The balancing act of living with symptoms

Patient-reported data and quality of care during and after treatment with proton beam therapy in patients with brain tumors

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Ge mig icke Din styrka
men stärk mig så jag kan finna min

Ge mig icke Din visdom
men säg mig var den har källan sin

Ge mig icke Ditt liv
men lev så jag kan leva mitt

Ge mig icke Din kärlek
men älska mitt hjärta fritt

Ge mig icke Din glädje
men var glad så jag kan finna min

Ta gärna ifrån mig min smärta
men gör den icke helt till Din

Björn Eidsvåg
/Sisela Kirkeby

Daniel

Elin

Mamma

ABSTRACT

This thesis focuses on patients with primary brain tumors undergoing proton beam therapy (PBT) and the consequences of the treatment. Quality of care (QoC) in a recently established clinic in Sweden was also evaluated. Furthermore, this thesis describes the development of the first comprehensive, prospective health and care science research project assessing patient-reported data related to PBT.

Study I - QoC in relation to health-related quality of life (HRQoL) was evaluated in patients with primary brain tumor given proton therapy. A need for quality improvement was identified for several aspects of care. More negative symptom experience during the treatment period led to greater perceived importance of specific support.

Study II - Symptom clusters among patients with primary brain tumor given PBT were explored. Three clusters were identified: *Mood*, *Reduced Appetit*e and *Reduced Energy*. Building knowledge about how these symptoms interact and are clustered can support healthcare professionals in more efficiently treating symptoms during and after PBT.

Study III - HRQoL, including acute side effects and associations between demographics and medical factors related to PBT, was investigated and compared with HRQoL related to conventional photon therapy (CRT). Global health/quality of life (QoL) deteriorated from baseline up to three months after treatment. The most pronounced symptom was fatigue.

Study IV - Grounded theory (GT) was applied and *The art of living with symptoms* emerged as the core concept in this qualitative study. It encompassed three interconnected symptom management processes expressed in the following concepts: *Adapting to limited ability*, *Learning about oneself* and *Creating new routines*. These concepts were summarized in a substantive theoretical model of symptom management.

The studies underlying this thesis revealed that patients with primary brain tumors experienced increased symptoms during the treatment period, and that they decreased gradually up to three months after the end of treatment. Healthcare professionals must clarify patients' needs for information and support related to symptoms and interventions and be aware that they change over time.

Keywords: brain tumor, proton beam therapy, conventional radiotherapy, illness, symptom experience, symptom cluster, health related quality of life, quality of care

SAMMANFATTNING PÅ SVENSKA

Det är väl känt att personer med hjärntumör besväras av olika symtom som är relaterade till sjukdomen och/eller till behandlingen. Tidigare forskning beskriver att kognitiva besvär, synrubbningar, huvudvärk, kramper och kraftlöshet är det som är mest besvärande. I Sverige får drygt 1400 personer diagnosen hjärntumör varje år. Tumörer i hjärnan drabbar människor i alla åldrar, men är vanligast bland personer över 60 år. Hjärntumörer kan vara både elakartade och godartade. Kirurgi och strålbehandling är de vanligaste metoderna för att behandla hjärntumörer. För att behandla elakartade hjärntumör krävs även cytostatika.

Strålbehandling med fotoner är den vanligaste metoden men idag finns även strålbehandling med protoner som alternativ i Sverige. Behandling med protonstrålning går att styra mer precist än konventionell strålning med fotoner, vilket kan minska risken för biverkningar. Avhandlingens huvudsakliga syfte var att beskriva och jämföra effekt, påverkan och upplevelse av symtom utifrån patientens perspektiv, där behandling med protonterapi ges, jämfört med konventionell strålbehandling. Vi har även undersökt hur patienterna upplever vårdkvalitén. Studierna har genomförts på Skandionkliniken i Uppsala samt strålbehandlingsavdelningarna på universitetssjukhusen i Lund, Göteborg, Linköping, Örebro, Stockholm, Uppsala och Umeå.

