Original article

Annals of Oncology 15: 1267–1273, 2004
DOI: 10.1093/annonc/mdh303

The difference between study recommendations, stated policy, and actual practice in a clinical trial

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Received 15 March 2004; accepted 18 March 2004

Background: We determined whether physicians involved in a clinical trial adhere to the study recommendations or the stated policy of their treatment centre with respect to the administration of boost radiation after breast conserving surgery.

Patients and methods: Boost radiation treatment policy was determined by survey at 25 oncology centres involved in a randomised trial of breast or breast plus nodal radiation in Canada. Actual practice was compared with stated policy and study recommendations.

Results: Among 248 subjects, 201 (81%) were treated according to stated policy [$\kappa = 0.40$, 95% confidence intervals (CI) 0.27–0.52; $P<0.0001$], indicating only a fair to moderate agreement between stated and actual practice, while 232 (94%) were treated according to study recommendations ($\kappa = 0.59$, 95% CI 0.40–0.77; $P<0.0001$), indicating moderate to near substantial agreement between study recommendations and actual practice ($P = 0.88$ for z-test of difference). In a multivariate analysis, subjects who had invasive disease at a resection margin were more likely to get a boost than those with margins clear of invasive tumour by 2 mm [odds ratio (OR) 49, 95% CI 7.6–322; $P<0.0001$].

Conclusions: Physicians appear compliant with study recommendations for a non-randomised manoeuvre in a clinical trial, possibly at the expense of compliance with stated local policy. Clinical trial protocols should incorporate standard practice.

Key words: clinical trials, data collection, radiotherapy

Introduction

Surveys of physicians have been used to assess a variety of practice patterns [1–7], but few studies have compared the stated practice of physicians with actual practice assessment. Research assessing compliance with screening recommendations has found that physicians tend to significantly overestimate their own compliance [8, 9]. In fact, physician self assessment can be less accurate than patient surveys of the same physicians' practices [10]. Lomas et al. found that even when physicians appeared to agree with guidelines for Caesarian section, they had poor knowledge of the content of those guidelines [11]. Furthermore, while physicians reported that they performed fewer Caesarian sections after guidelines were issued, the true procedural frequency changed very little. It thus appears that surveys of practice patterns may not reflect real practice and that compliance with recommended practice may frequently be suboptimal.

The ability to predict practice patterns is important to the conduct of clinical trials. Accurate estimations of accrual rates are required to assess trial timelines and feasibility. These estimates are usually based on both previous trial experience and physicians' assessment of their practice patterns. Physicians' assessment of their practice patterns may also be used as a basis for defining standard therapy in a trial and in order to set specific study treatment parameters. Inaccurate assessment of current physician practice or the subsequent failure of physicians to follow the treatment recommendations of a trial protocol can jeopardise modern resource-intensive studies.

The National Cancer Institute of Canada Clinical Trials Group (NCIC–CTG) is currently leading a trial, MA.20, to assess the benefit of regional radiation in women treated with breast conserving surgery for early breast cancer [12]. Substantial evidence exists to support the use of breast irradiation after tumour resection [13–16] and there is recent evidence that additional radiation to the primary tumour site, a 'radiation boost', can decrease local recurrence [17, 18]. As the role of regional nodal radiation therapy is more controversial, trial MA.20 will randomise subjects between radiation to the breast alone or radiation to the breast plus regional nodes.

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When the trial was originally designed, there was a lack of definitive evidence to support the use of radiation boost in patients with clear margins of excision following breast conserving surgery; a conservative approach was taken and it was recommended that only subjects who had tumours focally involving the resection margins receive radiation boost. The protocol compensated for any potential regional practice variations by stratifying accrual by centre. In October of 2001, the centres involved in the MA.20 trial were surveyed to assess centre policies and to reinforce awareness that a consistent practice was needed within each centre. This report addresses the question of whether physicians will comply with a non-randomised treatment manoeuvre specified in a clinical trial when they may have a centre specific policy that differs from protocol specifications. Factors associated with use of a boost are described.

