



A quantitative approach to the distress caused by symptoms in patients treated with radical radiotherapy

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Summary A computerised self-assessment instrument was used to capture data on the distress caused by symptoms in 110 patients treated with radical radiotherapy. Patients selected symptoms from a list of 34 problems and then quantified the distress associated with each problem using a linear Analogue self assessment (LASA)-type scale. The test instrument was feasible: 90% of assessments were completed in under 14 min. There was a significant increase in tiredness and significant decrease in anxiety and worries about the family, during treatment. Menopausal symptoms and post-surgical problems were important causes of distress in the patients with breast cancer. When the area under the curve method was used to quantify distress in the patients with breast cancer, difficulty concentrating, pain and sleep disturbances emerged as significantly troublesome problems. Computerised self-assessment may have a useful role in quantifying the distress caused by treatment with radiotherapy.

Keywords: radiotherapy symptoms; breast neoplasm; psychology

Patients treated with radiotherapy have physical and psychological symptoms related both to the underlying disease and to the treatment. The distress caused by these symptoms can only be assessed adequately by the patients themselves (Slevin *et al.*, 1988). Inability to measure accurately and feasibly the symptomatic distress experienced by patients undergoing treatment with radiotherapy has, to an extent, hindered the rational scientific development of clinical radiotherapy. Factors influencing tumour control have been carefully analysed, but the price paid for that control, in terms of subjective distress, has largely been ignored. Prescribing practices vary widely (Priestman *et al.*, 1989) and largely reflect previous training and/or institutional dogma (Maher, 1991). Insufficient quantitative information on what patients actually experience means that it is very difficult to incorporate patients' views into decisions about the optimal scheduling of treatment. Many of the problems experienced by patients during radiotherapy may be preventable or might be amenable to treatment. However, it is not possible to ameliorate, or to advise patients about, unrecognised problems. If we wish to improve the quality of care for patients then we need to know their views as to what the problems actually are: which symptoms are important and which symptoms are less distressing.

There are no standard instruments that address the specific concerns of patients during treatment with radiotherapy. There is an abundant literature on the assessment of 'quality of life' (Aaronson *et al.*, 1993; Ganz *et al.*, 1992; Selby *et al.*, 1984; Olschewski *et al.*, 1994), but these instruments do not deal in detail with the particular symptoms that radiation treatment might itself produce. The tendency has been to concentrate on collapsed global indices. Radiotherapy causes quite specific symptoms, distress from which will probably impinge upon overall quality of life, but which will only be one aspect of a much broader and more complex domain. Collapsed indices are of little help in these circumstances. In order to improve standards, we need to be able to focus on the distress caused by specific problems in patients undergoing a course of radiotherapy treatment. In the absence of any standard instrument we have had to design our own test instrument.

In a previous study (Munro *et al.*, 1989) we showed that it was possible to capture useful information on the distress caused by symptoms in patients being treated with radiotherapy. The technique used was adapted from the method originally described by Coates *et al.* (1983). The disadvantage of the method was that it was too time-consuming for routine use in clinical practice. Each assessment took around 30 min, and the data entry procedures were cumbersome. Based on this previous experience, we designed a computerised test-instrument that avoids some of the previous problems. We wanted an instrument that would be feasible for routine use, reasonably comprehensive, reliable and responsive. Responsiveness was a particularly important criterion as we wished to be able to track changes in levels of distress during and immediately after a course of treatment.

This paper presents data from over 400 assessments, performed with the computerised test instrument, from 110 patients treated with radical radiotherapy for cancers of the head and neck, bronchus and breast.

Patients and methods

All consecutive outpatients attending for radiotherapy under the care of one consultant were selected for entry into the study. The patients were treated on 6 MV linear accelerators. Three groups of patients were studied:

- (1) Patients with stage I or II breast cancer receiving post-operative radiotherapy to the breast (after local excision) or to the chest wall (after mastectomy). The majority of patients were treated with 40 Gy in 15 fractions over 3 weeks to tangential fields only; a minority received an additional boost of 10 Gy in five fractions over 1 week. The cervicoaxillary chain was not treated as nearly all patients had full axillary clearance.
- (2) Patients with head and neck cancer treated with radical radiotherapy. All patients were treated in a shell for immobilisation and doses ranged from 50 to 55 Gy in 20 fractions over 4 weeks.
- (3) Patients treated with more than five fractions of radiotherapy for localised lung cancer. The standard regimen for these patients was 22.5 Gy in five fractions over 1 week using parallel opposed fields to the chest followed by a 2-3 week gap. Patients who had tolerated the first phase of treatment well and who had not developed clinical or radiological evidence of progressive

disease were treated with a second phase of treatment 22.5 Gy in five fractions over 1 week using a two- or three-field plan to avoid the spinal cord.