Patienter har inkluderats i studierna under 4 år, 2015-2018. Data har insamlats med både kvantitativa och kvalitativa metoder genom enkäter som mäter symtom, hälsorelaterad livskvalitet, tillfredsställelse med vården samt intervjuer. I den första studien undersöktes hur patienterna upplevde vårdkvalitén på Skandionkliniken. Totalt deltog 186 patienter och vi identifierade att det fanns behov av förbättringar kring vården gällande information om symtomlindring. Ju högre grad av symptom desto mer behov av stöd gällande symtomhantering. I den andra studien undersöktes hur olika symtom påverkar varandra, en så kallad klusteranalys. Tre symtomkluster identifierades: sinnesstämning, nedsatt aptit samt nedsatt energi. Kunskap om hur dessa symtom påverkar varandra kommer att bidra till att vårdpersonal effektivt kan lindra symtom hos patienter som genomgår protonbehandling. I den tredje studien jämfördes upplevelsen av akuta symtom och hälsorelaterad livskvalité vid behandling med protoner eller konventionell behandling med fotoner. Resultatet visade ingen skillnad mellan grupperna. Inom protongruppen försämrades livskvalitén från start av behandling och upp till tre månader. I den fjärde studien genomfördes intervjuer med 22 patienter. Syftet var att förstå hur personer med hjärntumör som genomgår strålbehandling med protoner hanterar sina symtom. Resultatet visade att deltagarna använde sina egna resurser för att uppnå bättre symtomhantering. Deltagarna förmedlade att de levde ett tillfredsställande liv trots en mängd symtom.

Denna avhandling har identifierat att patienter med primär hjärntumör som genomgår protonbehandling upplever ökad grad av symtom under behandlingsperioden som gradvis minskar tre månader efter avslutad behandling. Dessa personer har specifika behov som sjukvården behöver ha kunskap om för att kunna stödja patienten i det akuta skedet och förändringen över tid.

Resultatet kommer att ligga till grund för kliniska beslutsprocesser, både under pågående projekttid och framöver. Vidare för studier där olika strategier för att förbättra patienternas hälsorelaterade livskvalitet och situation i samband med protonterapi kan undersökas.

LIST OF STUDIES

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Ulrica Langegård, MSc, RN, Karin Ahlberg, PhD, Assoc Prof, RN, Per Fransson, PhD, Assoc Prof, RN, Birgitta Johansson, PhD, Assoc Prof, RN, Katarina Sjövall PhD, RN, Thomas Bjork-Eriksson, PhD, Assoc Prof, MD, Emma Ohlsson-Nevo, PhD, RN.

Evaluation of quality of care in relation to health-related quality of life of patients diagnosed with brain tumor: A novel clinic for proton beam therapy.

Supportive Care of Cancer 2018; Nov 27

II. Ulrica Langegård, MSc, RN, Birgitta Johansson, PhD, Assoc Prof, RN, Thomas Bjork-Eriksson, PhD, Assoc Prof, MD, Per Fransson, PhD, Assoc Prof, RN, Emma Ohlsson-Nevo, PhD, RN, Katarina Sjövall PhD, RN, Karin Ahlberg, PhD, Assoc Prof, RN.

Symptom Clusters in Patients With Brain Tumors Undergoing Proton Beam Therapy.

Oncology Nursing Forum 2019; May 1

III. Ulrica Langegård, MSc, RN, Per Fransson, PhD, Assoc Prof, RN, Birgitta Johansson, PhD, Assoc Prof, RN, Thomas Bjork-Eriksson, PhD, Assoc Prof, MD, Emma Ohlsson-Nevo, PhD, RN, Katarina Sjövall PhD, RN, Karin Ahlberg, PhD, Assoc Prof, RN.

Protons or photons? Health-related quality of life in patients with brain tumors treated with proton beam therapy or conventional photon radiotherapy.

Submitted

IV. Ulrica Langegård, MSc, RN; Karin Ahlberg, PhD, Assoc Prof, RN ; Thomas Bjork-Eriksson, PhD, Assoc Prof, MD; Per Fransson, PhD, Assoc Prof, RN; Birgitta Johansson, PhD, Assoc Prof, RN; Emma Ohlsson-Nevo, PhD, RN; Petra Witt-Nyström, Phd, MD; Katarina Sjövall PhD, RN.

The art of living with symptoms: A qualitative study in patients with primary brain tumors receiving proton beam therapy.

Cancer Nursing, 2019; Jan 25.

