Original Study

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Physician Survey of Timing of Adjuvant Endocrine Therapy Relative to Radiotherapy in Early Stage Breast Cancer Patients

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Abstract

The optimal timing of adjuvant endocrine therapy with respect to radiotherapy in early breast cancer is unknown. We conducted a multicenter survey of oncologists to evaluate institutional and personal practices. Results showed that decisions around the timing of therapies were being based on personal opinion and preference. In the absence of data to support these decisions, appropriately powered trials are needed.

Background: Patients can start endocrine therapy before, concurrently with, or sequentially after radiotherapy. The optimal timing of starting adjuvant endocrine therapy is unknown. This survey was performed to evaluate physician recommendations. **Methods:** Canadian oncologists were surveyed to evaluate institutional and personal practices regarding the prescription of adjuvant endocrine therapy and radiotherapy. Perspectives regarding the design of a clinical trial to compare concurrent versus sequential therapy, and the optimum end points for such a trial, were also sought. **Results:** The overall response rate was 30% (65/220), with responses mainly from medical (35/65, 54%) and radiation (28/65, 43%) oncologists. Eighty-four percent of respondents reported an absence of institutional protocols. The majority of physicians (57%, 36/65) identified endocrine therapy provided after radiotherapy as the preferred sequence of treatments. Twenty-two percent (14/65) had no preference, while 21%, (14/65) started endocrine therapy either before or concurrent with radiotherapy. Practice patterns were largely based on the physician's own clinical experience. Thirty-two percent of physicians (21/65) had concerns regarding concurrent endocrine therapy and radiotherapy, including increased adverse effects with endocrine therapy (13/21, 62%), reduced efficacy of radiotherapy (4/21, 19%), reduced compliance with endocrine therapy (3/21, 14%), and increased radiation toxicity (1/21, 5%). Most thought a pragmatic clinical trial addressing this question would help standardize and improve patient care. **Conclusion:** Decisions around the timing of endocrine therapy and radiotherapy are largely being made on the basis of physicians' personal choices. In the absence of data to support these decisions, appropriately powered trials are needed.

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Introduction

Despite the majority of patients with early-stage breast cancer receiving adjuvant endocrine therapy and radiotherapy, the optimal way to sequence these treatments is unknown. As such, patients may commence adjuvant endocrine therapy before, concurrently with, or sequentially after radiotherapy. This results in variation in clinical practice. Traditional clinical practice has however favored sequential radiotherapy followed by endocrine therapy. This practice may have arisen from concerns that concurrent endocrine therapy may reduce the efficacy of radiotherapy or lead to increased toxicity.[1]

Concerns regarding efficacy likely relate to the cytostatic effect of endocrine therapy on breast cancer cells, which may render them radioresistant, as radiation is most effective in actively cycling cells.

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However, preclinical data on this subject have been conflicting, with some studies suggesting that aromatase inhibitors in particular may enhance radiosensitivity.[2-5] The latter has raised the question as to whether concurrent radiotherapy and aromatase inhibitor therapy might therefore improve local control, something that is currently under study in the prospective Study of Anastrozole and Radiotherapy Sequencing (STARS) trial (ClinicalTrials.gov, NCT00887380). However, with enhanced radiosensitivity comes the concern for greater toxicity. Although, data from animal studies regarding toxicity with concurrent endocrine and radiation treatment, particularly in the form of radiation-induced pulmonary fibrosis, has also been mixed.[6,7]

Clinical studies have been conducted, but they have failed to conclusively demonstrate a detrimental effect with concurrent radiotherapy and endocrine therapy on breast cancer–specific outcomes or treatment-related toxicity. Indeed, studies looking at the timing of radiotherapy and aromatase inhibitors[8-15] or tamoxifen[16-20] found no difference in local or distant control, overall survival, skin toxicity, or radiation-related pneumonitis with the sequence of therapy. However, these data were largely derived from older, small, retrospective studies.

The paucity of high-quality data on this subject is reflected in the lack of definitive clinical practice guidelines, which frequently fail to address the issue, or if they do, are nonspecific and often leave the choice of when to start endocrine therapy to physician preference. Determining the optimum sequence of endocrine therapy and radiotherapy is important, however, as it may reduce practice variability and avoid unnecessary delays in initiating endocrine therapy, particularly for those at higher risk of recurrence. Additionally, concurrent therapy may help to streamline and potentially shorten the adjuvant treatment process. The following survey was performed to identify current practices with respect to the timing of adjuvant radiotherapy and endocrine therapy in Canada in addition to providing data to inform the design of a pragmatic clinical trial to address this important but as yet unanswered clinical question.