The only patients excluded from the study were patients who were unable to comprehend written English. Accrual was from 1st April 1994 to 1 December 1994.

The assessment schedule for each group of patients is summarised in Table I; the schedule chosen for each group represents a compromise between the need to assess patients at the likely time of maximum treatment-related morbidity and the desire to keep extra attendances at hospital to a minimum.

Assessment procedure

All patients were asked about the same basic set of symptoms, the core symptoms, and in addition there was a specific set of additional symptoms for each diagnostic group (Appendix). The system was completed automated. After entering their hospital number, for identification, the patient was shown a series of symptoms on the computer screen. Each symptom appeared within a box in the centre of the screen, and at the bottom of the screen was the question 'Does this symptom trouble you Y or N?'. If the patient answered N the program moved on to the next symptom; if the patient answered Y a further screen was shown with the request 'Please indicate how much you are troubled by (symptom)'. Underneath was a box with a highlight within it which could move horizontally. There were 15 possible positions for the highlight within the box. The left end of the box was labelled 'not at all' and the right end of the box was labelled 'unbearably'. The patient was asked to place the highlight within the box at the position that corresponded to the level of distress produced by that particular symptom. The procedure was directly analogous to the completion of a LASA scale. The position chosen by the patient was recorded automatically and the assessment then moved on to the next question.

The list of symptoms was compiled on the basis of: previous experience; informal conversations with patients; consultations with staff within the department. An open request, 'Please enter any other problems that concern you, but about which we have not asked you, in the box below', was also included within the questionnaire.

Additional questions were added to the basic symptom inventory in order to permit some assessment of the validity of the approach. The McGill present pain index (PPI) and automated LASA scales for pain, overall quality of life [analogous to the Uniscale (Selby *et al.*, 1984)] and disruption due to treatment were added as well as the Hospital Anxiety and Depression (HAD) Scale (Zigmond and Snaith, 1983). The computer's internal time clock was used to record the duration of the assessment; the duration of the HAD assessment was separately recorded.

The assessments were carried out under the supervision of the research nurse (SP) in a private room. The nurse was available to help with any difficulties patients might have understanding the questions or the procedure; the nurse was seated so that patients were aware that their responses could not be seen directly by her. If, at the end of the session, patients had any problems or questions, these were dealt with.

Programs, data, analysis and statistics

The test instrument was written using an expert system (Crystal, Intelligent Environments), which then automatically exported responses to a standard relational database (Dbase for Windows, Borland). There was therefore no separate data entry procedure: the patients had directly entered the data and there was no editing of responses. The data were exported to Excel (Microsoft v5.0) for graphical presentation and spreadsheet analysis. The statistics were performed using Stata (Stata Corporation).

A symptom that was not troubling the patient was scored as zero. Symptoms that were causing problems were scored from 1 to 15 using the LASA bar scale. For each symptom it is possible in any group of patients to obtain a mean score for that symptom. An alternative method of analysis is to ignore the scores and simply record symptoms as being present or absent. The information has been analysed both ways.

Area under the curve (AUC) measurements could be obtained for each symptom for each individual patient. The calculation was performed according to the method described by Matthews *et al.* (1990). The area under the curve for symptom score plotted against time was estimated as the sum of the measurements:

$$(t_2 - t_1)(y_1 + y_2)/2$$

where $t_2 - t_1$ is the interval between the measurements and y_1 and y_2 are the symptom scores at the two time points.

Problems with the scheduling of interviews meant that complete data sets were not available for all patients. The problem of missing data was handled in three different ways:

- (1) only complete data sets were analysed;
- (2) zero was substituted for all missing values;
- (3) missing values were imputed using linear regression.

Correlation between the various components of the instrument has been assessed using Kendall's tau. The changes in responses over time have been assessed using the Wilcoxon matched-pairs signed-ranks test as well as the non-parametric test for trend described by Cuzick (1985).

Results

A total of 110 patients were eligible for the study: there were 72 patients with breast cancer, average age 53 years (range 31–74 years); there were 24 patients with lung cancer, average age 71 years (range 46–81 years); there were 14 patients with head and neck cancer, average age 63 years (range 32–82 years).

Feasibility

All patients were able to complete the computerised questionnaire. There were no problems with non-compliance or technical malfunction. The average duration of each assessment was 10.0 min (95% CI 7.8–12.2), the median

Table I Assessment schedules for the patients according to type of cancer and treatment

<i>All patients</i>	
1	immediately before planning
2	day 5–7
3	day 12–14
4	day 19–21
<i>Breast</i>	
Three week regimen	
5	day 49
Four week regimen	
5	day 28
6	day 56
<i>Bronchus (phase II only)</i>	
5	day 35
6	day 56
<i>Head and neck</i>	
5	day 26–28
6	day 33–35
7	day 40–42
8	day 54–56

duration was 7.3 min and 90% of assessments were completed in under 14 min. There was evidence of a possible learning effect: the average duration of first interviews was 12.0 min (95% CI 10.0–14.), whereas the mean duration of the fourth interviews was 7.2 min (95% CI 6.6–7.7). The *P*-value for this difference is 0.0001 ($z=6.67$) using the Wilcoxon signed-ranks matched-pairs test. It took an average of 2.3 min (95% CI 2.2–2.4) to administer the Hospital Anxiety and Depression scale in its computerised form; 90% of the HAD assessments were completed in less than 6.5 min.

