we conducted the present study to estimate secular trends in waiting time for radiation therapy after breast cancer surgery and to identify factors that may influence waiting time.

Subjects and Methods

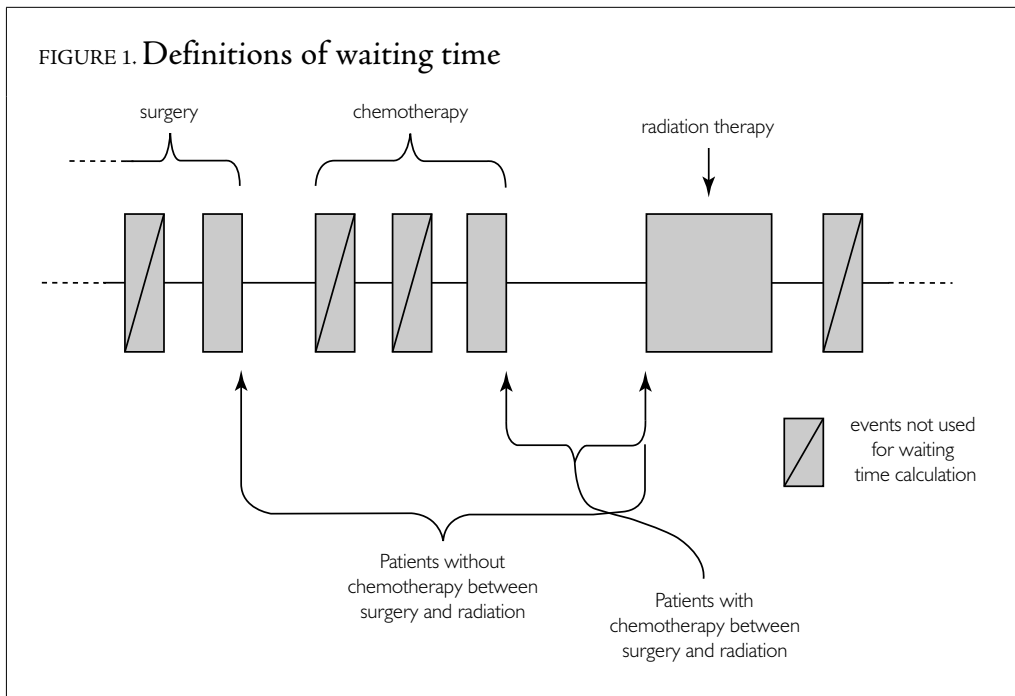
This study was approved by the McGill University Faculty of Medicine Institutional Review Board and by the Commission d'accès à l'information du Québec. It was population based and included all women aged 20 years and over who had an invasive procedure for the diagnosis or treatment of breast cancer in the province of Quebec between 1992 and 1998.

We used the database of physician fee-for-service claims maintained by the Régie de l'Assurance Maladie du Québec (RAMQ) to obtain data on diagnostic and surgical procedures related to the breast including chemotherapy, radiotherapy and visits to radio-oncologists. This was possible because all these procedures have specific codes and are performed by specific specialists, namely, surgeons, oncologists and radiation oncologists, who have unique specialty identifiers. The validity of the RAMQ database has been verified and shown to be high in another setting (Tamblyn et al. 2000). Since no radiation therapy facility in Quebec is private and doctors must bill specific procedure codes to the RAMQ in order to get paid, completeness of the data was expected to be high. During the study period, all breast cancer related procedures were performed in day surgery, thus requiring hospitalization. For that reason, the hospital discharge file (MedEcho) was used to capture additional details concerning the treatments and any missing breast cancer episodes. MedEcho is a mandatory database concerning all the procedures performed during hospital stays. For confidentiality reasons, the only personal patient information provided in the dataset from RAMQ was the women's age in 1992, in five-year categories.

