Development and initial psychometric evaluation of a radiotherapy-related symptom assessment tool, based on data from patients with brain tumours undergoing proton beam therapy

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Background: Currently, no available tool easily and effectively measures both the frequency, intensity and distress of symptoms among patients receiving radiotherapy. A core symptom set (fatigue, insomnia, pain, appetite loss, cognitive problems, anxiety, nausea, depression, constipation, diarrhoea and skin reaction) has been identified and assessed across oncology research to better understand the pattern of symptoms and treatment side effects.

Aim: The aim was to develop a tool measuring the multiple-symptom experience in patients undergoing radiotherapy and evaluate its psychometric properties (validity, reliability and responsiveness).

Design: This study has a prospective, longitudinal and quantitative design.

Methods: We developed a patient-reported outcome questionnaire, the Radiotherapy-Related Symptoms Assessment Scale to assess the frequency, intensity and distress associated with symptoms. Patients (n = 175) with brain tumours undergoing proton beam therapy completed the Radiotherapy-Related Symptoms Assessment Scale and

the health-related quality of life questionnaire (EORTC QLQ-C30) during treatment. We assessed the validity, reliability and responsiveness of the Radiotherapy-Related Symptoms Assessment Scale and evaluated the validity against QLQ-C30.

Results: There were significant questionnaire–questionnaire correlations regarding selected items, primarily fatigue, insomnia and pain, indicating satisfactory criterion-related validity. The Radiotherapy-Related Symptoms Assessment Scale had fair to good retest reliability.

Conclusion: The Radiotherapy-Related Symptoms Assessment Scale is a valid instrument for assessing symptom intensity and distress in patients with brain tumour undergoing PBT, with psychometric properties within the expected range. The Radiotherapy-Related Symptoms Assessment Scale provides nurses with substantial information on symptom experience but requires little effort from the patient. Additional studies are required to further assess the psychometric properties in patients with different cancer diagnoses receiving conventional radiotherapy.

Keywords: self-administered questionnaire, radiotherapy, symptom experience, validity, reliability, responsiveness.

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Introduction

When a person is diagnosed with a tumour or cancer, s/he is often concerned about the symptoms s/he experiences and will experience. Symptoms may be a result of

the disease itself and/or of the associated treatment and may have a major impact on daily life or remain unnoticed and underdiagnosed. The number of available health status questionnaires has increased over recent decades. A systematic review revealed a large number of published questionnaires assessing specific concepts in specific populations (1–5). The European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ) is an integrated system for assessing the health-related quality of life of patients with cancer participating in international clinical trials. The QLQ-C30 questionnaire (6) was designed to be cancer-specific, multidimensional in structure, appropriate for self-administration and applicable across a range of cultural settings. An essential component of the EORTC QLQ strategy involves the use of supplementary questionnaire modules, for example the QLQ-BN20 (7) which, when combined with the QLQ-C30, can provide more detailed information for evaluating health-related quality of life in specific patient populations. These questionnaires contain 50 items together. When having a discussion about symptoms, the nurse needs an easy tool to quickly and effectively report the frequency and intensity of symptoms related to radiotherapy and the related distress. To our knowledge, such tool is not yet available. Therefore, we designed the Radiotherapy-Related Symptoms Assessment Scale to evaluate symptom experiences in patients undergoing radiotherapy. This instrument comprises a core symptom set of 13 items: fatigue, insomnia, pain, loss of appetite, dyspnoea, cognitive impairment, worry, anxiety, nausea, sadness, constipation, diarrhoea and skin reactions. The reliability and validity of the items are key indicators of the quality of an instrument. Moreover, the responsiveness of an instrument to change is of interest in many healthcare applications, as outcome improvement from treatment is a primary research focus. The Radiotherapy-Related Symptoms Assessment Scale was completed together with, and compared with, the validated Health-Related Quality of Life Questionnaire (EORTC QLQ-C30) (6).

Symptom theories

A symptom is defined as an individual's subjective experience of altered functioning, sensation or cognition that cannot be objectively observed (8). A previous study showed that patients have difficulty distinguishing between the intensity of, and distress caused by, symptoms (9). Middle-range theories, such as the Theory of Unpleasant Symptoms (10, 11), provide a structured and comprehensive way to understand symptoms. They have direct applications in clinical practice and can aid in the description, explanation and prediction of the phenomena (12). The Theory of Unpleasant Symptoms is distinct from other models in that it asserts that symptom

experience includes a quality dimension in addition to intensity, timing and distress. Therefore, the Theory of Unpleasant Symptoms provided a good basis for developing the Radiotherapy-Related Symptoms Assessment Scale with the objective of evaluating multiple symptoms.