Comparison between components of the computerised questionnaire and standard measures

The correlation matrix in Table II shows values for Kendall's tau and *P*-values for those elements of the test instrument for which standard tests were available. The data come from the initial assessments on all 110 patients in the study. The reasonable correlation for appropriate comparisons (pain, the separate LASA scale for pain and the PPI) and, conversely, the poor correlations for inappropriate comparisons (for example, depression and the PPI) suggests that the components of the test instrument have both criterion validity and discriminant validity (Nunnally, 1978).

Core questions (all 110 patients)

The following 13 symptoms were selected by less than 30% of patients; sickness, weight loss, constipation, hoarseness, inconvenience of attending for treatment, not enough information about disease and its treatment, inadequate support, unable to care for self, difficulty swallowing, vomiting, pain on swallowing, decreased appetite, headache. They will therefore not be analysed in detail in this section. The data scores and counts for the 14 most frequently mentioned of the core symptoms are presented in Figure 1. At the start of treatment 55% of patients selected tiredness as a symptom; by the end of treatment the figure was 71%. Anxiety seemed to diminish as a problem: 62% of patients mentioned anxiety at the beginning of treatment, but by the end of treatment only 42% selected anxiety from the list of problems. The data show a disparity in the relative ranking of symptoms according to whether the symptoms are ranked according to frequency or whether the ranking is by mean score for each problem. Frequent symptoms do not necessarily cause the most distress: the data on indigestion illustrate this point. Over 35% of patients complained of indigestion, but the mean score for indigestion was 1.96 and it ranked only 11th in terms of the distress it apparently caused.

Our primary aim was to estimate distress rather than simply enumerate problems and the rest of the analysis is therefore based on the scoring, rather than the counting, of symptoms and problems.

Inspection of the data in Figure 1 suggests that there may be significant changes in some of the core symptoms during a course of radiotherapy. The only symptom to increase significantly during treatment was tiredness: *P* by Wilcoxon matched-pairs signed-rank test was 0.002. The following symptoms were significantly less distressing by the end of treatment: worry about effects of disease and treatment upon the family ($P=0.0003$) and feeling anxious ($P=0.0002$). The apparent changes in ability to concentrate, depression, taste, sweating and itch were not statistically significant.

It was possible to derive, by simple addition, a total score for the core symptoms for each individual patient. The data in Table III show that there is no clear evidence that the total distress caused by the core group of symptoms is worse in any particular group of patients or at any particular time.

The open question was answered on 34 different occasions: there were four problems which we had failed to include in our original list. These items were subsequently added to the inventory: increased sweating, headache, hot flushes, indigestion.

Disease-specific symptoms and core symptoms in the different groups of patients

Figure 2 shows the data for all symptoms which, on any occasion, had an average score >2 for each group of patients. The data are shown for the initial assessment (week 0), the end of treatment (week 3) and the first follow-up visit (week 7). There were too few patients with lung cancer or cancer of the head and neck for meaningful statistical analysis.

The data from the patients with breast cancer showed significant changes over time during the study period. Tiredness significantly increased between the start of treatment for breast cancer and the completion of radiotherapy ($P=0.009$, Wilcoxon). It then decreased so that by the first follow-up visit there was no significant difference from the pretreatment baseline ($P=0.9$). There were no statistically significant changes during the first 2 weeks of treatment, but when the second week was compared with the third week there was a significant increase in the scores for tiredness ($P=0.007$, Wilcoxon). The sequential mean scores and 95% confidence intervals were: week 0, 3.9 (2.9–4.9); week 1, 4.77 (3.6–5.9); week 2, 5.25 (4.2–6.3); week 3, 6.85 (5.62–8.1); week 7, 4.2 (2.9–5.5). Other, more obviously direct, effects of radiotherapy followed a similar pattern: distress at not being able to wash properly increased between week 0 and week 3 ($P=0.016$) then decreased between week 3 and week 7 ($P=0.004$). Similarly, changes in the skin of the breast increased during treatment (week 0 vs week 3, $P=0.0003$) then appeared to decrease (week 0 vs week 7, $P=0.06$). Similar, but statistically non-significant, patterns were seen for heaviness of the treated breast and itching of the treated skin.