We made use of prior (1980–1991) and subsequent (1999) data to avoid truncating episodes that spanned administrative time periods. The 1996 Canadian census database was used to obtain, for each Forward Sorting Area (first three characters of the postal code), the median income (categorized as high if the median income was higher than the 75th percentile), the proportion of households in which one or more persons had completed high school (categorized as “educated” if more than two-thirds of households in the area included at least one person with a high school diploma) and the distance of the patient's residence to the nearest radiation therapy facility (categorized as 0–100 km, 101–400 km and ≥ 401 km because the often very wide geographical area covered by each Forward Sorting Area did not permit finer stratification). There were 10 radiation therapy centres in Quebec in 1991, and three new centres were opened in the province during the study period.

Since routine mammograms are usually spaced at intervals of at least six months, we considered consecutive surgical procedures to the breast that were separated in time by five months or less to be related to a single breast cancer that was operated on more than once (e.g., the biopsy, the definitive surgery and then a re-excision for positive surgical margins) and not to multiple breast cancers. Any non-surgical treatments delivered later than one year after breast cancer surgery were considered not to be related to that surgical procedure but rather to another cancer event. Topography and morphology codes listed in the hospital discharge database were used to estimate the stage of breast cancer.

Only episodes including breast surgery followed by adjuvant radiotherapy were retained. Excluded were episodes with a diagnosis of disseminated disease, with localized breast cancer occurring after an episode for metastatic cancer and where radio-



therapy was begun before surgery.

For patients who did not receive chemotherapy between their surgery and radiation therapy, waiting time was calculated as the number of days between the last surgery in an episode (accounting for possible multiple surgeries) and radiotherapy. For patients who received chemotherapy, the time before the end of the chemotherapy was considered as part of planned treatment and, thus, the waiting time was calculated as the time from the last post-operative chemotherapy code to the initiation of radiation therapy (Figure 1).

Statistical methods

Secular trends were analyzed using simple linear regression and logistic regression. To evaluate factors associated with waiting time, hierarchical linear regression models were used. We used the natural logarithm scale for waiting time because it was log-normally distributed. We used hierarchical models because waiting times may be more similar for patients treated in a given hospital (Bryk and Raudenbush 1992). We used a two-level hierarchical model to try to isolate the effects of individual-level variables on waiting time (e.g., tumour stage, type of surgery) from the variation in waiting times explained by the radiation therapy centres' differing waiting lists. This model allowed each radiation therapy centre to have its own median value for waiting time. The effect of any individual-level variable was then analyzed according to that centre-specific median.

All statistical tests were two-sided. The reported confidence intervals (CI) were evaluated at the 95% level, and all covariates were adjusted for the others in the retained model.

Results

Demographic characteristics

Between 1992 and 1998, there were 30,446 episodes of surgically treated breast cancers among 27,734 patients. Of these, 1,374 episodes were metastatic, thus leaving 29,072 cancer episodes for analysis.

Table 1 shows that the distributions of age and stage of breast cancer were fairly stable during the study period. Apparent changes in the age distribution over time are

TABLE 1. Selected characteristics of the 29,072 non-metastatic breast cancer episodes among the 27,734 patients surgically treated in Quebec between 1992 and 1998

	Total (%)	1992	1993	1994	1995	1996	1997	1998
Women's age in 1992		%	%	%	%	%	%	%
20–34	1488 (5.1)	2.6	3.6	3.9	4.8	5.9	6.2	7.5
35–49	8968 (30.9)	25.4	28.4	28.9	30.5	31.6	34.1	34.6
50–64	10 092 (34.7)	33.5	33.7	34.6	34.8	35.1	34.8	36.0
65–79	7364 (25.3)	31.3	28.3	27.6	25.7	24.5	22.5	20.3
≥ 80	1160 (4.0)	7.3	6.1	4.9	4.2	2.9	2.4	1.6
Cancer stage								
Benign In situ	199 (0.7)	0.6	0.8	0.9	0.7	0.6	0.5	0.8
Localized	19 336 (66.51)	66.2	67.0	66.8	65.4	66.6	66.5	67.0
Regional	7431 (25.6)	28.4	26.8	26.7	26.4	24.8	24.1	23.1
Unspecified	2106 (7.2)	4.8	5.3	5.7	7.5	8.1	8.8	9.1
Surgery in a centre with a radiation therapy service	8420 (29.0)	29.9	29.5	28.2	28.3	29.8	29.0	29.1
Highest quartile for median income	5846 (24.8)	22.9	24.2	24.9	24.2	25.6	26.0	28.3
Residential distance from a radiation therapy centre								
0–100 km	25 960 (89.4)	88.5	89.8	89.8	88.8	89.0	89.6	89.9
101–400 km	2933 (10.1)	10.9	9.8	9.6	10.6	10.4	10.0	9.7
≥401 km	158 (0.5)	0.5	0.4	0.7	0.7	0.6	0.5	0.5