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CONTENT

ABBREVIATIONS

CNS	Central nervous system
CRT	Conventional radiotherapy
GT	Grounded Theory
HRQoL	Health Related Quality of Life
PBT	Proton beam therapy
PCC	Person-centered care
PCSG	Proton Care Study Group
PR	Perceived reality
PRO	Patient-reported outcome
QoC	Quality of Care
QoL	Quality of life
ROS	Reactive oxygen species
RT	Radiotherapy
SD	Standard deviation
SI	Subjective importance
TOUS	The Theory of Unpleasant Symptoms
WHO	World Health Organization

INTRODUCTION

This thesis investigates patient-reported outcomes (PROs) in patients with primary brain tumors who have undergone radiotherapy (RT). Patients with both malignant and benign tumors who required RT were included. Symptoms and PROs related to benign CNS tumors are often overlooked, as they are not categorized as cancer and patients are, in many cases, not followed up.

When a person is diagnosed with a tumor 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.

Today, conventional radiotherapy therapy (CRT) with photons is the most common RT technique for treatment of primary brain tumors. Numerous PROs for patients who have undergone CRT can be found in the literature. There is ongoing research in the field of RT, aimed at finding a treatment method that spares healthy tissue and generates fewer unpleasant symptoms.

In August 2015, the first proton beam therapy (PBT) clinic in Scandinavia, the Skandion Clinic, began treating patients. PBT offers the possibility to reduce non-desirable radiation doses to healthy brain tissue, mainly due to the advantageous physical properties of protons, compared to CRT. The evidence base regarding brain tumor patients' experiences of PBT is sparse and there was thus an urgent need to evaluate the PROs evidence for this technique.

Previous research has demonstrated substantial unmet needs in this group of patients. When introducing a new treatment modality, it is important to investigate Quality of Care (QoC) in relation to Health-Related Quality of Life (HRQoL), including symptoms. It was thus necessary to study patients' experienced HRQoL and associated symptoms related to PBT. This thesis aimed at investigating symptom experience and HRQoL during and up to three months after PBT, and the related importance of the QoC.

BACKGROUND

Protons have more advantageous dosimetric properties than photons. The question is whether this makes any difference to patients treated with PBT instead of CRT when it comes to their experienced HRQoL, including treatment-related symptoms. This thesis is based on patient-reported data, thus enabling inclusion of a personal aspect in the description of symptoms. Incorporating patients' perspectives is critical when evaluating treatment outcomes, clinical care and quality performance. Patient-reported data can be compiled either by self-reports or through interviews (U.S. Department of Health et al., 2006; Patrick et al., 2007). The main studied concepts in this thesis are symptom experience, symptom clusters, HRQoL and QoC. These concepts were chosen as they represent the implications of living with a brain tumor during treatment and up to three months after the end of treatment.

The Skandion clinic

The construction of Skandion Clinic was initiated in June 2011, and the first patients were treated on August 31, 2015. The initial and most frequently treated group at the Skandion Clinic is patients with primary brain tumors. The Skandion Clinic is designed to treat 1 000 patients with PBT per year, with the option of future expansion. Given the Swedish population of 10 million inhabitants, approximately 2 200 patients per year may potentially benefit from PBT. This constitutes approximately 15% of all irradiated patients, although there is substantial variation between tumor types. The Skandion Clinic is expected to provide the opportunity to scientifically assess whether PBT can reduce the side effects associated with other modern forms of RT applied for curative purposes. The goal was that at least 80% of patients at the Skandion Clinic should be included in different clinical trials (Glimelius et al., 2005). During the treatment period, (five-six weeks), most of the patients stay in single rooms at a hotel located in the same building as the Skandion Clinic, accompanied by a family member if they wish. All meals are served in the hotel dining room. On each floor, there are lounges for common activities. No healthcare staff work in this part of the building.

The ProtonCare Study Group

The ProtonCare Study Group (PCSG) was established in the autumn of 2013, when members were commissioned by the Skandion Clinic management to conduct research in conjunction with PBT. The group's goal was to conduct research from a health and care science perspective, in collaboration with the diagnosis-specific research groups at the Skandion Clinic, for instance concerning the protocol for CNS tumors (PRO-CNS, 2015). The PCSG members are nurses with various knowledge

profiles from different universities and from the seven Swedish university hospitals, all of which share the governance of the Skandion Clinic. The group members have extensive experience in health and care science research in the area of cancer care, including PROs in conjunction with RT, as well as broad knowledge of various qualitative and quantitative research methods. The PCSG also collaborates with other professionals, such as dieticians and physiotherapists.