Table II Correlation matrix for item scores: the values shown are for Kendall's tau with *P*-values for each comparison in brackets

	Anxious	Depressed	PPI	HAD anxiety	HAD depression	LASA pain	pain
Anxious	1						
Depressed	0.35 (0.00001)	1					
PPI	0.08 (0.21)	0.06 (0.36)	1				
HAD anxiety	0.39 (0.00001)	0.25 (0.03)	0.01 (0.86)	1			
HAD depression	0.02 (0.72)	0.29 (0.00001)	0.14 (0.02)	0.26 (0.00001)	1		
LASA pain	0.06 (0.35)	0.13 (0.22)	0.79 (0.00001)	0.04 (0.52)	0.18 (0.004)	1	
Pain	0.09 (0.13)	0.15 (0.16)	0.44 (0.00001)	0.15 (0.02)	0.10 (0.11)	0.46 (0.00001)	1

The distress caused by the following symptoms steadily decreased between the initial assessment and the follow-up visit: numbness ($P=0.001$, Wilcoxon); worry about effects of disease and treatment upon family ($P=0.0001$, Wilcoxon); feeling anxious ($P=0.003$, Wilcoxon). Using the non-parametric test for trend only the change in worry about family was significant ($P=0.001$).

The data on the AUC measurements in the patients with breast cancer are shown in Table IV. The method used to allow for missing data did not seem materially to affect the interpretation of the results: the only significant change in rank order according to the method used was for sleep disturbances. The data clearly show, when taken in conjunction with Figure 2, the importance of not relying on a single time point for assessing the distress caused by

Table III Total symptom scores (means and confidence interval) according to type of cancer and time of assessments – all available data have been used

Group	Time (weeks)	Mean score	95% CI
Breast	0	41	32–49
	3	36	31–47
	7	30	22–38
Bronchus	0	40	31–50
	3	42	20–65
	7	51	30–74
Head and neck	0	31	14–46
	3	34	15–53
	7	26	0–55