Patients and methods

Survey

In October 2001, the MA.20 trial committee surveyed 25 Canadian centres to assess boost radiation policy for breast cancer (Table 1). The survey was designed to be easily completed and requested information as to whether the site had a policy on boosting, asked how a positive margin was defined, inquired about what proximity of invasive carcinoma or ductal carcinoma *in situ* (DCIS) to a margin would precipitate boost, and inquired about age and dose policies.

Trial

On 9 March 2000, NCIC–CTG trial MA.20 began accruing subjects with node-positive or high-risk node-negative breast cancer treated with breast conserving surgery and axillary dissection. The study was approved by ethics review boards at all centres and all subjects signed informed consent. All patients in the trial were to receive chemotherapy and/or tamoxifen. Subjects were randomised between radiation to the breast alone or breast plus regional lymph node bearing areas. Node-negative patients were eligible if they had tumour size ≥5 cm, or ≥2 cm with <10 nodes resected and either estrogen receptor negativity, grade 3 histology [19] or lymphovascular invasion.

Patients on the control arm were treated with a tangent pair to the breast with a dose of 50 Gy in 25 fractions, 5 days each week. Patients randomised to receive regional nodal radiation were treated at the same dose and fractionation but with fields that also included ipsilateral internal mammary nodes in the first to third interspaces, the supraclavicular nodes, and the apex (level III) of the axilla generally using a modified wide-tangent technique [20]. Patients with four or more nodes involved or <10 nodes resected had the regional nodal fields extended to include the full axilla.

Re-excision of the breast was recommended if there was gross or diffuse disease at margins. In both treatment arms, a radiation boost of 10 Gy in five fractions was recommended for patients with focally positive resection margins postlumpectomy. An amendment dated 8 January 2001 confirmed the boost indication for patients with focally positive margins and requested that each centre participating in the study have a policy for the use of a boost. A trial amendment of 31 August 2001 added the suggestion that a radiation boost might also be used for close margins (invasive carcinoma or DCIS within 2 mm of a marked margin).

Table 1. Survey results

Question	*n* (%)
Do you have a policy regarding indication for a boost dose of radiation?	
Yes	20 (80)
No	5 (20)
How do you define a positive margin?[a]	
Tumour cells at inked margin	15 (75)
Tumour cells <1 mm from inked margin	1 (5)
Tumour cells <2 mm from inked margin	4 (20)
Do you always boost for a positive margin?[a] (yes response)	20 (100)
Do you give a radiation boost if there is 'invasive tumour':[a]	
At the inked margin	20 (100)
Within 1 mm	18 (90)
1 to <2 mm	14 (70)
2 to <3 mm	5 (25)
3 to <5 mm	2 (10)
Do you give a boost if there is 'DCIS/LCIS':	
At the inked margin	19 (95)
Within 1 mm	17 (85)
1 to <2 mm	13 (65)
2 to <3 mm	6 (30)
3 to <5 mm	3 (15)
Do you base the use of boost on patient age?[a] (yes response)	8 (40)
If yes, what age is an indication for boost?[a]	
≤40 years	3
≤50 years	4
<60 years	1
What do you prescribe to a positive margin?[a]	
Median	10 Gy
Range	10–16 Gy
If delivering a 10 Gy boost, where is the prescription point?[a]	
Median	100% isodose
Range	80–100% isodose

[a]Answers account only for those sites with a group policy.
DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*.