Brain tumors

Primary brain tumor is a relatively infrequent disease that is subdivided into benign and malignant types and classified according to the World Health Organization (WHO) classification (Louis et al., 2016), ranging, for instance, from grade I meningioma to grade IV glioblastoma. Brain tumors are unlike systemic tumors, as they tend to be unifocal and they do not metastasize outside the CNS. Although malignant brain tumors predominantly occur in adults around age 60, they are also common solid tumors in children (Vargo, 2017). Benign tumors are often discovered incidentally or present with only mild symptoms and indolent growth patterns (Combs et al., 2013; El Shafie et al., 2018). About 296 000 people are diagnosed with brain tumors annually worldwide (1.6 % of tumor sites) (Bray et al., 2018). In Sweden, approximately 1 400 people are diagnosed with primary brain tumors each year, and approximately 50% of these tumors are malignant (National Board of Health and Welfare, 2017).

The vast majority of intracranial malignancies are grade IV astrocytomas, more commonly referred to as glioblastomas, which account for 66% of all malignant brain tumors (Vargo, 2017). A grade IV tumor will most likely already have disseminated throughout the brain. It has been estimated that only 0.4-2.0% of all glioblastomas metastasize; this low number might be due to the fact that glioblastoma is a very rapidly progressing disease, leaving only a small time window for cells to migrate before having a lethal effect (Beauchesne, 2011). Glioblastoma almost invariably recurs 2-3 cm from the initial tumor location, leading to the patient´s demise within approximately 15 months after diagnosis (Giese, Bjerkvig, Berens, & Westphal, 2003; Wen & Kesari, 2008). Due to this invasive nature, radiation oncologists previously considered this malignancy to be a systemic disease and thus irradiated the whole brain, but concerns over toxicity have led to more localized treatment. Glioma classifications include lower grade (I-III) astrocytoma, oligodendroglioma, ependymoma, and some additional rare tumors (Vargo, 2017). Anaplastic and diffuse astocytoma (grades II and III) can progress to secondary glioblastoma, which make up less than 10% of all glioblastomas (Ohgaki & Kleihues, 2013). Other primary brain tumors include pituitary and nerve sheath tumors and meningioma, which are usually benign (Vargo, 2017). Meningiomas are slow-growing tumors and account for 20% of intracranial tumors, roughly 94% of which are regarded as benign. This

thesis includes patients with malignant brain tumors and those with life-threatening benign brain tumors that require PBT or CRT treatment.

Symptom experience in patients with primary brain tumors

Brain tumors differ significantly from other forms of cancer due to the unique neurocognitive symptoms and the higher symptom load (Ford, Catt, Chalmers, & Fallowfield, 2012). Upon diagnosis, patients must deal with the implications of a life-limiting illness while coping with the symptoms, which can be severe and progressive (Cavers et al., 2012). Malignant and benign CNS tumors may not be two distinct separate categories when it comes to symptom experience prior to treatment, during treatment and months after treatment (Combs et al., 2013; Combs, Ganswindt, Foote, Kondziolka, & Tonn, 2012; El Shafie et al., 2018). The effect on quality of life (QoL) related to the symptoms may be just as severe, and the tumor may also be incurable in some cases with a benign diagnosis (Combs et al., 2012). Many of the symptoms, and degree of symptom severity, related to CNS tumors are similar, regardless of whether they are benign or malignant, or low-grade (I-II) or high-grade (III-IV). This may also apply to the acute and late toxicity related to RT, that frequently increases during treatment. The primary symptoms in brain tumor patients are headache, anorexia, nausea, vomiting, seizures, sleeping longer at night and drowsiness (Armstrong et al., 2015; Butowski & Chang, 2007; Catt, Chalmers, & Fallowfield, 2008a; Janda et al., 2008; Levin, Leibel, & Gutin, 2001; Omuro & DeAngelis, 2013). Most patients also experience symptoms such as fatigue and double vision (Flechl et al., 2017; Wen & Kesari, 2008). For patients with brain tumors, cognitive decline is reported to have a significant impact on QoL (Jzerman-Korevaar, Snijders, de Graeff, Teunissen, & de Vos, 2018; Li, Bentzen, Li, Renschler, & Mehta, 2008). These impairments are a major cause of disability for individuals with brain tumors and are frequently identified by patients and their caregivers as the single greatest cause of suffering (Locke et al., 2008). Seizures are common and this may impact employment, social interactions and independence (Englot, Chang, & Vecht, 2016). Another source of suffering and decreased QoL is emotional distress (Pelletier, Verhoef, Khatri, & Hagen, 2002). Previous research shows that these symptoms are commonly amplified during CRT, and negatively affect patients' daily life (Durand et al., 2015; Giovagnoli et al., 2014; Scoccianti et al., 2012) and HRQoL (Bitterlich & Vordermark, 2017).