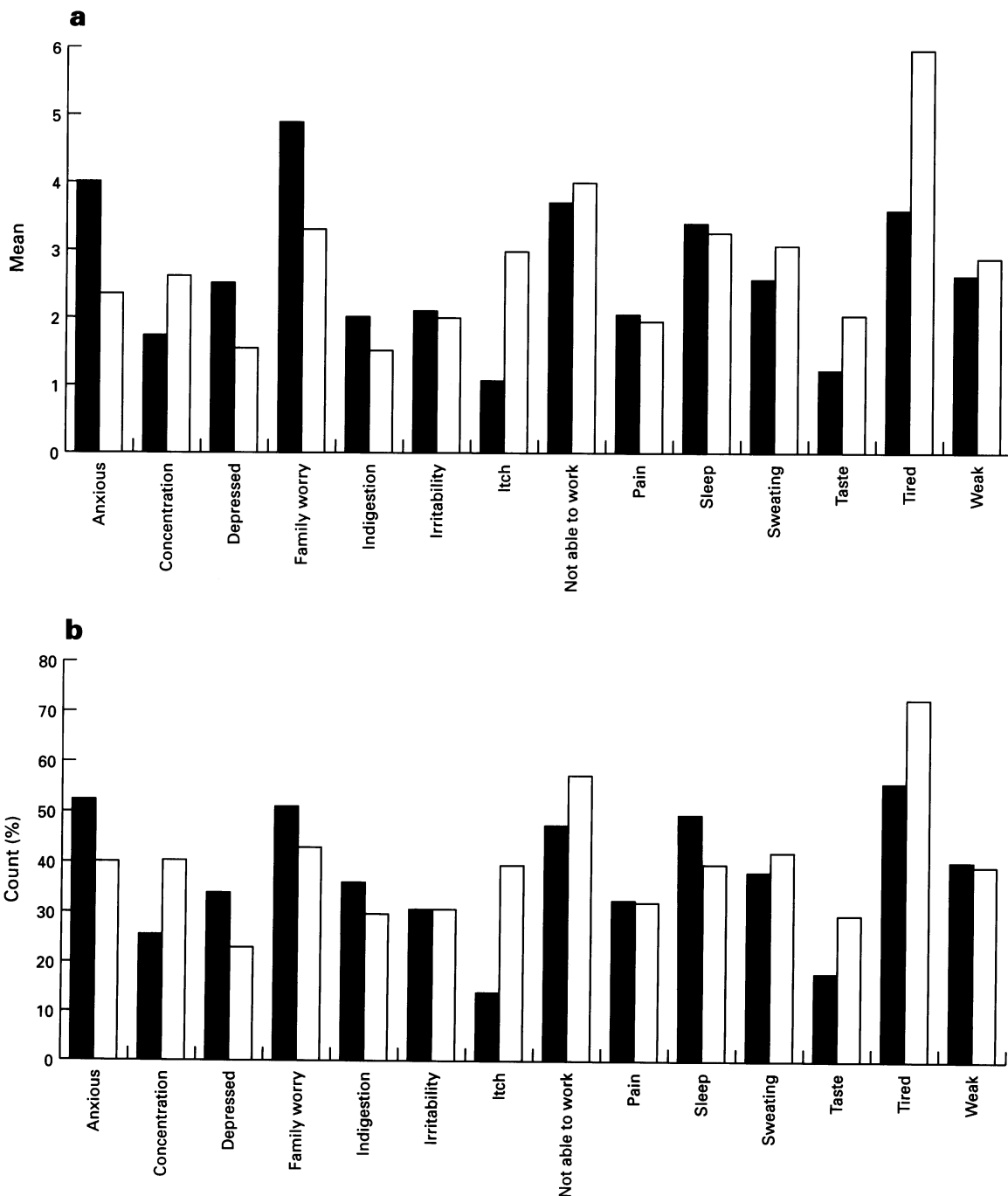
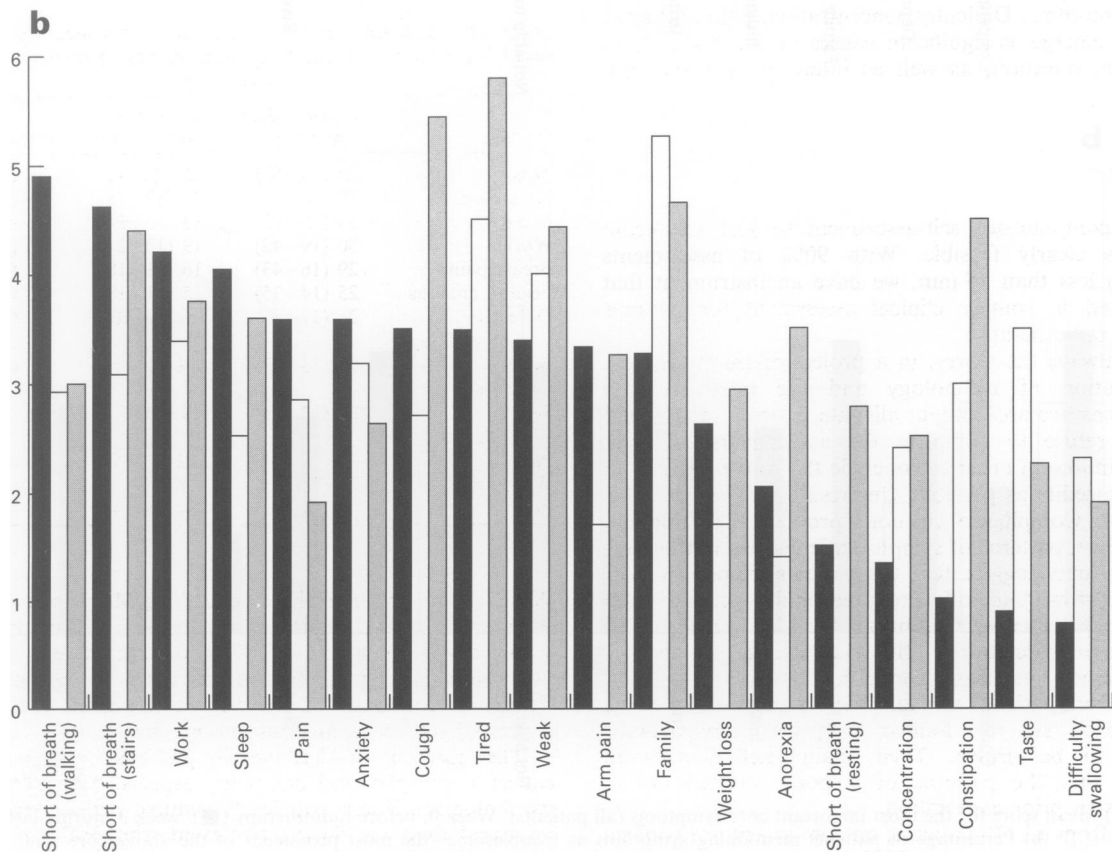