Actual practice data collection

Actual practice of the surveyed radiation oncologists was determined by acquiring radiation treatment data from the clinical trial database maintained by the NCIC–CTG in Kingston, Ontario, Canada. Patient data were collected from MA.20 trial records from the date of study opening up to and including any patient who underwent their first radiation fraction on or before 8 November 2001. This latter date was chosen as it was the date of publication of the European Organisation for Research and Treatment of Cancer (EORTC) paper that demonstrated improved local control for women receiving boost radiation to the tumour bed after breast irradiation [17]. For each patient, data were abstracted on patient age, the pathological characteristics of the malignancy, the status of the resection margins with respect to either invasive or *in situ* disease, randomisation arm, treating

Table 2. Patient characteristics

Characteristic	*n* (%)
Age (years)	
Median	53.0
Range	30.2-80.7
T stage	
T1	136 (55)
T2	106 (43)
T3	6 (2)
T4	0
Tumour grade	
I	43 (17)
II	94 (38)
III	111 (45)
Estrogen receptor status	
Positive	141 (57)
Negative	54 (22)
Unknown	53 (21)
Progesterone receptor status	
Positive	85 (34)
Negative	45 (18)
Unknown	118 (48)
Lymph node status	
Positive	219 (88)
Negative	29 (12)
Invasive tumour margin status	
Positive	9 (4)
Negative, <1 mm from margin	23 (9)
Negative, 1 to <2 mm from margin	40 (16)
Negative, 2 to <3 mm from margin	20 (8)
Negative, 3 to <5 mm from margin	28 (11)
Negative, ≥5 mm from margin	59 (24)
Negative, distance not specified	69 (28)
Unknown margin	0 (0)
DCIS/LCIS tumour margin status[a]	
No DCIS/LCIS	46 (19)
DCIS/LCIS not mentioned	27 (11)
Positive margin	5 (2)
Negative, <1 mm from margin	7 (3)
Negative, 1 to <2 mm from margin	11 (4)
Negative, 2 to <3 mm from margin	6 (2)
Negative, 3 to <5 mm from margin	1 (0.4)
Negative, ≥5 mm from margin	8 (3)
Unknown margin	137 (55)
Adjuvant chemotherapy	
Anthracycline based chemotherapy	194 (78)
Non-anthracycline chemotherapy	33 (13)
No chemotherapy	21 (8)
Adjuvant tamoxifen	
Yes	136 (55)
No	112 (45)
Adjuvant radiation	
Local	125 (50)
Local plus regional	123 (50)
Use of boost radiation	
Yes	25 (10)
No	223 (90)
Boost dose	
4 Gy	1 (4)
10 Gy	23 (92)
Unspecified	1 (4)

Percentage totals do not sum to 100 for reasons of rounding.
[a]The presence of DCIS/LCIS at a margin was only collected as a variable in the trial database after 1 October 2001.
DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*; T, tumour.

centre and radiation oncologist, and whether a boost was given. If a boost was used, the prescribed dose and prescription point were abstracted.

Individual patient treatment was compared to the declared policy of the treating centre for the conditions of that patient. For centres that did not have policies, the individual who completed the form was asked to describe his or her own policy, and this was compared with the patients that he or she treated. A patient was considered to have been treated in compliance with centre policy if she received boost radiotherapy (RT) when there was a centre-defined indication for a boost or if she did not receive boost RT when there was no centre-defined indication for a boost.

Individual patient treatment was also compared to study protocol recommendations. Until 31 August 2001, this meant that treatment was in compliance if resection margins were focally positive with invasive tumour or DCIS and the patient received boost radiation or if margins were negative and no boost was given. After 31 August 2001, the date of the relevant amendment, for patients with negative resection margins but with tumour or DCIS within 2 mm of a marked margin, treatment was also in compliance regardless of whether radiation boost was administered.

Statistical analysis

The κ statistic and associated 95% confidence interval (CI) were used to describe the agreement relationship between actual practice and stated policy as well as the relationship between actual practice and study recommendations (>0.8, near perfect agreement; 0.61–0.8, substantial agreement; 0.41–0.6, moderate agreement; 0.21–0.4, fair agreement; >0–0.2, slight agreement; 0, no agreement or random association) [21]. The *P* value of the exact test for the hypothesis that κ equals zero was also calculated. The equality of two κs was compared using the *z*-test [22].