Symptoms in brain tumor patients

Patient with brain tumours often experience symptoms such as headache, loss of appetite, nausea, vomiting, seizures, sleeping longer at night and drowsiness with daytime napping (13). Most patients also experience fatigue and double vision (14), as well as neurological deficits and cognitive impairment (15). Personality changes, mood disturbances and decreased mental capacity and concentration can occur later in the disease trajectory (13, 16). Most of these symptoms may be amplified during radiotherapy (17–20).

In August 2015, the Skandion Clinic in Uppsala, Sweden, the first proton beam therapy clinic in Sweden, started treating patients. Proton beam therapy is a radiotherapy modality in which proton particles penetrate deep into the target and stop at a certain depth, depending on their energy (21). Studies of proton beam therapy side effects based on patient-reported outcomes are lacking, and studies exploring how patients experience and conceptualise symptom dimensions are thus needed. Furthermore, instruments that assess multiple dimensions of symptoms must be evaluated and psychometrically tested. This study aimed at developing and conducting an initial evaluation of the psychometric properties (validity, reliability and responsiveness) of a self-administered tool assessing multiple-symptom experience and distress among patients undergoing radiotherapy.

Methods and variables

Design

This study has a prospective, longitudinal and quantitative design. This study is part of Proton Care, a large-scale multicentre project that aims at assessing proton beam therapy, compared with modern photon-based radiotherapy techniques, with regard to short- and long-term patient-reported outcomes.

Participants and setting

A consecutive sample of 234 patients aged ≥18 years, diagnosed with a primary brain tumours and undergoing proton beam therapy at the Skandion Clinic between August 2015 and December 2017, were invited to participate in this study. The exclusion criterion was inability to communicate in Swedish. Information about the study

was provided to potential participants by the first author (UL) via telephone. Written information about the study was then sent to interested patients by mail. This information covered the voluntary nature of participation, confidentiality and freedom to withdraw from the study. Participating in studies can lead to being reminded of one's illness, which might prompt unpleasant memories and thoughts. Therefore, participants were advised they could contact healthcare providers or the principal investigator if they needed to discuss such feelings. All participants provided informed consent.

Data collection

In order to examine the symptom pattern, data were collected every day during the treatment period (35 days) using the newly created Radiotherapy-Related Symptoms Assessment Scale (see below). In addition, participants responded to the EORTC QLQ-C30 (6) at the start of treatment (baseline), after 3 weeks and at the end of treatment. Data were collected via online or paper questionnaires, according to patients' choice. Online questionnaires were e-mailed to participants every day during the treatment period and a reminder was sent each day that the questionnaire was not completed. Participants who chose paper were handed one questionnaire and a prepaid envelope for each treatment day by an oncology nurse at the Skandion Clinic at the start of treatment, and asked to return the questionnaires at the end of treatment. A reminder was sent out if the questionnaires were not returned within 1 week after the end of treatment.

Questionnaires

The Radiotherapy-Related Symptoms Assessment Scale. Creation of the questionnaire–The content of the Radiotherapy-Related Symptoms Assessment Scale was developed in accordance with published guidelines from expert advisory bodies (22). Reeves et al. (23) suggested that a core set of 12 symptoms should be used as a basis for the Radiotherapy-Related Symptoms Assessment Scale. These symptoms—fatigue, insomnia, pain, loss of appetite, dyspnoea, cognitive problems, anxiety (including worry), nausea, depression (including sadness), sensory neuropathy, constipation and diarrhoea—are recommended to be considered for inclusion in all cancer studies investigating patient-reported outcomes. The theoretical basis used to develop the Radiotherapy-Related Symptoms Assessment Scale was the middle-range Theory of Unpleasant Symptoms. Application of this theory transformed the Radiotherapy-Related Symptoms Assessment Scale from a purely linear to a more interactive questionnaire and allowed for the

simultaneous experience of multiple symptoms. Furthermore, the Radiotherapy-Related Symptoms Assessment Scale was created inspired by the design of the Quality from the Patient's Perspective instrument developed by Wilde et al. (24). Therefore, it includes assessment of symptom intensity (1 = not at all, to 4 = very much) and symptom distress (1 = of no concern, to 4 = of greatest concern). Each item score is converted to a score ranging from 0–100, analogous to the QLQ scoring process (25). On average, the Radiotherapy-Related Symptoms Assessment Scale requires 4–5 minutes to complete.