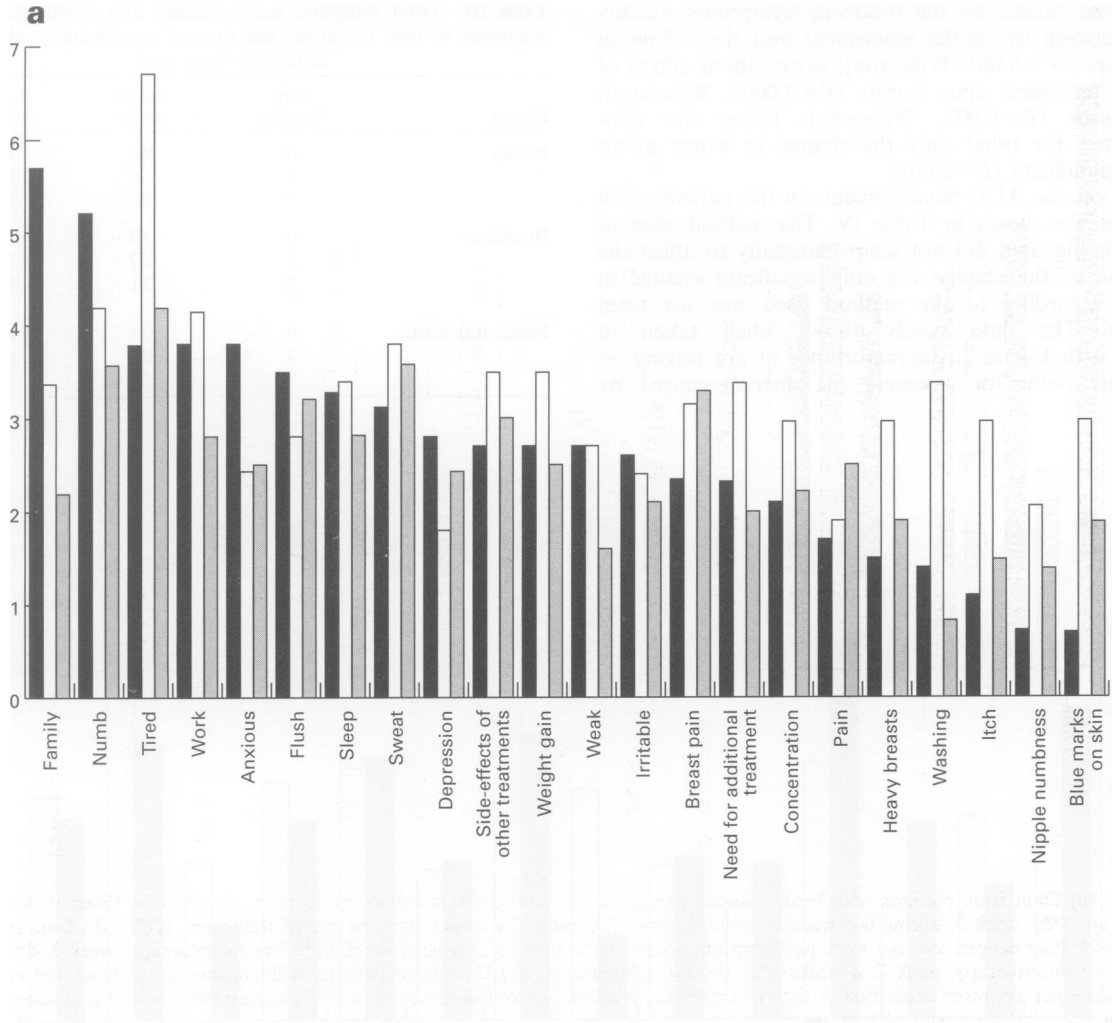