The following variables were included in the logistic regression analyses to identify factors which might induce oncologists to add boost radiation: age (as a continuous variable), tumour stage (as an ordinal categorical variable with three levels: T1, T2 and T3), tumour grade (as an ordinal categorical variable with three levels: 1, 2 and 3), estrogen receptor status (as two binary variables: positive versus negative

and positive versus unknown), nodal status (positive versus negative), adjuvant chemotherapy (administered versus not), adjuvant hormonal therapy (administered versus not), the use of breast versus breast plus nodal radiation, and the resection margin status (categorised as invasive tumour present at margin, tumour <2 mm from margin, tumour = 2 mm from margin, and distance to margin unknown but no invasive tumour at the resection margin). All statistical analyses were performed using SAS software (SAS Institute, Inc., Cary, North Carolina).

Results

Survey

All 25 surveyed sites returned the survey (Table 1) and 20 centres stated that their institution had a policy on administering boost. Four sites accrued no patients, including one site that did not have a group policy. Most centres with a group policy (75%) described a positive margin as indicating the presence of tumour cells at the invasive margin, with the remainder indicating that cells within 1 or 2 mm defined a positive margin. All centres indicated that they would give a boost if a positive margin were present. Eight centres with a group policy (40%) used age criteria when deciding on boost therapy. Sixteen centres (80%) used a 10 Gy boost dose and 11 centres (55%) exclusively recommended a 100% isodose prescription point.

Patients

A total of 250 patients received their first radiation fraction on or before 8 November 2001. Two patients were excluded because they were treated at a centre that had an individual physician policy but were not treated by the physician responding to the survey. Of the 248 patients included in the analysis, 225 were treated at centres that declared a group policy and 23 were treated at centres with policy determined by individual physicians.

Characteristics of the 248 patients are shown in Table 2. The median age was 53.0 years (range 30.2–80.7). Most patients (98%) had T stage 1 or 2 tumours, 45% had high grade disease and 57% were recorded as having estrogen receptor-positive tumours. As this study focused on patients at higher risk for locoregional failure, 88% had lymph node involvement. Only 4% of patients had a resection margin involved with invasive tumour. Information on the status of DCIS/LCIS was sparse, in part because the data were not collected routinely until 1 October 2001.

As regards adjuvant therapy, 91% received chemotherapy and half of the patients (55%) received tamoxifen. As it was the randomised variable, half of the patients (50%) received both local and regional radiation. A boost was given to only 10% of subjects, typically at a dose of 10 Gy.

Adherence to centre policy

Of 248 patients whose treatment was compared with declared policy, 201 (81%) were considered to have been treated according to stated centre policy (Table 3). This results in a κ of 0.40 (95% CI 0.27–0.52; $P<0.0001$), indicating only a fair to moderate agreement between stated policy and actual practice. In 107 of 248 subjects (43%), insufficient data precluded declaring noncompliance with centre policy, and so these subjects were assumed to have received treatment in accordance with policy. The missing data related to inadequate reporting of DCIS/LCIS status in 67 cases, inadequate information regarding invasive tumour margin in 23 instances, or both in a further 17 cases. If these 107 patients are excluded from the analysis, the resulting κ is 0.30 (95% CI 0.17–0.43; $P<0.0001$).

Table 3. Actual practice compared to policy

In practice used a boost	Policy indicates boost, *n* (%)		
	Yes	No	Total
Yes	22 (9)	3 (1)	25 (10)
No	44 (18)	179 (72)	223 (90)
Total	66 (27)	182 (73)	248 (100)

Subgroup analyses achieved similar results to the overall analysis. When only subjects treated under group policy were analysed, 193 of 225 (86%) were treated according to policy, resulting in a κ value of 0.41 (95% CI 0.28–0.55; $P<0.0001$). Among 23 patients treated in four centres without a group policy, 18 (78%) were treated according to policy ($\kappa = 0.23$, 95% CI −0.15–0.61; $P = 0.26$). Comparing these two κ values, no significant difference was found. However, this comparison must be interpreted cautiously given the wide confidence intervals around the smaller subgroup.