Methods

The survey was developed by clinicians and researchers with expertise in survey design, oncology, epidemiology, and knowledge translation. Important themes were identified, and survey questions were drafted and reviewed by members of the research team (Supplemental Appendix 1 in the online version). The survey was approved by the Ottawa Health Sciences Network research ethics board.

Survey

Physicians involved in the treatment of patients with early-stage breast cancer across Canada, particularly those involved in the initiation of adjuvant endocrine therapy, were approached to participate. A collection of publically available physician e-mail addresses that have been used in previous surveys of this type[21] was used to contact physicians for participation. The online survey was run through Google Forms, and physicians were also given the opportunity to complete paper-based surveys. Physicians were sent an information sheet and a link to the survey via e-mail 3 times over a 12-week period.

The survey was designed to evaluate: (1) institutional and personal practices regarding the timing of adjuvant endocrine therapy and radiotherapy, (2) opinions on the need for a clinical trial to compare concurrent versus sequential therapy and potential end points for such a trial, and (3) physicians' experience of endocrine therapy compliance.

Data Analysis

Data from the questions was input and analyzed using Microsoft Excel. Summative proportional data were generated, and free-text responses were collated.

Results

Study Population

Canadian physicians working in the field of oncology were surveyed between August and October 2017. The overall response rate was 30% (65/220). Respondents were predominantly medical (35/65, 54%) and radiation (28/65, 43%) oncologists. Physicians practiced in academic (teaching) hospitals with a cancer center (51/65, 79%), nonacademic (community) hospitals with a cancer center (10/65, 15%), academic hospitals without a cancer center (2/65, 3%), and nonacademic hospitals without a cancer center (2/65, 3%). The cohort covered a broad range of experience, with 57% in postresidency practice for more than 10 years [$\leq$ 5 years 14/65 (21%), 6 to 10 years 14/65 (21%), 11 to 20 years 20/65 (31%), and $>$ 20 years 17/75 (26%)].

Institutional Policies and Practices

Most respondents (54/65, 83%) identified medical oncologists as the group typically responsible for initiating endocrine therapy, while 11% (7/65) thought it varied between members of the

Table 1 Institutional Practices Regarding Initiation of Endocrine Therapy

Question	Options	Response (N = 65)
In your institution, who is typically responsible for initiating adjuvant endocrine therapy?	Medical oncologist	54 (83%)
	Radiation oncologist	1 (1%)
	Surgical oncologist	3 (5%)
	Varies	7 (11%)
When is endocrine therapy typically initiated at your institution?	Before radiation	8 (12%)
	During radiation	1 (2%)
	After radiation	33 (51%)
	Other	4 (6%)[a]
	Varies from physician to physician	19 (29%)[a]
Do you have an institutional protocol specifying timing of endocrine therapy and radiotherapy?	Don't know	6 (10%)
	No	53 (84%)
	Yes	4 (6%)
If yes, is your institutional policy?	Sequential	4 (100%)
	Concurrent	0

[a]A summary of the free text themes from the responses include (n): Depends on the preference of the radiation oncologist (7), medical oncologist (2) and/or patient (2); depends on the nature of the disease and risk of recurrence (7); depends on whether chemotherapy was provided (2); depends on the type of endocrine therapy planned (1).