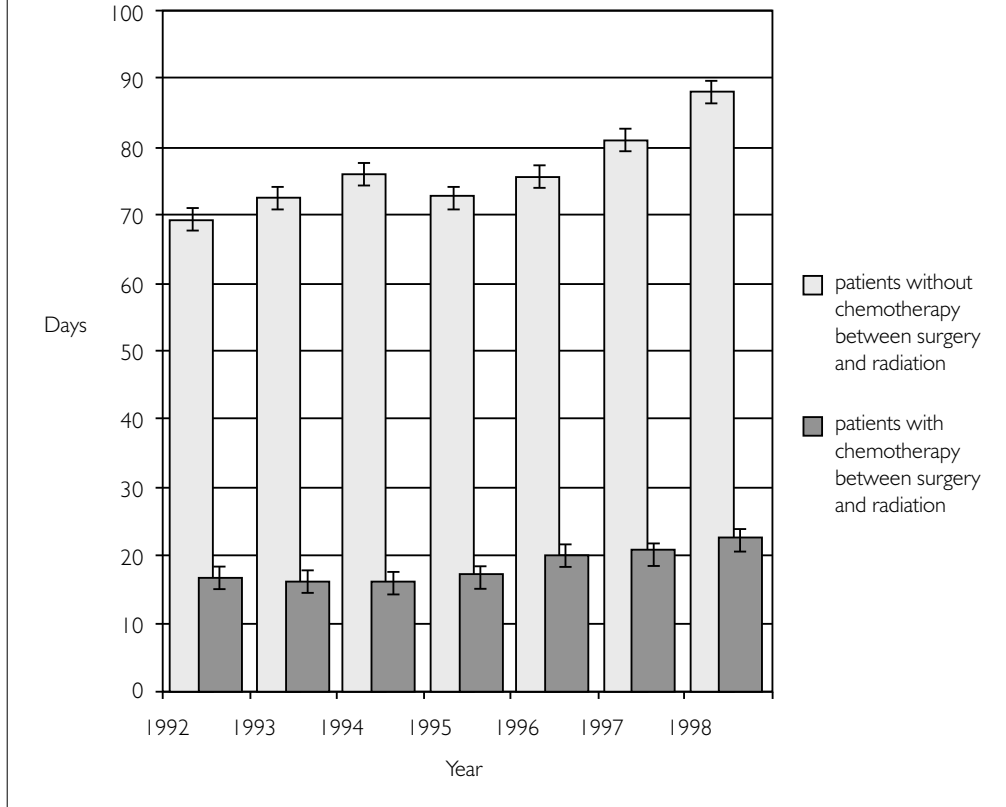
TABLE 2. Distribution of the number of cases by type of treatment and calendar year