Pilot study and adaptions–A qualitative pilot study was conducted to test the understanding and interpretability of the Radiotherapy-Related Symptoms Assessment Scale (26). The main purposes were to evaluate whether the instructions and questions were easy to understand, identify potentially problematic questions and examine participants' thoughts when answering the questionnaire. Content and face validity require a sample that ensures the target population and different subgroups of it are represented (27). Therefore, participants were included if they had a brain tumour, older than 18 years and both men and women were included. A total of 10 patients (four women and six men) participated by being interviewed in the pilot study.

During the interviews, the pilot study participants were asked, inspired by the EORTC (7), whether they had found any of the questions difficult or confusing, whether the questionnaire contained words that upset them or whether there were any other difficulties. Participants were also asked whether they had any rephrasing suggestions.

This initial study showed that patients found two items unclear: anxiety (including worry) and depression (including sadness). Therefore, anxiety, worry and sadness were transformed into individual items. The depression item was excluded because the Radiotherapy-Related Symptoms Assessment Scale was meant to evaluate self-reported symptoms, and depression is a psychiatric diagnosis. We also added skin reactions, as the Radiotherapy-Related Symptoms Assessment Scale was intended for radiotherapy patients. This resulted in 13 items in the final version of the Radiotherapy-Related Symptoms Assessment Scale: fatigue, insomnia, pain, loss of appetite, dyspnoea, cognitive impairment, worry, anxiety, nausea, sadness, constipation, diarrhoea and skin reactions. Our previous interview-based study confirmed that patients commonly experienced several of the symptoms included in the Radiotherapy-Related Symptoms Assessment Scale during the treatment period (28). The 10 patients included in the pilot study were not included in the final analysis.

The EORTC QLQ-C30–Participants were asked to complete the EORTC QLQ-C30 (6). This is a generic cancer-specific questionnaire covering physical, social and psychological functioning, as well as cancer-specific symptoms. The instrument consists of 30 items covering five functioning scales (*physical, role, emotional, cognitive* and *social function*), three symptom scales (*fatigue, pain* and *nausea/vomiting*) and two *global health/QoL* items. Six single items address additional symptoms commonly reported by patients with cancer (*loss of appetite, insomnia, dyspnoea, diarrhoea* and *constipation*) and *financial difficulties* are also included. The two *global health status/QoL* items were scored from 1 = *very poor* to 7 = *excellent*. The items in all symptom scales were scored 1 = *not at all*, 2 = *a little*, 3 = *quite a bit* or 4 = *very much*. Scores for each scale were transformed into scores ranging from 0 to 100, first by calculating the raw scores, that is estimating the average of the items contributing to each scale, and second, by using linear transformation to standardise the raw scores. This procedure is in accordance with the scoring manual (25). High functioning scores represent better HRQoL, and high symptom scores are related to more severe symptoms. The Swedish version of QLQ-C30 has been widely used and has demonstrated high reliability and validated in different groups of patients with cancer (6).

Statistical analyses

Mean, standard deviation, minimum and maximum were used for age, while number and per cent were used for categorical variables. All analyses were performed using SAS version 9.3. A p-value of <0.05 was considered statistically significant.

Reliability. Test-retest reliability –Stability or reliability is determined in both dimensions (symptom experience and symptom distress) by administering a test to the same individual at two different points and determining the degree of agreement between the two sets of scores. The timing of the second administration is critical when tests are administered repeatedly. Ideally, the interval between tests should be long enough so that results of the second test will not be affected by the previous one. However, the interval should not be so long that memorising questionnaire details or a change in health status could alter responses to the second test. As the Radiotherapy-Related Symptoms Assessment Scale was completed each of the 35 treatment days, we calculated the weighted kappa and absolute agreement at two time points (day 1 vs. day 2), when completing the questionnaire was not yet routine for participants. We knew that there were differences in the respective symptoms on days 1 and 14 and we therefore chose to compare day 7 to day 14, as we considered this to be a more stable

interval. Kappa of 0–0.20 indicated slight, 0.21–0.40 indicated fair, 0.41–0.60 indicated moderate, 0.61–0.80 indicated substantial, and 0.81–1.0 indicated almost absolute, agreement (29).