Compared to stated policy, 44 patients (18%) were not treated when policy would dictate that they should be treated with a boost (Table 3). In contrast, three patients (1%) were treated with a radiation boost when policy would dictate that they should not be treated. Variation from centre-stated policy in the 44 untreated patients was due to failure to follow the invasive tumour margin policy (30 patients), the DCIS/LCIS margin policy (five patients), both margin criteria (seven cases) and stated age policy (two patients) (Table 4). In the cases of undertreatment relative to age, both subjects were <40 years of age and had clear margins but were treated at a centre where every patient <40 years of age, regardless of margin, was offered a boost. This strict age criterion was verified with the centre. At no other site was age interpreted in this strict sense, either for patients under or over stated age criteria. The three subjects who received a boost against centre policy all had clear margins.

Of 25 patients who did receive boost radiation, 14 (56%) were treated according to stated boost method, inadequate treatment detail was available in six (24%) cases, and in five (20%) instances boost radiation was not given in accordance with stated method. Of the latter, four subjects received a different dose and one subject received a different prescription point.

Table 4. Deviations from policy

Deviation from policy	*n* (%) (*n* = 47)
Among subjects not receiving boost radiation	44 (94)
Not treated: 'invasive disease' policy indicated boost	37 (79)
Invasive disease at margin	2 (4)
Invasive disease close to margin	35 (74)
Not treated: DCIS/LCIS policy indicated boost	12 (26)
DCIS/LCIS at margin	3 (6)
DCIS/LCIS close to margin	9 (19)
Not treated: policy indicated boost if age <40 years	2 (4)
Among subjects receiving boost radiation	3 (6)
Treated: 'invasive disease' policy indicated no boost	3 (6)
Treated: DCIS/LCIS policy indicated no boost	2 (4)
Treated: policy indicated no boost for age	0

Percentages do not total 100 as more than one violation occurred for nine subjects.
DCIS, ductal carcinoma *in situ*; LCIS lobular carcinoma *in situ*.

Adherence to study recommendations

Of the 248 patients whose treatment was assessed, 232 (94%) were considered to have been treated according to study recommendations (Table 5). This results in a κ of 0.59 (95% CI 0.40–0.77; $P<0.0001$), indicating moderate to near substantial agreement between study recommendations and actual practice.

Prior to the 31 August 2001 study amendment, 207 subjects were treated. Nine received boost for positive margins according to study recommendations, while four did not receive boost despite positive margins. While 194 subjects had negative margins, 12 of them still received a boost; nine of these were treated according to centre-specific policy while three were treated despite adequate margins according to centre policy. After 31 August 2001, when the study allowed a boost for close margins, all 41 subjects were treated in accordance with study recommendations, with four receiving boost radiation.

Study recommendations for the boost method were a dose of 10 Gy with a prescription point at 90–100% isodose. Of the 25 subjects who received boost radiation, 15 were treated in this manner (60%), two were not (8%) and inadequate information was available for eight (32%).

When the κ value of practice versus centre policy (0.40, 95% CI 0.27–0.52) is compared to the κ value of practice versus study recommendations (0.59, 95% CI 0.40–0.77), the *P* value for the *z*-test for equality is 0.88.

Table 5. Actual practice compared to protocol recommendation

In practice used a boost	Protocol indicates boost, *n* (%)		
	Yes	No	Total
Yes	13 (5)	12 (5)	25 (10)
No	4 (2)	219 (88)	223 (90)
Total	17 (7)	231 (93)	248 (100)

Factors influencing the decision to give boost radiation

In the regression analysis of 248 patients, patients with invasive tumour at the resection margin were much more likely to receive boost than those with a margin clear by ≥2 mm (OR 49, 95% CI 7.6–322; $P<0.0001$) (Table 6). Subjects with invasive tumour <2 mm from margin may have been more likely to receive boost radiation than those with tumour = 2 mm from margin (OR 2.46, 95% CI 0.86–7.09; $P = 0.09$). Other variables were non-significant. The analysis did not change if anthracycline-based adjuvant chemotherapy was compared with non-anthracycline-based adjuvant chemotherapy.