	1992	1993	1994	1995	1996	1997	1998	Average absolute annual change (95% CI)*
Total number of cases	3532	3675	3904	4062	4231	4503	5165	5.5% (3.7 to 7.4)
Proportion with breast-conserving surgery	78%	78%	78%	80%	81%	80%	82%	0.7% (0.3 to 1.1)
Number receiving radiotherapy, any surgery	1966	2125	2306	2393	2592	2886	3398	9.0% (5.7 to 12.4)
Proportion receiving radiotherapy, any surgery	56%	58%	59%	59%	61%	64%	68%	1.8% (1.2 to 2.4)
Radiotherapy given, breast-conserving surgery episodes only	1783 (65%)	1963 (68%)	2125 (70%)	2217 (68%)	2410 (70%)	2681 (75%)	3279 (77%)	1.8% (1.0 to 2.6)
Radiotherapy given, mastectomy episodes only	183 (23%)	162 (20%)	181 (21%)	176 (22%)	182 (22%)	205 (22%)	219 (24%)	0.3% (-0.3 to 0.8)
Proportion receiving chemotherapy	27%	26%	25%	25%	25%	27%	28%	0.3% (-0.4 to 1.0)

*Modelled using simple linear regression

explained by the fact that age was provided in the database as the patient's five-year age category in 1992 rather than when she was diagnosed. Table 2 shows that there was a statistically significant average increase in the number of breast cancer cases (5.5% per year, 95% CI 3.7%–7.4%), in the proportion of patients treated with breast-conserving surgery (average of 0.7% per year, 95% CI 0.3%–1.1%) and in the number of patients receiving radiation (9% per year; 95% CI 5.7%–12.4%). For patients treated with breast-conserving surgery, the proportion of subjects receiving radiation increased from 65% to 77% (annual increase of 1.8%; 95% CI 1.0%–2.6%). The overall use of chemotherapy (26% of patients) and radiation therapy for patients treated with mastectomy (22%) was stable.

FIGURE 2. Median waiting time for radiation therapy, by calendar year, for groups with and without chemotherapy. Vertical bars represent the 95% confidence intervals



Waiting time for radiation therapy

Post-operative radiation therapy was provided in 17,684 (60.8%) of the cancer episodes. Of these, 4,821 contained an indication that chemotherapy was received after surgery and before radiation.

Figure 2 shows the median and 95% CI of the waiting time, by year of treatment, for the group without chemotherapy and for the group with chemotherapy. For the former group, the median waiting time was 69 days in 1992 and 88 days (28% longer) in 1998; for the group receiving post-surgery chemotherapy, the median waiting time was 17 days in 1992 and 22 days (32% higher) in 1998.

For patients not receiving chemotherapy, the unadjusted proportion of patients having to wait more than eight weeks before radiation therapy increased from 70% in 1992 to 82% in 1998 (Figure 3). If a 12-week cut-off is used, the proportion increased from 36% in 1992 to 57% in 1998.

Tables 3 and 4 show the predictors of waiting time, expressed as the percentage

TABLE 3. Predictors of waiting time for radiotherapy in the group not receiving chemotherapy

Patient-level predictors:	Hierarchical modelling	
	% change in median waiting time (95% CI)	95% CI for mean change in median waiting times across RT centres
1993 vs. 1992	9% (2 to 16%)	-10 to 31%
1994 vs. 1992	10% (1 to 21%)	-16 to 45%
1995 vs. 1992	5% (-8 to 20%)	-30 to 59%
1996 vs. 1992	12% (0 to 24%)	-20 to 55%
1997 vs. 1992	14% (-4 to 37%)	-36 to 103%
1998 vs. 1992	63% (35 to 97%)	-11 to 199%
Regional cancer spread	9% (4 to 14%)	-5 to 25%
For mastectomy vs. breast-conserving surgery	25% (15 to 36%)	-3 to 61%
If seen pre-op by a radio-oncologist	-30% (-37 to -23%)	-48 to -6%
If surgery done in a centre where there is a radiotherapy service	-13% (-17 to -8%)	-25 to 2%
Living more than 100 km from a radiotherapy centre	10% (4 to 17%)	-8 to 32%
Living in an area where at least one person completed high school in 2/3 of households	-3% (-5 to -1%)	-6 to 1%
Missing information for household education	-20% (-32 to -4%)	-53 to 39%
Hospital-level predictors:		
Proportion of patients from high median income area, per 10% increase	-2% (-3 to -1%)	n.a.