Table 2 Personal Practice Regarding Initiation of Endocrine Therapy

Question	Options	Response (N = 65)
When do you typically prefer to start adjuvant endocrine therapy?	Before radiation	12 (18%)
	With radiation	2 (3%)
	After radiation	37 (57%)
	No preference	14 (22%)
Is there a reason for this?	No	7 (11%)
	Don't know	0
	Advised per clinical trials and/or other evidence based studies	8 (12%)
	Advised per treatment guidelines (eg, CCO, NCCN)	0
	Personal experience/practice (ie, just standard practice)	23 (36%)
	It's the way I was taught	4 (6%)
	Other; please explain	23 (35%)[a]
Are your recommendations affected by the risk of cancer recurrence? Tick all that apply.	No	33 (52%)
	Yes; for patients with more aggressive disease I recommend starting endocrine therapy sooner rather than waiting for completion of radiotherapy	29 (45%)
	Other	2 (3%)
Are you aware of any evidence-based treatment guidelines around the timing of endocrine therapy and radiotherapy?	No	44 (68%)
	Unsure	14 (21%)
	Yes	7 (11%)
If you answered yes above, please specify.	NCCN	1
	ASCO	1
	ESMO	0
	CCO	3
	BC Cancer Agency	2
	St Gallen	1
	Other	3
If starting endocrine therapy radiotherapy, when do you advise patients to start?	Immediately	12 (21%)
	Within 1-2 wk	28 (48%)
	Within 2-4 wk	13 (22%)
	After 4 wk	4 (7%)
	Varies	1 (2%)
Do you have any concerns regarding concurrent endocrine therapy and radiotherapy?	No	44 (68%)
	Yes	21 (32%)
If you answered yes above, please indicate (tick all that apply) whether these concerns relate to:	Reduced efficacy of endocrine therapy and subsequently, systemic control.	0
	Increased endocrine therapy adverse effects causing reduced tolerability.	13 (62%)
	Reduced compliance with endocrine therapy.	8 (38%)
	Reduced efficacy of radiotherapy and subsequently, locoregional control.	10 (48%)
	Increased radiation toxicity (eg, fatigue, radiation skin burn, lung fibrosis)	6 (29%)
	Increased clinical workload/responsibility for the radiation oncologist	1 (5%)
	Other	2 (10%)

Abbreviations: ASCO = American Society of Clinical Oncology; CCO = Cancer Care Ontario; ESMO = European Society of Medical Oncology; NCCN = National Comprehensive Cancer Network.
[a]A summary of the themes from the responses include (N): Concerns regarding endocrine therapy tolerance with over-lapping side-effects and implications for compliance (10), concerns regarding treatment related toxicity (6), depends on the nature of the disease and risk of recurrence (5), lack of conclusive data to guide treatment either way (5), concerns regarding treatment efficacy (4), concerns regarding workflow and efficiency (2), opinion that total duration of endocrine therapy is prolonged, so the exact timing does not matter (1), and depends on the preference of the radiation oncologist (1) or patient (1).

Table 3 Potential Clinical Trial Designs

Question	Options	Response (N = 65)
Do you think a trial looking at the timing of endocrine therapy relative to radiotherapy would help to standardize and improve patient care?	Yes	33 (51%)
	No	15 (23%)
	Don't know	17 (26%)
If such a study was to be performed, in which study arm would you prefer endocrine therapy be started?	a. Before radiation	24 (37%) [a, c]
	b. With radiation	14 (22%) [b, c]
	c. After radiation	13 (20%) [a, b, c]
	d. Don't know	4 (6%) [c]
		4 (6%) [d]
		3 (5%) [b]
		2 (3%) [a]
		1 (1%) [a, b]
If you selected after radiation, how long after completion of radiotherapy?	Immediately	7 (12%)
	Within 1-2 wk	26 (46%)
	Within 2-4 wk	19 (33%)
	After 4 wk	5 (9%)
	Other; please specify	0
What do you think the most important end point(s) of such a study should be?	Locoregional control/recurrence	38 (58%)
	Systemic control/recurrence	33 (51%)
	Endocrine therapy adverse effects/tolerability	37 (57%)
	Endocrine therapy compliance	40 (62%)
	Radiation toxicity (eg, fatigue, radiation skin burn, lung fibrosis)	41 (63%)
Do you think that standardizing the timing of adjuvant endocrine therapy will affect survival outcomes?	Yes	1 (1%)
	No	46 (71%)
	Unsure	18 (28%)

multidisciplinary team (Table 1). The majority of institutions (53/65, 84%) had no formal protocol in place specifying the preferred timing of endocrine therapy with respect to radiotherapy. However, for those who did report an institutional protocol (4/65, 6%), it always favored sequential therapy.

When asked what the standard timing of endocrine therapy and radiotherapy was within their institution, 51% (33/65) reported sequential treatment with endocrine therapy started after radiotherapy (Table 1). Fourteen percent stated endocrine therapy was started either before (8/64, 12%) or during (1/65, 2%) radiotherapy. The remaining respondents (23/65, 35%) stated that varied practices were seen in their institution. The free-text explanations for these practices stated that they were dependent on the radiation oncologist's preference (7/22, 32%), and to a lesser extent the medical oncologist's (2/22, 9%) and/or patient's preference (2/22, 9%). Others cited the risk of disease recurrence as a factor influencing when endocrine therapy was started (7/22, 32%), in addition to whether or not chemotherapy was provided (2/22, 9%) and the type of endocrine therapy planned (ie, tamoxifen vs. an aromatase inhibitor) (1/22, 5%) (Table 1).