Validity. Criterion-related validity (30) was assessed using Spearman's rank correlations between selected Radiotherapy-Related Symptoms Assessment Scale items and the corresponding QLQ-C30 items at baseline, after 3 weeks and at the end of treatment. Correlations were classified as low (<0.30), moderate (0.3–0.60) or strong (>0.6) (4).

Responsiveness. Responsiveness is the ability of an instrument to detect clinical changes over time (increase, unaltered or decrease). It was evaluated by calculating the per cent agreement and Spearman's rank correlations between Radiotherapy-Related Symptoms Assessment Scale items and the corresponding QLQ-C30 items, for changes between baseline and 3 weeks, as well as between baseline and end of treatment.

Results

The response rate was 94% and the final sample comprised 175 participants, 51% women and 49% men. The mean age was 47 years (range 18–77 years). Eight per cent had elementary education (<10 years), 45% had secondary education, and 43% had university education or higher (Table 1). The mean values and frequencies for each variable are presented in Tables S1 and Table S2.

Table 1 Participants' demographics (N = 175)

Parameters	n	%
Sex		
Women	90	51
Men	85	49
Age, years		
Mean	47	
Standard deviation	14.2	
Min	18	
Max	77	
Marital status		
Married	124	71
Single	51	29
Education		
Elementary school	14	8
Secondary school	78	45
University	75	43
Missing	8	4
Questionnaire format		
Paper	119	68
Online	56	32

Reliability

The analysis of test–retest reliability of Radiotherapy-Related Symptoms Assessment Scale symptom intensity showed absolute agreement for day 1 vs. day 2, ranging from 64%–95% (Table 2). Weighted kappa demonstrated moderate agreement (K_w = 0.46–0.59). There was particularly high agreement for cognitive impairment and anxiety (K_W = 0.67 and 0.65, respectively) and fair agreement for nausea (K_w = 0.30). For day 7 vs. day 14, the absolute agreement ranged from 66% to 92%. The weighted kappa ranged from 0.33 to 0.68, that is poor to strong agreement. There was high absolute agreement for symptom distress, ranging from 77% to 99% for day 1 vs. day 2. The weighted kappa demonstrated moderate to strong agreement (K_w = 0.44–0.68), except for fatigue, loss of appetite, dyspnoea and nausea that showed fair agreement (K_w = 0–0.39). For day 7 vs. day 14, absolute agreement ranged from 79% to 96%. The weighted kappa ranged from 0.22 to 0.64, that is poor to strong agreement.

Criterion-related validity

Correlations between the instruments were statistically significant in the majority of cases (Table 3). The correlations ranged from 0.19 to 0.66 at baseline, from 0.40 to 0.71 after 3 weeks and from 0.30 to 0.71 at the end of treatment (Table 4). The strongest correlations were found for fatigue, insomnia, pain, cognitive impairment, sadness and constipation. Most correlations were moderate to strong (31).

Responsiveness

Comparison of the Radiotherapy-Related Symptoms Assessment Scale and the QLQ-C30 showed that the absolute agreement between baseline and 3 weeks ranged from 51%–75%. The highest correlation between the two questionnaires was found for nausea (0.32). When it came to the change from baseline to end of treatment, the absolute agreement ranged from 48% to 73%. Nausea also showed the highest correlation during this period (Table 3).

Discussion

This study aimed at an initial evaluation of the reliability, responsiveness and validity of the Radiotherapy-Related Symptoms Assessment Scale, a self-administered tool measuring the frequency and intensity of multiple symptoms and related distress. The Radiotherapy-Related Symptoms Assessment Scale was found to be a reliable and valid questionnaire that was suitable for assessing symptom experience and distress in patients with brain tumour undergoing proton beam therapy. The psychometric properties (test–retest reliability, responsiveness and criterion-related validity) of the Radiotherapy-