Figure 1 (a) Mean score for the most important core symptoms (all patients). Week 0, before radiotherapy (■); week 3, during last week of radiotherapy (□). (b) Percentage of patients mentioning symptoms as troublesome – the most prominent of the above core symptoms (all patients). Week 0, before radiotherapy, (■); week 3, during last week of radiotherapy, (□).



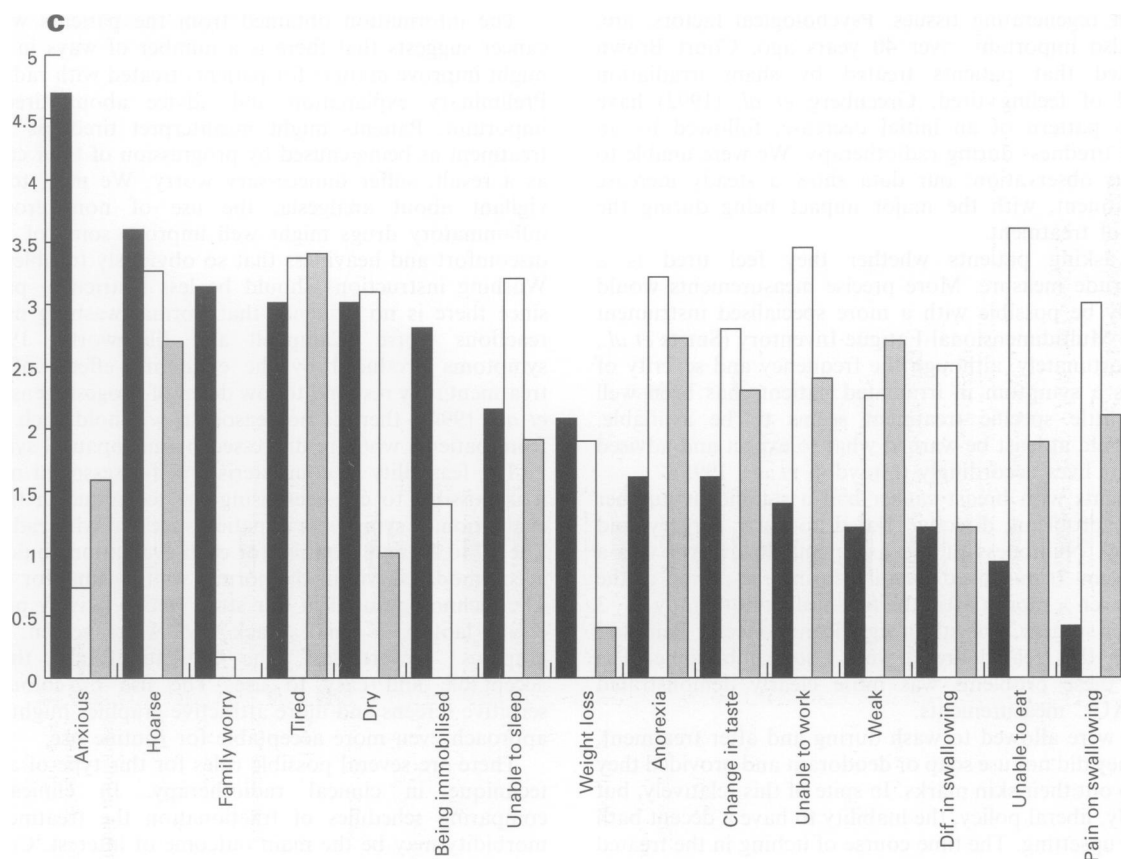


Figure 2 (a) Data from patients with breast cancer: average score per symptom according to time of interview. Week 0, before radiotherapy (■); week 3, during last week of radiotherapy (□); week 7, 4 weeks after the end of treatment. (b) Data from patients with lung cancer: average score per symptom according to time of interview. Week 0, before radiotherapy; week 3, during last week of radiotherapy; week 7, 4 weeks after the end of treatment. (c) Data from patients with cancers of the head and neck: average score per symptom according to time of interview. Week 0, before radiotherapy, week 3, during last week of radiotherapy; week 7, 4 weeks after the end of treatment.

particular symptoms. Difficulty concentrating, pain and sleep disturbances emerge as significant causes of distress in these patients when duration, as well as intensity, is taken into account.

Discussion

The use of computerised self-assessment to sort and score symptoms is clearly feasible. With 90% of assessments completed in less than 15 min, we have an instrument that could be used in routine clinical assessment for patients treated with radiotherapy.

There is always the worry, in a project of this type, that the combination of technology and the intrusion into potentially sensitive areas might alienate patients, who might then either refuse to complete the assessments or press buttons at random in order to conclude the whole unpleasant business as speedily as possible. Our results suggest that this is not the case. Compliance was not a problem. The different, and appropriate, patterns of symptomatic distress in the three groups of patients suggest that the patients' responses were not produced at random and were a reasonable guide to what they were experiencing. Capturing the data was not a problem; the interpretation of the data, teasing out its true meaning, is much less straightforward.

The data from patients with lung cancer and cancers of the head and neck are too limited to permit any detailed conclusions to be drawn. Their main usefulness is to demonstrate that the patterns of response elicited are in accordance with prior expectation.

The data, from all 110 patients, on core symptoms confirm previous observations (Smets, 1993; Lamszus *et al.*, 1994;

Table IV Data on the area under the curve measurements (for details of calculations, see text), data is from patients with breast cancer only

Problem	Complete data sets only	Missing data points at zero	Imputed data
Tired	45 (33–57)	28 (22–33)	39 (34–44)
Numbness	39 (26–51)	23 (17–28)	29 (24–34)
Family worry	30 (15–43)	18 (13–24)	24 (18–31)
Work	30 (19–42)	19 (13–24)	26 (20–32)
Breast pain	29 (16–43)	16 (11–18)	22 (17–28)
Feeling anxious	25 (14–35)	15 (11–18)	20 (16–24)
Difficulty concentrating	25 (11–38)	14 (9–18)	19 (13–25)
Breast heaviness	25 (13–37)	12 (8–17)	17 (12–22)
Sleep difficulties	24 (12–36)	18 (14–23)	25 (20–30)
Pain	23 (12–34)	12 (8–15)	17 (12–21)
Washing	22 (11–33)	14 (9–18)	17 (12–23)
Itch	22 (11–33)	11 (6–14)	14 (10–19)

Wallace *et al.*, 1993; Irvine *et al.*, 1994; Maraste *et al.*, 1992). Patients starting a course of radiotherapy mention anxiety, worry about the effects of their disease and its treatment upon their families, and problems related to work as being significant concerns. At the end of treatment they are less distressed by feeling anxious and are significantly more tired.