Discussion

There is considerable evidence suggesting that physicians overestimate their compliance with practice recommendations [8–11]. These studies were based on comparisons of physician practice with the recommendations of national societies. Our data add another dimension to the compliance issue by assessing compliance with both treatment centre policy and research protocol recommendations in the setting of a clinical trial.

Using a survey conducted during a clinical trial, we were able to determine the actual use of radiation boost as compared with treatment centre policy and research protocol recommendations. We found that 47 of 248 study patients (19%) were not treated in accordance with declared centre policies regarding the use of boost radiation therapy. This corresponds to a κ value of 0.40, indicating only a fair to moderate agreement between local policy and practice. In fact, given that we assumed compliance in 107 instances in which there was inadequate information for certainty, our results are likely an overestimate of the true concordance between policy and practice. If these patients are excluded, the agreement between practice and policy results in a κ of only 0.30.

When comparing actual practice to study recommendations, only 16 patients (6%) were not treated according to protocol recommendations. The resulting κ of 0.59 indicates moderate to near substantial agreement. While this result appears superior to the agreement between centre policy and practice ($\kappa = 0.40$), the *z*-test did not reach statistical significance, possibly because of the limited sample size. Compliance with the trial recommendations was likely improved to some extent by the 31 August 2001 amendment, which extended indications for a boost to subjects with close margins (tumour or DCIS/LCIS within 2 mm of a resection margin).

Several factors may account for the disagreement between local policy and actual practice. Most importantly, the physicians involved in this clinical trial may have felt obligated to follow the protocol recommendations regarding boost radiation, and these recommendations were seldom in complete agreement with centre policy. There may also be disagreement

Table 6. Logistic regression analysis of factors influencing the decision to give boost

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (increase per year)	0.98 (0.94–1.02)	0.33	0.97 (0.92–1.02)	0.21
Tumour stage (II versus I)	1.02 (0.48–2.16)	0.97	1.11 (0.42–2.98)	0.83
Nuclear grade (increase per grade)	1.10 (0.62–1.94)	0.74	1.02 (0.48–2.16)	0.97
Estrogen receptor negative versus positive	1.14 (0.41–3.13)	0.81	0.99 (0.24–4.17)	0.99
Invasive tumour proximity to margin				
Positive versus ≥2 mm from margin	50.5 (8.79–290)	<0.001	49.4 (7.55–323)	<0.0001
<2 mm[a] versus ≥2 mm from margin	2.45 (0.86–6.95)	0.09	2.46 (0.86–7.09)	0.09
Unknown[a] versus ≥2 mm from margin	0.43 (0.09–2.14)	0.30	0.44 (0.09–2.20)	0.32
Lymph node positive versus negative	1.58 (0.35–7.1)	0.55	1.88 (0.31–11.49)	0.50
Local versus local plus regional	2.26 (0.94–5.46)	0.07	1.29 (0.47–3.53)	0.63
Radiation therapy				
Chemotherapy administered	0.71 (0.19–2.67)	0.61	0.43 (0.07–2.57)	0.36
Hormonal therapy administered	0.84 (0.35–2.03)	0.70	0.94 (0.28–3.11)	0.91

[a]But not present at resection margin.

CI, confidence interval; OR, odds ratio of receiving boost.

on optimal practice, particularly when the literature is underdeveloped, and this may have hindered compliance with both local policy and study recommendations [23]. Physicians may feel that specific treatment recommendations infringe upon physician autonomy [24] or they may not be adequately knowledgeable about recommended standards [11]. Finally, practice may be tailored based on other unspecified factors, such as performance status, comorbidity and patient preference.