Table 2 Reliability of the self-administered Radiotherapy-Related Symptoms Assessment Scale

| Variables | Symptom experience | | | | Symptom distress | | | |
| | Reliability Test–retest: day 1 vs. day 2 | | Reliability Test–retest: day 7 vs. day 14 | | Reliability Test–retest: day 1 vs. day 2 | | Reliability Test–retest: day 7 vs. day 14 | |
	% agreement	Weighted kappa	% agreement	Weighted kappa	% agreement	Weighted kappa	% agreement	Weighted kappa
Fatigue	65	0.53	68	0.55	77	0.39	79	0.48
Insomnia	69	0.55	66	0.50	83	0.55	83	0.59
Pain	82	0.56	80	0.62	90	0.56	88	0.64
Loss of appetite	88	0.54	82	0.57	97	0.39	91	0.48
Dyspnoea	95	0.30	92	0.42	98	0	96	0.32
Cognitive impairment	86	0.67	84	0.62	90	0.44	93	0.51
Worry	64	0.46	82	0.63	86	0.57	87	0.43
Anxiety	85	0.65	89	0.68	91	0.68	90	0.55
Nausea	91	0.54	82	0.50	94	0.20	86	0.26
Sadness	79	0.58	82	0.52	93	0.66	91	0.45
Constipation	93	0.56	91	0.53	98	0.66	96	0.54
Diarrhoea	91	0.59	87	0.40	98	0.39	91	0.22
Skin reaction	94	0.47	79	0.33	99	0.66	91	0.30

The table shows the absolute agreement and weighted kappa for the symptom experience and symptom distress dimensions in the Radiotherapy-Related Symptoms Assessment Scale. Comparisons: day 1 vs. 2 and day 7 vs. 14.

Table 3 Criterion validity: correlations between the Radiotherapy-Related Symptoms Assessment Scale and the Health-Related Quality of Life Questionnaire at baseline, after 3 weeks and at the end of treatment

	Baseline	After 3 weeks	End of treatment
Fatigue	0.61*	0.69*	0.45
Insomnia	0.66*	0.71*	0.62*
Pain	0.59	0.67*	0.71*
Loss of appetite	0.47	0.58	0.60*
Dyspnoea	0.19	0.31	0.30
Cognitive impairment	0.55	0.64*	0.53
Worry	0.57	0.57	0.63*
Nausea	0.43	0.52	0.57
Sadness	0.51	0.60*	0.55
Constipation	0.37	0.61*	0.62*
Diarrhoea	0.56	0.40	0.43

Spearman's correlation coefficient was used for the analysis.
*Indicates a correlation equal to or higher than the prespecified correlation level of 0.60.

Related Symptoms Assessment Scale were within the expected range. The stringent validation process helped establish its comparability with that of the QLQ-C30. It was also well accepted by participants, most of whom reported that it was easy to use. Our findings resonate with those of previous researchers who stated that single-item questionnaires have the advantage of simplicity at the cost of details, although they are useful for minimising burden on the patients (32). Some participants felt that it was gruelling to complete the questionnaire every day during the treatment period, and it may be

assumed that the questionnaire was completed by rote on some days. This might have influenced the responses, and response bias should thus be acknowledged (12). A total of 32% of the participants chose to complete the questionnaires online. We believe that this did not affect the results, as previous research suggests that there is little or no difference in reliability between paper and digital questionnaires (33, 34).

The investigation of validity showed moderate to strong correlations between the Radiotherapy-Related Symptoms Assessment Scale and the selected items in the QLQ-C30, suggesting that the constructs were similar and measured the same concepts for nine symptoms (fatigue, insomnia, pain, loss of appetite, cognitive impairment, worry, nausea, sadness and diarrhoea). However, the correlation for dyspnoea was poor, possibly because this item was not directly related to the brain tumour diagnosis.

Participants completed the Radiotherapy-Related Symptoms Assessment Scale every day during the treatment period (35 days). To rule out changes in the symptom experience being evaluated, we analysed the test–retest reliability based on two time points. The test–retest reliability for all items in the Radiotherapy-Related Symptoms Assessment Scale was reasonably high between baseline and both retest points. The high degree of agreement and good weighted kappa further support the reliability of the Radiotherapy-Related Symptoms Assessment Scale. The test–retest values confirmed that patients were following instructions correctly. Test–retest reliability studies should be performed in a stable but

Table 4 Responsiveness of the self-administered Radiotherapy-Related Symptoms Assessment Scale (RSAS) and the Health-Related Quality of Life Questionnaire (symptom experience)