The question of tiredness in patients being treated for cancer is complex and has many aspects, both physical and psychological. There are clearly genuine physical reasons for increased tiredness during treatment—the strain of unaccustomed daily travel (Junor *et al.*, 1992), the metabolic

demands of regenerating tissues. Psychological factors, are, however, also important: over 40 years ago, Court Brown (1953) noted that patients treated by sham irradiation complained of feeling tired. Greenberg *et al.* (1992) have described a pattern of an initial decrease, followed by an increase, in tiredness during radiotherapy. We were unable to confirm this observation: our data show a steady increase during treatment, with the major impact being during the final week of treatment.

Simply asking patients whether they feel tired is a relatively crude measure. More precise measurements would undoubtedly be possible with a more specialised instrument such as the Multidimensional Fatigue Inventory (Smets *et al.*, 1995). Unfortunately, although the frequency and severity of tiredness as a symptom in irradiated patients has been well described, little specific treatment seems to be available. Patients should at least be warned what to expect and advised to pace their lives accordingly (Graydon *et al.*, 1995).

The patients with breast cancer had a significant number of physical problems directly related to their surgery and radiotherapy. Numbness of the axilla and inner arm was a major problem. It improved steadily during the period of the study but, even a month after the finish of radiotherapy, 2–3 months after surgery, was still a significant concern. Pain and heaviness in the treated breast were also troublesome. The impact of these problems was more clearly demonstrated using the AUC measurements.

Patients were allowed to wash during and after treatment, provided they did not use soap or deodorant and provided they did not rub out their skin marks. In spite of this relatively, but insufficiently, liberal policy, the inability to have a decent bath was clearly upsetting. The time course of itching in the treated skin was in accordance with expectation—maximal during the last week of treatment and settling thereafter. Adjuvant treatment caused significant upset. Hot flushes and increased sweating were consistent and distressing problems.

The rank order of symptoms in terms of the distress caused depended upon the timing of the assessment. Feeling anxious and numbness of the axilla and arm were the dominant problems at the start of the treatment; by the end of treatment tiredness and numbness predominated; by the first follow-up visit tiredness, sweating and breast discomfort were the major causes of distress.

The AUC data, by and large, confirm the visual impression given by the data in Figure 2. Sleep difficulties fell in rank, and breast pain rose in rank, when AUC rather than mean score was used as the measure of distress. The interpretation and ranking of AUC measurements is not simple. Although such measurements are clearly useful in assessing the 'total' upset caused by an individual symptom during the period of observation (Matthews *et al.*, 1990) there is, inevitably, oversimplification. A mildly troublesome, but persistent, symptom might well have an AUC value equal to that of a much more distressing problem of shorter duration. We are still left with the question of which is worse: a bang on the thumb with a hammer or persistent mild backache?

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Appendix

Core symptoms

Cough
Feeling tired
Loss of appetite
Unable to sleep properly
Nausea (feeling sick)
Vomiting (feeling sick)
Difficulty concentrating
Weight loss
Not enough support from family and friends
Feeling bad-tempered or irritable
The inconvenience of attending hospital
Unable to work or perform my usual activities
Hoarse voice
Not given enough information about my disease or its treatment
Difficulty swallowing
Pain when swallowing
Pain
Feeling weak
Constipation
Feeling anxious
Feeling depressed
Change in taste

Breast patients only

Pain in the breast
Swelling of the arm or hand
Pain in the nipple
Numbness in the armpit or arm
Heavy feeling in the breast
Discomfort in the skin of treated breast
Having to have blue marks on the skin
Worry about the possible need for additional treatment (e.g. tamoxifen or chemotherapy)
Itching of the skin
Gain in weight
Not being able to wash properly

Head and neck patients only

Sore mouth or tongue
Unable to eat properly

Itching of the skin
Not being able to wash or shave properly
People having difficulty understanding what I'm saying
Dry mouth
Being immobilised in shell for treatment

Lung cancer patients only

Coughing up blood
Short of breath at rest
Short of breath on walking
Short of breath on stairs
Chest pain
Pain in the arm or shoulder

Problems added after interim analysis of responses

Headache
Hot flushes
Increased sweating
Indigestion

Supplementary questions (all patients)

LASA pain

Please indicate how much pain you have had over the past 24 hours
no pain _____ unbearable pain

McGill PPI

How would you describe your pain over the past 24 hours?
No pain
Mild pain
Discomforting pain
Distressing pain
Horrible pain
Excruciating pain