Although our study could not account for all factors, we undertook a logistic regression analysis to determine whether known variables might have influenced the decision to give boost radiation. On multivariate analysis, subjects with invasive disease at a resection margin were far more likely to get a boost than those with margins clear of invasive tumour by ≥ 2 mm (OR 49, 95% CI 7.6–322; $P<0.0001$). Interestingly, subjects with resection margins clear by <2 mm had only a trend toward more boost therapy than those with margins clear by ≥ 2 mm (OR 2.46; $P = 0.09$), in apparent contradiction to survey results from 70% of centres that suggested patients with close margins should receive boost radiation. This discrepancy may have been the result of physicians following the study recommendations, whereby prior to the 13 August 2001 amendment, only subjects with focally positive margins were to undergo boost radiation. Patient age, adjuvant systemic therapy, randomisation arm and tumour characteristics other than margin status were not related to use of a boost.

A potential criticism of the current study is that it is not certain that the policy recorded on the survey represents the actual policy of each centre as applied to trial patients. However, the survey and accompanying cover letter were explicit in this regard. Furthermore, in examining the subset of 23 patients treated in centres without a group policy, we found κ similar to or lower than for the overall group ($\kappa = 0.23$). While this suggests that physician reporting of personal policy is no more accurate with respect to practice than is reporting of group policy (difference between κs not significant), the wide confidence limits around the subset test value preclude a definitive conclusion. Finally, the policy survey was distributed near the end of our data collection period. Although this 20 month period was relatively short, presentation of the EORTC study findings [17] at scientific meetings may have led to some evolution of policies over the period.

When planning clinical trials, accurate assessment of current treatment policies and habits is critical. Trial treatment parameters that reflect common current practice are most likely to optimise recruitment to a study and maximise compliance. When uncertainty exists about existing practice, surveys or practice audits may help to determine practice patterns. Multicentre studies may need to accommodate varying local practices when clinical standards are less clear. In addition, new data may result in the evolution of certain aspects of therapy during a given study. In the MA.20 study, the desire and policy of many physicians to boost subjects with close margins was taken into account with the 31 August 2001 study amendment. During the subsequent post-amendment period assessed by our study, all 41 subjects were treated in compliance with the study protocol.

Our study does not allow the assessment of pre-trial boost practice compared with centre policy. Previous studies have suggested that compliance with guidelines is suboptimal, and that this is even the case when physicians themselves have had input into the guidelines, as might be expected for the policy of an individual cancer centre [25, 26]. However, our study does suggest that in the setting of uncertain data regarding best practice, physicians involved in a clinical trial are likely to follow study treatment recommendations, possibly at the expense

of compliance with centre policies. Good compliance with the clinical trial protocol even when not consistent with centre policy may suggest ways to improve compliance with clinical practice guidelines in general. Clearly defining the target population that should undergo the procedure, describing the procedure in detail and indicating that practices will be reviewed all may facilitate compliance. Other factors may also be at work: physicians and patients that participate in research protocols may be more inclined to conform to practice guidelines.

Implementing a real-time review process may be another method by which to ensure high levels of compliance with intended practice. In the MA.20 trial, a real-time review process is employed to improve compliance with mandated radiation treatment parameters. To date, while 17% of initial radiation treatment plans had a major protocol violation, this number fell to 3% after real-time review (M. Valsangkar-Smyth, unpublished data). Our data suggest physicians maintain a good degree of compliance with study recommendations for a non-randomised manoeuvre in a clinical trial, while a lesser degree of compliance is kept with centre-specific policy. The compliance with trial recommendations is unlike the poor compliance with general guidelines as assessed by other studies [8–11]. It also appears that compliance may be improved when treatment recommendations are in line with each centre's practice policy. Accurate methods to incorporate current practice into study protocols and audits of non-randomised interventions should be considered when planning and implementing clinical trials.

Acknowledgements

We thank Monica Valsangkar-Smyth and Eric Bacon for assistance with the database of the National Cancer Institute of Canada Clinical Trials Group. J.R.G. was supported by the National Cancer Institute of Canada, Clinical Trials Group/ AstraZeneca Clinical Research Fellowship.