n.a.: not applicable; CI: confidence interval

For the chemotherapy group (Table 4), the radiation therapy centre at which a given patient was treated explained only 2% of the variation in waiting times, while the patient-level variables explained 10% of that variation. The association between individual-level variables and waiting time in this group was similar in direction to what was found in the non-chemotherapy group: regional cancer spread (28% increase), having had a mastectomy instead of breast-conserving surgery (31% increase) and having surgery in a centre with a radiotherapy service (-18%). A trend towards longer waiting times was found in the later years (35% longer in 1998 than in 1992). The parameters estimates in the chemotherapy group are less stable because the cohort was smaller.

TABLE 4. Predictors of waiting time for radiotherapy in the group receiving chemotherapy

Patient-level predictors:	Hierarchical modelling	
	% change in median waiting time (95% CI)	95% CI for mean change in median waiting times across RT centres
1993 vs. 1992	5% (-10 to 23%)	-21 to 39%
1994 vs. 1992	-5% (-27 to 24%)	-55 to 100%
1995 vs. 1992	-3% (-29 to 31%)	-60 to 135%
1996 vs. 1992	25% (-14 to 82%)	-60 to 287%
1997 vs. 1992	19% (-17 to 72%)	-60 to 259%
1998 vs. 1992	35% (-3 to 88%)	-50 to 269%
Regional cancer spread	28% (15 to 43%)	-4 to 72%
For mastectomy vs. breast-conserving surgery	31% (16 to 48%)	3 to 67%
If surgery done in a centre where there is a radiotherapy service	-18% (-35 to 4%)	-61 to 74%

CI: confidence interval

Discussion

The main findings from this study are that waiting times for receiving radiation therapy after surgery for breast cancer increased over the study period. The increase in the group receiving chemotherapy is disturbing, because there should have been sufficient time to schedule radiotherapy during the planned delay of three to six months.

Most of the variation in waiting times cannot be explained by the available data. This result is not surprising given that this study is based on administrative databases that contain very little data on personal characteristics, medical histories and limited contextual variables. This should not, however, affect the validity of the findings. It was troubling to find an increase in waiting time by distance from the nearest radiation therapy centre. This finding may have been due to difficulties in communication between the treating surgeon and the radiation oncologist. Supporting this observation was a favourable effect on waiting time for patients who had surgery in a centre with a radiation therapy facility on site. These centres are located mainly within large tertiary centres. Some possible explanations for this effect include improved communication between specialists, faster access to diagnostic tests and higher volumes of patients treated by these surgeons.

Other factors adversely affecting waiting time were having had a mastectomy and having regional disease spread. The longer waiting time could have been due to longer

healing time after a more extensive surgery or to more thorough investigation and treatment for a more severe disease.

In addition, the effect of socio-economic status and education on waiting time, though small, was surprising considering the universal health insurance coverage in the province of Quebec. This finding may reflect an ability of some women to influence more timely treatment.

... physicians are paid on the basis of services rendered ... completeness and accuracy of reporting have monetary incentives attached.

Some radiation therapy centres performed better than others. Because each hospital designation code was encrypted, it is difficult to explore possible causes such as total radiation therapy workload, staff shortages and case mix. However, it is likely that some of the radiation centres were newly

created and thus may not have had the same backlog as the older ones. It also demonstrates that during the study period, patients could have waited less if they had been transferred from centres with long waiting lists to centres with shorter ones.

A strength of this study is that it is population based and that the data are robust: physicians are paid on the basis of services rendered, and completeness and accuracy of reporting have monetary incentives attached. Because of the universality of medicare, very few procedures would have been performed at private clinics and, thus, coverage of the data is close to 100%. The waiting times for radiation therapy reflected in this study are thus a precise depiction of the situation in Quebec between 1992 and 1998.