Variables	Responsiveness, RSAS vs. QLQ-C30 Change[a] from baseline to 3 weeks		Responsiveness, RSAS vs. QLQ-C30 Change[a] from baseline to end of treatment	
	% agreement	Correlation RSAS vs. QLQ-C30	% agreement	Correlation RSAS vs. QLQ-C30
Fatigue	51	0.19*	48	0.17***
Insomnia	57	0.29**	58	0.36*
Pain	63	0.27**	62	0.40*
Loss of appetite	66	0.28**	71	0.40*
Dyspnoea	66	0.06	64	0.05
Cognitive impairment	60	0.30**	52	0.22**
Worry	55	0.29*	56	0.31*
Nausea	68	0.32*	73	0.48*
Sadness	59	0.24**	58	0.30*
Constipation	75	0.30*	73	0.37*
Diarrhoea	72	0.22***	73	0.32*

RSAS, Radiotherapy-Related Symptoms Assessment Scale; QLQ-C30, Health-Related Quality of Life Questionnaire.
[a]Changes classified as increase, equal or decrease.
***<0.05,
**<0.01,
*<0.0001.

heterogeneous population (35). The least stable response in this analysis was for the dyspnoea item. All of the above comparisons indicated that the Radiotherapy-Related Symptoms Assessment Scale was responsive to different circumstances. Further testing of responsiveness to change is required, particularly by repeated administration of the questionnaire in the same group of individuals over a sufficiently long period of time, so that comparisons can be made with other changes related to radiotherapy.

The Radiotherapy-Related Symptoms Assessment Scale included many of the symptoms experienced by patients with cancer according to Reeve at al. (23) and was inspired by and validated against an existing questionnaire (the EORTC QLQ C-30). In creating the Radiotherapy-Related Symptoms Assessment Scale, we also drew on the Theory of Unpleasant Symptoms, described by Lenz et al. (11). This theory describes three major perspectives: symptoms that the individual experiences, influencing factors that give rise to or affect the nature of and the consequences of the symptom experience. The Theory of Unpleasant Symptoms asserts that symptoms can occur alone or sequentially but that multiple symptoms are more often experienced simultaneously. Intensity is the most commonly measured symptom dimension. Furthermore, Lenz and colleagues discussed the quality of a symptom, which was defined as a description of what the symptom felt like. Quality can include the location of a given sensation and the degree to which a patient responds to a particular intervention and can also be used to distinguish among various pathological causes or to indicate severity. With the Radiotherapy-Related Symptoms Assessment Scale, we wanted to implement the theory in a more interactive fashion, as well as evaluating the distress dimension, which is why both symptom experience and distress are Radiotherapy-Related Symptoms Assessment Scale components. We found that patients experienced more than one symptom. The Radiotherapy-Related Symptoms Assessment Scale was created with this in mind, as well as specifically for patients with brain tumour undergoing proton beam therapy. Indeed, it proved useful in our study investigating symptom clusters in this precise group (36).

Limitations and strengths

Our findings must be interpreted in light of the limitations of this study. Given the structure of the questionnaire, it was not possible to assess all psychometric properties, such as internal consistency. Moreover, four symptoms could not be evaluated against the EORCTC QLQ-C30, indicating a need for further testing using more comprehensive criteria. Another limitation was that the questionnaire was only tested among patients with brain tumour.

Its applicability in other disorders has to be validated in future studies, by adapting the symptoms to other cancer diagnoses. One strength was that we were able to analyse longitudinal data, which allowed us to calculate responsiveness, a psychometric property rarely reported. That scales content validity is reinforced by including the most frequently reported symptoms among patients with cancer.

Implications for nursing

In health care, patients should be seen as partners not only in care, but in research. It is important for nurses to actively involve patients in the development and validation of tools to improve the quality of care. The present study included the target population during face and content validity, which potentially enhances the relevance of the scale for the target group. Clinically, the use of Radiotherapy-Related Symptoms Assessment Scale enables the patients to answer questions about their individual symptom experiences and the related distress. This can help the nurse and the patients design appropriate care plans that adjusts to their symptoms experience. The scale provides nurses with substantial information and requires little effort from the patient, given its short length. The instrument is useful for both research and clinical practice.