Personal Practice

Regarding individual practice, 57% (37/65) of respondents preferred to start endocrine therapy after radiotherapy, while 21% preferred to start endocrine therapy either before (12/65, 18%) or during (2/65, 3%) radiotherapy. Twenty-two percent (14/65) had no preference (Table 2). When asked how soon after radiotherapy they would recommend starting endocrine therapy, clinicians responded as follows: immediately (12/65, 21%), within 1 to 2 weeks (28/65, 48%), within 2 to 4 weeks (13/65, 22%), after 4 weeks (4/65, 7%), and varies (1/65, 2%) (Table 2).

Overall, practice patterns were largely based on the physician's own clinical experience or how they were taught (27/65, 42%). However, 35% (23/65) of respondents cited other reasons guiding their decision regarding when to start endocrine therapy. The most common reason given was concern regarding the impact of concurrent endocrine therapy and radiotherapy on treatment tolerability and compliance (10/23, 48%), in addition to treatment-related toxicity (6/23, 26%). The preference of the patient was only cited by a single respondent (1/23, 4%). When asked if a higher risk of breast cancer recurrence influenced when endocrine therapy was provided, 52% (33/65) answered no, while 45% (29/65) said yes (Table 2).

The majority of respondents (68%, 44/65) were not aware of any evidence-based guidelines describing the optimum timing of endocrine therapy and radiotherapy in early breast cancer. Eleven percent (7/65) answered that they were aware of guidelines, and cited the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), Cancer Care Ontario (CCO), the BC Cancer Agency, and St Gallen (Table 2).

Table 4 Endocrine Therapy Compliance

Question	Options	Response (N = 65)
How often do you encounter problems with endocrine therapy compliance among your patients?	Never	0
	≤ 10% of patients	8 (12%)
	11%-25% of patients	35 (54%)
	26%-40% of patients	17 (26%)
	41%-75% of patients	3 (5%)
	> 75% of patients	1 (1%)
	Don't know	1 (2%)
Do you think the timing of starting endocrine therapy affects compliance with endocrine therapy?	Yes	19 (29%)
	No	17 (26%)
	Unsure	29 (45%)
When should patients ideally be seen to evaluate their tolerance, adverse effects, and compliance after starting adjuvant endocrine therapy?	Less than 1 mo after starting treatment	5 (8%)
	3 mo after starting treatment	55 (87%)
	6 mo after starting treatment	1 (2%)
	12 mo after starting treatment	0
	Does not matter	2 (3%)
Which of the following strategies do you think might help to increase compliance? Tick all that apply.	Greater physician contact to manage adverse effects and encourage compliance.	27 (43%)
	Great contact with health care providers when starting endocrine therapy (eg during daily visits for radiotherapy)	19 (30%)
	Increased patient education regarding the role and importance of endocrine therapy.	51 (81%)
	More patient education/support with management of treatment adverse effects.	49 (78%)
	Enrolment of patients in survivorship programs.	26 (42%)
	Shorter duration of total treatment course including surgery, radiation, endocrine therapy.	15 (24%)
	Other	4 (6%)

Although the majority of physicians (44/65, 68%) had no concerns regarding concurrent endocrine therapy and radiotherapy, 32% (21/65) did indicate some level of concern (Table 2). Of the 21 respondents who had concerns, the most common reasons cited were: increased endocrine therapy adverse effects causing reduced tolerability (13/21, 62%), reduced efficacy of radiotherapy (10/21, 48%), reduced compliance with endocrine therapy (8/21, 38%), and increased radiation toxicity (6/21, 29%) (Table 2).

Potential Clinical Trials

Fifty-one percent (33/65) of respondents thought that a pragmatic clinical trial looking at the timing of endocrine therapy relative to radiotherapy would help to standardize and improve patient care, while 17% (26/65) were unsure (Table 3). The preferred combination of study arms for such a trial included: endocrine therapy started before versus after radiotherapy (24/65, 37%), endocrine therapy started with versus after radiotherapy (14/65, 22%), or a 3-arm trial of endocrine therapy started before versus with versus after radiotherapy (13/65, 20%). For the postradiotherapy arms, starting endocrine therapy was recommended within 1 to 2 weeks of finishing radiotherapy (46%, 26/57) (Table 3).

When presented with a number of the most important end points for study, those selected were (in order of decreasing preference): radiation toxicity (41/65, 63%), endocrine therapy compliance and adherence (40/65, 62%), locoregional control (38/65, 58%), endocrine therapy adverse effects and tolerability (37/65, 57%), and systemic control (33/65, 51%). When asked whether or not the sequence of therapies would affect patient survival outcomes, most respondents (99%) where either unsure (18/65, 28%) or did not think that therapy sequence would affect survival (46/65, 71%) (Table 3).