A limitation of this study is that these results cannot be used to distinguish system delays from patient delays, as our data sources contain only records for procedures performed by physicians. Nevertheless, in an oncology setting, the delay for which the patient is responsible is often only the time from the appearance of symptoms until the first contact with a healthcare professional, as subsequent diagnostic and therapeutic procedures are usually scheduled on behalf of the patient.

There are no data to suggest an optimal waiting time. As treatment decisions involve major life-altering choices for women, an "appropriate" amount of time is required to choose the best treatment approach (Coates 1999), and this may vary considerably among women. On the other hand, women and their families may face considerable anxiety because of delays. What is of more concern is that long waits may also affect recurrence and survival, as suggested by theory and experience with other cancer sites (Robertson et al. 1998; van der Voet et al. 1998; Petereit et al. 1995; Fortin et al. 2002).

There is only one randomized clinical trial (Recht et al. 1996) and few retrospective studies investigating the effects of delays on breast cancer control (Buchholz et al. 1993; Clarke et al. 1985; Nixon et al. 1994; Buzdar et al. 1993; Vujovic et al. 1998; Froud et al. 2000; Slotman et al. 1994; Recht et al. 1991; Hartsell et al. 1995). In the randomized trial, 244 patients with early breast cancer were assigned, after breast-conserving surgery, to receive a 12-week course of chemotherapy given either before or after breast radiotherapy. There was lower overall survival (73% vs. 81%) and a higher incidence of distant metastasis (36% vs. 25%), but a lower rate of local recurrence (5% vs. 14%), in the group receiving radiotherapy early (thus delaying chemotherapy). These observations have led to the practice of prioritizing chemotherapy over radiation therapy for patients who require it.

A pooled analysis of the retrospective studies (Huang et al. 2003) compared local breast cancer recurrence rates for patients treated later than eight weeks to those receiving their post-operative radiation therapy within eight weeks. The pooled odds ratio of recurrence among patients treated later compared to those treated within eight weeks was 1.62 (95% CI 1.21–2.03), representing a 62% higher risk of recurrence among those receiving radiation more than eight weeks after surgery.

The existing data do not show a relationship between local cancer recurrence rates and survival. The usually slow tumour kinetics of breast cancer (which lead to under-detection of late recurrences in studies with short observation periods) and the option to perform a mastectomy in patients with local recurrence after breast-conserving surgery are possible explanations for this lack of obvious relationship between local recurrences and cancer death.

Because waiting time usually reflects accessibility to services, some measures have been implemented in the province since 1998 to address this issue – for example, centralized management of the waiting lists of all radiation therapy centres and transfer of patients to centres with shorter waiting lists, opening of new radiation therapy units and a significant increase in admissions to the radiation oncology residency program and the radiation technologist training programs.

One has to remain conscious, though, of the unrelenting increase in the total number of breast cancer cases over the years, as shown in this study. As a consequence, we believe that the problem of waiting lists must be kept under close scrutiny if we want to maintain the highest standards of cancer treatment for our population, and the available administrative databases provide a tool to do so.

Correspondence may be directed to: Dr. Bernard Fortin, Dept. of Radiation Oncology, Centre Hospitalier de l'Université de Montréal, 1560 Sherbrooke East, Montréal, QC H2L 4M1.