Conclusions

The findings in this study suggest that the Radiotherapy-Related Symptoms Assessment Scale is a reliable and valid instrument that can be used as to quantify symptom intensity and distress in patients with brain tumour undergoing PBT. Additional studies are ongoing to further assess its psychometric properties in patients with different cancer diagnoses undergoing conventional RT. We recommend that the Radiotherapy-Related Symptoms Assessment Scale be used to investigate patterns of single symptoms or concurrent symptom clusters among patients with cancer undergoing RT.

Conflicts of interest

All the authors declare no conflicts of interest.

Author contributions

UL, PF, BJ, EON, KS and KA were responsible for the study conception and design and also obtained funding. UL collected data and provided administrative, technical and material support. UL also drafted the manuscript and carried out data analyses. All authors made critical revisions of the manuscript for important intellectual content. Statistical expertise was provided by UL and KA who were responsible for supervision.

Ethical approval

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References

1 Atroshi I, Johnsson R, Sprinchorn A. Self-administered outcome instrument in carpal tunnel syndrome: reliability, validity and responsiveness evaluated in 102 patients. *Acta Orthopaedica Scand* 1998; 69: 82–8.

2 Mattsson M, Möller B, Lundberg I, Gard G, Boström C. Reliability and validity of the Fatigue Severity Scale in Swedish for patients with systemic lupus erythematosus. *Scand J Rheumatol* 2008; 37: 269–77.

3 Revicki DA, Wood M, Wiklund I, Crawley J. Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease. *Qual Life Res* 1997; 7: 75–83.

4 Revicki DA, Rentz AM, Luo MP, Wong RL. Psychometric characteristics of the short form 36 health survey and functional assessment of chronic illness Therapy-Fatigue subscale for patients with ankylosing spondylitis. *Health Qual Life Outcomes* 2011; 9: 36.

5 Bakhsh H, Ibrahim I, Khan W, Smitham P, Goddard N. Assessment of validity, reliability, responsiveness and bias of three commonly used patient-reported outcome measures in carpal tunnel syndrome. *Ortop Traumatol Rehabil* 2012; 14: 335–40.

6 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC, Kaasa S. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993; 85: 365–76.

7 Taphoorn MJB, Claassens L, Aaronson NK, Coens C, Mauer M, Osoba D, Stupp R, Marimanoff R, van den Bent M, Bottomley A. An international validation study of the EORTC brain cancer module (EORTC QLQ-BN20) for assessing health-related quality of life and symptoms in brain cancer patients. *Eur J Cancer* 2010; 46: 1033–40.

8 Dodd MJ. Occurrence of symptom clusters. *JNCI Monographs* 2004; 2004: 76–8.

9 Henoch I, Olsson C, Larsson M, Ahlberg K. Symptom dimensions as outcomes in interventions for patients with cancer: a systematic review. *Oncol Nurs Forum* 2018; 45: 237–49.

10 Lenz ER, Suppe F, Gift AG, Pugh LC, Milligan RA. Collaborative development of middle-range nursing theories: toward a theory of unpleasant symptoms. *ANS Adv Nurs Sci* 1995; 17: 1–13.

11 Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F. The middle-range theory of unpleasant symptoms: an update. *Adv Nurs Sci* 1997; 19: 14–27.

12 Polit DF, Beck CT. *Nursing Research: Generating and Assessing Evidence for Nursing Practice*. Philadelphia: Lippincott Williams & Wilkins, 2008.

13 Levin VA, Leibel SA, Gutin PH. Neoplasms of the central nervous system. In *Cancer: Principles and Practice of Oncology* (DeVita Jr VT, Rosenberg SA, Hellman S eds). Philadelphia, PA: Lippincott Williams and Wilkins, 2001; 2100–60.

14 Bitterlich C, Vordermark D. Analysis of health-related quality of life in patients with brain tumors prior and subsequent to radiotherapy. *Oncol Lett* 2017; 14: 1841–6.

15 Butler JM, Rapp SR, Shaw EG. Managing the cognitive effects of brain tumor radiation therapy. *Curr Treat Options Oncol* 2006; 7: 517–23.

16 Armstrong TS, Cohen MZ, Eriksen LR, Hickey JV. Symptom clusters in oncology patients and implications for symptom research in people with primary brain tumors. *J Nurs Schol* 2004; 36: 197–206.