Compliance With Endocrine Therapy

A series of questions was designed to explore physician experience with compliance. All respondents had encountered problems with compliance with endocrine therapy, with 54% (35/65) stating that it was an issue they encountered with 11% to 25% of patients, and 26% (17/65) in > 25% of their patients (Table 4). When asked to rank the factors that may be related to poor compliance, respondents selected (in order of decreasing importance): medication adverse effects (42/63, 67%), the prolonged duration of treatment overall (21/62, 34%), insufficient physician follow-up and encouragement (17/63, 27%), failure to understand the importance of endocrine therapy (18/62, 29%), and finally financial factors (15/63, 24%). Although 29% (19/65) of respondents thought the timing of endocrine therapy could affect compliance, the majority were either unsure (29/65, 45%) or thought it would not affect compliance (17/65, 26%) (Table 4). Potentially beneficial strategies

Table 5 Review of Select Clinical Practice Guidelines

Organization	Guideline Title	Study, Year	Sequencing of RT and ET Addressed?	Guidance Statement
ASCO	Update on Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer	Burstein, 2010[22]	Not directly	"The optimal timing and duration of endocrine treatment remains unresolved."
ASTRO	Radiotherapy for the Whole Breast	Smith, 2018[23]	No	None
BCCA	Breast Cancer Guidelines—Radiotherapy	BCCA, 2017[24]	Yes	"Adjuvant hormonal therapy may be commenced prior to or after radiotherapy."
CCO	Optimal Systemic Therapy for Early Female Breast Cancer	Eisen, 2014[25]	Not directly	"The optimal timing and duration of endocrine treatment remains unresolved."
	Adjuvant Systemic Therapy for Node-Negative Breast Cancer	Breast Cancer Disease Site Group, 2011[26]	No	None
	Breast Irradiation in Women with Early Stage Invasive Breast Cancer Following Breast Conserving Surgery	Breast Cancer Disease Site Group, 2016[27]	No	None
ESMO	Primary Breast Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-up	Senkus, 2015[28]	Yes	"Radiotherapy can be delivered during endocrine therapy."
NCCN	Breast Cancer Guidelines	NCCN, 2017[29]	Yes	"Available data suggests that sequential or concurrent ET with RT is acceptable."
St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer	15th Annual Meeting Consensus Guideline	Curigliano, 2017[30]	No	None
	14th Annual Meeting Consensus Guideline	Coates, 2015[31]	No	None
	13th Annual Meeting Consensus Guideline	Goldhirsch, 2013[32]	No	None

Abbreviations: ASCO = American Society of Clinical Oncology; ASTRO = American Society for Radiation Oncology; BCCA = British Columbia Cancer Agency; CCO = Cancer Care Ontario; ESMO = European Society of Clinical Oncology; ET = endocrine therapy; NCCN = National Comprehensive Cancer Network; RT = radiotherapy.

to increase compliance were identified as greater patient education regarding the importance of endocrine therapy (51/65, 81%), and greater patient education and support with respect to the management of treatment adverse effects (49/65, 78%) (Table 4).

Discussion

Despite the large numbers of breast cancer patients receiving adjuvant endocrine therapy and radiotherapy, uncertainty remains regarding the optimum sequence of these therapies. It would appear from clinical practice and the results of this survey that the majority of patients commence endocrine therapy after the completion of radiotherapy.

Defining the optimum timing of adjuvant endocrine therapy and radiotherapy would help to ensure all patients receive treatments in a sequence that maximizes clinical efficacy and outcomes while minimizing the risk of toxicity and adverse effects. Furthermore, it would help to avoid unnecessary delays in the commencement of endocrine therapy, particularly for patients at higher risk for recurrence. It may even help to expedite the overall treatment process and reduce the number of required specialist follow-up appointments if treatment is started concurrently. Finally, starting endocrine therapy concurrently with radiation, when patients are already receiving close follow-up and monitoring, may help increase compliance by providing them with greater support at the outset of treatment when adverse effects may be greatest and discontinuation rates can be high.