REFERENCES

- Benk, V., V. Ho, P.R. Fortin, G. Zhang, C. Levinton and C.R. Freeman. 1998. "Predictors of Delay in Starting Radiation Treatment for Patients with Early Stage Breast Cancer." *International Journal of Radiation Oncology, Biology, Physics* 41(1): 109–115.
- Blichert-Toft, M., C. Rose, J.A. Andersen, M. Overgaard, C.K. Axelsson, K.W. Andersen et al. 1992. "Danish Randomized Trial Comparing Breast Conservation Therapy with Mastectomy: Six Years of Life-Table Analysis." Danish Breast Cancer Cooperative Group. *Journal of the National Cancer Institute Monographs* 11: 19–25.
- Bryk, A.S. and S.W. Raudenbush. 1992. *Hierarchical Linear Models: Applications and Data Analysis Methods*. Newbury Park: Sage Publications.
- Buchholz, T.A., M.M. Austin-Seymour, R.E. Moe, G.K. Ellis, R.B. Livingston, J.G. Pelton et al. 1993. "Effect of Delay in Radiation in the Combined Modality Treatment of Breast Cancer." *International Journal of Radiation Oncology, Biology, Physics* 26(1): 23–35.
- Buzdar, A.U., S.W. Kau, T.L. Smith, F. Ames, E. Singletary, E. Strom et al. 1993. "The Order of Administration of ChemoTherapy and Radiation and Its Effect on the Local Control of Operable Breast Cancer." *Cancer* 71(11): 3680–3684.
- Clarke, D.H., M.G. Le, D. Sarrazin, M.J. Lacombe, F. Fontaine, J.P. Travagli et al. 1985. "Analysis of Local–Regional Relapses in Patients with Early Breast Cancers Treated by Excision and Radiotherapy: Experience of the Institut Gustave-Roussy." *International Journal of Radiation Oncology, Biology, Physics* 11(1): 137–145.
- Coates, A.S. 1999. "Breast Cancer: Delays, Dilemmas, and Delusions." *Lancet* 353(9159): 1112–1113.
- Esco, R., A. Palacios, J. Pardo, A. Biete, J.A. Carceller, C. Veiras et al. 2003. "Infrastructure of Radiotherapy in Spain: A Minimal Standard of Radiotherapy Resources." *International Journal of Radiation Oncology, Biology, Physics* 56(2): 319–327.
- Fisher, B., J.H. Jeong, S. Anderson, J. Bryant, E.R. Fisher and N. Wolmark. 2002. "Twenty-Five-Year Follow-up of a Randomized Trial Comparing Radical Mastectomy, Total Mastectomy, and Total Mastectomy Followed by Irradiation." *New England Journal of Medicine* 347(8): 567–575.
- Fortin, A., I. Bairati, M. Albert, L. Moore, J. Allard and C. Couture. 2002. "Effect of Treatment Delay on Outcome of Patients with Early-Stage Head-and-Neck Carcinoma Receiving Radical Radiotherapy." *International Journal of Radiation Oncology, Biology, Physics* 52(4): 929–936.
- Froud, P.J., D. Mates, J.S. Jackson, N. Phillips, S. Andersen, S.M. Jackson et al. 2000. "Effect of Time Interval between Breast-Conserving Surgery and Radiation Therapy on Ipsilateral Breast Recurrence." *International Journal of Radiation Oncology, Biology, Physics* 46(2): 363–372.
- Gouvernement du Québec. 2001. *Surveillance de la mortalité au Québec 1977–1998*.
- Hartsell, W.F., D.C. Recine, K.L. Griem and A.K. Murthy. 1995. "Delaying the Initiation of Intact Breast Irradiation for Patients with Lymph Node Positive Breast Cancer Increases the Risk of Local Recurrence." *Cancer* 76(12): 2497–2503.
- Huang, J., L. Barbera, M. Brouwers, G. Browman and W.J. Mackillop. 2003. "Does Delay in Starting Treatment Affect the Outcomes of RadioTherapy? A Systematic Review." *Journal of Clinical Oncology* 21(3): 555–563.
- Jacobson, J.A., D.N. Danforth, K.H. Cowan, T. d'Angelo, S.M. Steinberg, L. Pierce et al. 1995. "Ten-Year Results of a Comparison of Conservation with Mastectomy in the Treatment of Stage I