17 Durand T, Bernier MO, Leger I, Taillia H, Noel G, Psimaras D, Ricard D. Cognitive outcome after radiotherapy in brain tumor. *Curr Opin Oncol* 2015; 27: 510–5.

18 Li J, Bentzen SM, Li J, Renschler M, Mehta MP. Relationship between neurocognitive function and quality of life after whole-brain radiotherapy in patients with brain metastasis. *Int J Radiat Oncol Biol Phys* 2008; 71: 64–70.

19 Scoccianti S, Detti B, Cipressi S, Iannalfi A, Franzese C, Biti G. Changes in neurocognitive functioning and quality of life in adult patients with brain tumors treated with radiotherapy. *J Neurooncol* 2012; 108: 291–308.

20 Tallet AV, Azria D, Barlesi F, Spano JP, Carpentier AF, Goncalves A, Metellus P. Neurocognitive function impairment after whole brain radiotherapy for brain metastases: actual assessment. *Radiat Oncol* 2012; 7: 77.

21 Durante M, Loeffler JS. Charged particles in radiation oncology. *Nat Rev Clin Oncol* 2010; 7: 37.

22 Stucky B, Pereira C, de Vet Henrica CW, Terwee CB, Mokkink LB, Knol DL. Measurement in medicine: a practical guide. *Qual Life Res* 2012; 21: 371–3.

23 Reeve BB, Mitchell SA, Dueck AC, Basch E, Cella D, Reilly CM, Minasian LM, Denicoff AM, O'Mara AM, Fisch MJ, Chauhan C, Aaronson NK, Coens C, Bruner DW. Recommended patient-reported core set of symptoms to measure in adult cancer treatment trials. *J Natl Cancer Inst* 2014; 106 7:

24 Wilde Larsson G, Larsson M, Starrin B. Quality of care. Development of a patient-centred questionnaire based on a grounded theory model. *Scand J Caring Sci* 1994; 8: 39–48.

25 Fayers PM, Aaronson NK, Bjordal K, Curran D, Grønvold M. *The EORTC QLQ C-30 Scoring Manual*, 3rd edn. 2001, European Organisation for Research and Treatment of Cancer, Brussels.

26 Patrick DL, Burke LB, Powers JH, Scott JA, Rock EP, Dawisha S, O'neill R, Kennedy DL. Patient-reported outcomes to support medical

product labeling claims: FDA perspective. *Value Health* 2007; 10: S125–S37.

27 Streiner DL, Norman GR, Cairney J. *Health Measurement Scales: A Practical Guide to Their Development and Use.* 2015. Oxford University Press, United Kingdom.

28 Langegård U, Ahlberg K, Björk-Eriksson T, Fransson P, Johansson B, Ohlsson-Nevo E, Witt-Nyström P, Sjövall K. The art of living with symptoms: a qualitative study among patients with primary brain tumors receiving proton beam therapy. *Cancer Nurs* 2020; 43: E79–E86.

29 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33: 159.

30 Kimberlin CL, Winterstein AG. Validity and reliability of measurement instruments used in research. *Am J Health Syst Pharm* 2008; 65: 2276–84.

31 Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn, 1988. Erlbaum, Hillsdale, NJ.

32 Bowling A. Just one question: if one question works, why ask several? *J Epidemiol Community Health* 2005; 59: 342.

33 Alfonsson S, Maathz P, Hursti T. Interformat reliability of digital psychiatric self-report questionnaires: a systematic review. *J Med Internet Res* 2014; 16: e268.

34 Wilde Larsson B. Touch-screen versus paper-and-pen questionnaires: effects on patients' evaluations of quality of care. *Int J Health Care Qual Assur* 2006; 19: 328–38.

35 Osoba D, Aaronson NK, Muller M, Sneeuw K, Hsu M-A, Yung WKA, Brada M, Newlands E. The development and psychometric validation of a brain cancer quality-of-life questionnaire for use in combination with general cancer-specific questionnaires. *Qual Life Res* 1996; 5: 139–50.

36 Langegard U, Johansson B, Bjork-Eriksson T, Fransson P, Ohlsson-Nevo E, Sjovall K, Ahlberg K. Symptom clusters in patients with brain tumors undergoing proton beam therapy. *Oncol Nurs Forum* 2019; 46: 349–63.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Responses to the Radiotherapy-Related Symptoms Assessment Scale (n = 175).

Table S2. Responses to selected items in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (n = 175).