References

1. Hill LD, Erickson K, Holzman GB et al. Practice trends in outpatient obstetrics and gynecology: findings of the Collaborative Ambulatory Research Network, 1995-2000. Obstet Gynecol Surv 2001; 56: 505–516.
2. Ehresmann KR, Mills WA, Loewenson PR, Moore KA. Attitudes and practices regarding varicella vaccination among physicians in Minnesota: implications for public health and provider education. Am J Public Health 2000; 90: 1917–1920.
3. Power ML, Holzman GB, Schulkin J. Knowledge and clinical practice regarding folic acid among obstetrician-gynecologists. Obstet Gynecol 2000; 95: 895–898.
4. Scott I, Heyworth R, Fairweather P. The use of evidence-based medicine in the practice of consultant physicians. Results of a questionnaire survey. Aust N Z J Med 2000; 30: 319–326.
5. Valentini M, Mari E, Belfiglio M, Nicolucci A. Is adjuvant tamoxifen used optimally in the treatment of breast cancer? Results of an Italian survey. Ann Oncol 1999; 10: 789–793.
6. Wong T, Foote EF, Lefavour GS et al. Physician knowledge and practice patterns relating to diabetic nephropathy. J Am Pharm Assoc 1999; 39: 785–790.
7. Barrison AF, Smith C, Oviedo J et al. Colorectal cancer screening and familial risk: a survey of internal medicine residents' knowledge and practice patterns. Am J Gastroenterol 2003; 98: 1410–1416.
8. Zack DL, DiBalse JK, Quigley EM, Roy HK. Colorectal cancer screening compliance by medicine residents: perceived and actual. Am J Gastroenterol 2001; 96: 3004–3008.
9. Saver BG, Taylor TR, Treadwell JR, Cole WG. Do physicians do as they say? The case of mammography. Arch Fam Med 1997; 6: 543–548.
10. Montano DE, Phillips WR. Cancer screening by primary care physicians: a comparison of rates obtained from physician self-report, patient survey and chart audit. Am J Public Health 1995; 85: 795–800.
11. Lomas J, Anderson GM, Domnick-Pierre K et al. Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. N Engl J Med 1989; 321: 1306–1311.
12. Olivotto IA, Chua B, Elliott EA et al. A clinical trial of breast radiation therapy versus breast plus regional radiation therapy in early-stage breast cancer: the MA20 trial. Clin Breast Cancer 2003; 4: 361–363.
13. Early Breast Cancer Trialists' Collaborative Group. Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials. Lancet 2000; 355: 1757–1770.
14. The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Canadian Association of Radiation Oncologists. Breast Radiotherapy After Breast-Conserving Surgery. CMAJ 1998; 158 (Suppl 3): S35–S42.
15. Fisher B, Anderson S, Bryant J et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347: 1233–1241.
16. Veronesi U, Cascinelli N, Mariani L et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227.
17. Bartelink H, Horiot JC, Poortmans P et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. N Engl J Med 2001; 345: 1378–1387.
18. Romestaing P, Lehingue Y, Carrie C et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997; 15: 963–968.
19. Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991; 19: 403–410.
20. Marks LB, Hebert ME, Bentel G et al. To treat or not to treat the internal mammary nodes: a possible compromise. Int J Radiat Oncol Biol Phys 1994; 29: 903–909.
21. Landis JR, Koch GG. A one-way components of variance model for categorical data. Biometrics 1977; 33: 671–679.
22. Donner A, Shoukri MM, Klar N, Bartfay E. Testing the equality of two dependent kappa statistics. Stat Med 2000; 19: 373–387.
23. Wortman PM, Vinokur A, Sechrest L. Do consensus conferences work? A process evaluation of the NIH Consensus Development Program. J Health Polit Policy Law 1988; 13: 469–498.
24. Tunis SR, Hayward RS, Wilson MC et al. Internists' attitudes about clinical practice guidelines. Ann Intern Med 1994; 120: 956–963.
25. Wachtel TJ, O'Sullivan P. Practice guidelines to reduce testing in the hospital. J Gen Intern Med 1990; 5: 335–341.
26. Putnam RW, Curry L. Physicians' participation in establishing criteria for hypertension management in the office: will patient outcomes be improved? CMAJ 1989; 140: 806–809.