- and II Breast Cancer." *New England Journal of Medicine* 332(14): 907–911.
- Mackillop, W.J., H. Fu, C.F. Quirt, P. Dixon, M. Brundage and Y. Zhou. 1994. "Waiting for Radiotherapy in Ontario." *International Journal of Radiation Oncology, Biology, Physics* 30(1): 221–228.
- Mackillop, W.J., Y. Zhou and C.F. Quirt. 1995. "A Comparison of Delays in the Treatment of Cancer with Radiation in Canada and the United States." *International Journal of Radiation Oncology, Biology, Physics* 32(2): 531–539.
- Mayo, N.E., S.C. Scott, N. Shen, J. Hanley, M.S. Goldberg and N. MacDonald. 2001. "Waiting Time for Breast Cancer Surgery in Quebec." *Canadian Medical Association Journal* 164(8): 1133–1138.
- Nixon, A.J., A. Recht, D. Neuberg, J.L. Connolly, S. Schnitt, A. Abner et al. 1994. "The Relation between the Surgery–Radiotherapy Interval and Treatment Outcome in Patients Treated with Breast-Conserving Surgery and Radiation Therapy without Systemic Therapy." *International Journal of Radiation Oncology, Biology, Physics* 30(1): 17–21.
- Petereit, D.G., J.N. Sarkaria, R. Chappell, J.F. Fowler, T.J. Hartmann, T.J. Kinsella et al. 1995. "The Adverse Effect of Treatment Prolongation in Cervical Carcinoma." *International Journal of Radiation Oncology, Biology, Physics* 32(5): 1301–1307.
- Recht, A., S.E. Come, R.S. Gelman, M. Goldstein, S. Tishler, S.M. Gore et al. 1991. "Integration of Conservative Surgery, Radiotherapy, and Chemotherapy for the Treatment of Early-Stage, Node-Positive Breast Cancer: Sequencing, Timing, and Outcome." *Journal of Clinical Oncology* 9(9): 1662–1667.
- Recht, A., S.E. Come, I.C. Henderson, R.S. Gelman, B. Silver, D.F. Hayes et al. 1996. "The Sequencing of Chemotherapy and Radiation Therapy after Conservative Surgery for Early-Stage Breast Cancer." *New England Journal of Medicine* 334(21): 1356–1361.
- Robertson, C., A.G. Robertson, J.H. Hendry, S.A. Roberts, N.J. Slevin, W.B. Duncan et al. 1998. "Similar Decreases in Local Tumor Control Are Calculated for Treatment Protraction and for Interruptions in the Radiotherapy of Carcinoma of the Larynx in Four Centers." *International Journal of Radiation Oncology, Biology, Physics* 40(2): 319–329.
- Sarrazin, D., M.G. Le, R. Arriagada, G. Contesso, F. Fontaine, M. Spielmann et al. 1989. "Ten-Year Results of a Randomized Trial Comparing a Conservative Treatment to Mastectomy in Early Breast Cancer." *Radiotherapy and Oncology* 14(3): 177–184.
- Slotman, B.J., O.W. Meyer, K.H. Njo and A.B. Karim. 1994. "Importance of Timing of Radiotherapy in Breast Conserving Treatment for Early Stage Breast Cancer." *Radiotherapy and Oncology* 30(3): 206–212.
- Tamblyn, R., T. Reid, N. Mayo, P. McLeod and M. Churchill-Smith. 2000. "Using Medical Services Claims to Assess Injuries in the Elderly: Sensitivity of Diagnostic and Procedure Codes for Injury Ascertainment." *Journal of Clinical Epidemiology* 53(2): 183–194.
- van der Voet, J.C., R.B. Keus, A.A. Hart, F.J. Hilgers and H. Bartelink. 1998. "The Impact of Treatment Time and Smoking on Local Control and Complications in T1 Glottic Cancer." *International Journal of Radiation Oncology, Biology, Physics* 42(2): 247–255.
- van Dongen, J.A., H. Bartelink, I.S. Fentiman, T. Lerut, F. Mignolet, G. Olthuis et al. 1992. "Randomized Clinical Trial to Assess the Value of Breast-Conserving Therapy in Stage I and II Breast Cancer, EORTC 10801 Trial." *Journal of the National Cancer Institute Monographs* 11: 15–18.