To obtain real-world data on current clinical practices, we conducted a survey of Canadian physicians with responsibility for the administration of radiation and/or endocrine therapy to women with early-stage breast cancer. The aim was to identify common practice patterns and the rationale behind them. In addition, we wished to assess potential interest in and design of a pragmatic clinical trial on the subject. Our results showed that although more than half of physicians initiated endocrine therapy after the completion of radiotherapy, the remainder administered treatment concurrently (with endocrine therapy starting either before or during radiotherapy), or stated that their practice varied. The variability in clinical practice observed in this survey likely stems from the lack of definitive clinical guidance on the subject, with the decision often left up to the personal experience and/or preference of the treating physician.

It is of interest that 11% (7/65) of respondents stated that they were aware of evidence-based guidelines. We reviewed several key regional and international clinical practice guidelines on the management of early breast cancer (Table 5), and we found that the issue was frequently not addressed,[23,26,27,30-32] or if it was, the guidance was vague and nonspecific.[22,24,25,28,29] For example, CCO[25] and ASCO[22] state, "The optimal timing and duration of endocrine treatment remains unresolved." while the NCCN states, "Available data suggests that sequential or concurrent ET with RT is acceptable."[29]

Given this lack of specific guidance, it was also interesting that many physicians cite the potential for worsening of endocrine therapy adverse effects with concurrent endocrine therapy and radiotherapy when this has not been explored in any clinical studies that we are aware of. Furthermore, the potential for worsening of radiation toxicity with concurrent therapy has not been definitively demonstrated in previous clinical studies.[8-20]

Overall, physicians were in agreement with the need to standardize clinical practice with the aim of improving patient care, with most stating that they thought a pragmatic clinical trial designed to determine the optimum timing of adjuvant endocrine therapy and radiotherapy was warranted. The key study arms for such a trial were identified by the majority (37%) of respondents as adjuvant endocrine therapy commenced before, compared to after, after radiotherapy. Furthermore, they highlighted important end points for such a trial as the incidence of radiation toxicity and the ability to tolerate and persist with adjuvant endocrine therapy. These results are important because the current ongoing trials assessing the sequence of adjuvant tamoxifen (Concurrent Versus Sequential Tamoxifen With Radiotherapy in Breast Cancer Patients; CONSENT) (ClinicalTrials.gov, NCT00896155) and aromatase inhibitors (STARS) with radiation in breast cancer do not address physician concerns regarding patient ability to tolerate and persist with endocrine therapy in the setting of overlapping toxicities.

Our study has several important limitations. These include a small sample size composed of physicians from a single country, who are predominantly from institutions with an academic affiliation. However, the data obtained from such in-depth questions will help investigators design appropriate trials to answer the ongoing questions that both physicians and patients have. In addition, this is the only survey we are aware of that has asked questions specifically about the timing of endocrine therapy and radiotherapy. Future surveys involving patients are also needed.

We also did not explore thoughts and practices regarding the timing of endocrine therapy in the setting of hypofractionated adjuvant breast radiation, which is becoming increasingly common for selected patients.[33] However, to facilitate a shorter duration of treatment, patients receive a higher daily radiation dose. A potential concern here would be increased radiation toxicity with concurrent endocrine therapy, particularly aromatase inhibitors, which are thought to enhance radiosensitivity. We identified 2 prospective studies looking at concurrent hypofractionated radiotherapy and either tamoxifen[17] or letrozole.[15] These studies found no difference in skin or pulmonary toxicity,[15,17] local or distant control,[17] or overall survival[17] with the sequence of therapies. However, the studies were small and are only available in abstract form. The impact of endocrine therapy timing and fractionated radiation on outcomes, particularly toxicity, is thus an important question that should be addressed in future trials.

In conclusion, this survey demonstrated that clinical equipoise exists as to the optimum timing of adjuvant endocrine therapy and radiotherapy, leading to significant variability in patient care. Given the importance of adjuvant radiotherapy and endocrine therapy in reducing the risk of locoregional and systemic breast cancer recurrence, respectively, it is critical that it is provided in the optimal sequence, and Canadian physicians are in agreement with this. We are currently designing a pragmatic clinical trial to address the concerns raised by physicians in the survey with the aim of improving the efficacy and quality of patient care.

Clinical Practice Points

- The optimal timing of adjuvant endocrine therapy relative to RT is unknown.
- This multicenter survey of oncologists highlights variability in the timing of endocrine therapy and RT, with decisions being based largely on physician preference.
- Adequately powered clinical trials are required to guide clinical practice in this area.

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Disclosure

The authors have stated that they have no conflict of interest.

Supplemental Data

Supplemental appendix accompanying this article can be found in the online version at https://doi.org/10.1016/j.clbc.2018.08.012.

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