Treatment modalities in patients with primary brain tumors

Glioblastoma is managed by surgically removing as much of the tumor bulk as is considered safe, followed by fractionated RT (typically 60 Gy in 30-35 fractions), and concurrent chemotherapy, which is given continuously for at least an additional six months after cessation of RT (Mrugala, 2013; Stupp et al., 2005; Thurin et al., 2018). Small asymptomatic meningiomas can be monitored frequently until they

become symptomatic (Combs et al., 2012). Total surgical resection of meningioma is generally the treatment of choice, since it results in long-term disease-free survival in a majority of patients. Adjuvant RT can be administered as necessary. RT does not eradicate a benign tumor but removes its capability for growth (Lesueur et al., 2019). The follow-up for patients in this category may be long, even as long as for tumors that are more malignant.

Radiotherapy

Currently, RT is given to about half of all cancer patients (Begg, Stewart, & Vens, 2011; Grunert et al., 2018). The mechanism of action is to induce single- and double-stranded breaks in the DNA, leading to chromosomal abnormalities and, consequently, cell death (Thompson, 2012). Moreover, reactive oxygen species (ROS) are produced by the ionizing radiation that is a component of RT. ROS can have some anti-tumorigenic effects, which enhance RT effects and can lead to cell death via several mechanisms. It is currently still common to use photons as the source of radiation. The CRT dose is highest at the point of entry to the target. It diminishes as it goes through the body, so that the radiation is higher entering the body and lower when it exits the body. Photons also pass through the tumor, so that the radiation affects healthy tissue. Extensive previous research has shown that CRT causes acute and long-term side effects (Durand et al., 2015). Acute side effects occur during and immediately after completion of treatment, while late side effects may occur from months (<90 days) to several years after completion (Bentzen, 2006).

PBT is a type of RT in which protons rather than photons are used. The difference between photon and proton therapy is that proton beams can be more precisely controlled in depth. PBT uses the unique dose distribution of protons, as they slow down at the site of the tumor and release their energy inside the tumor (Figure 1).
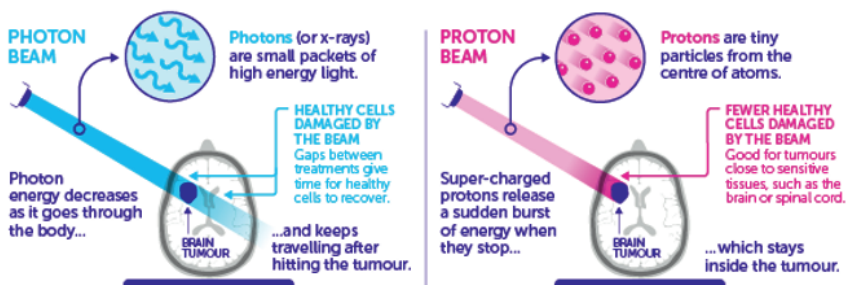

Figure 1. The difference between photon and proton RT. RT targets tumors with a beam of energy that damages DNA and leads to apoptosis.

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However, the proton beam does not go beyond the tumor. The clinical benefit of PBT thus consists of a lower risk of normal tissue toxicity due to the lower delivered dose outside the target tissue, compared with CRT (Adeberg et al., 2016; Glimelius et al., 2005; Hu, Jiang, Cui, Zhang, & Yu, 2018; Maquilan, Grover, Alonso-Basanta, & Lustig, 2014; Thurin et al., 2018; Yuh et al., 2004).

Theoretical concepts and framework

This thesis is based in health and care science research, in which the discipline of nursing plays an important role in generating knowledge. Furthermore, middle-range theories are part of the discipline of nursing and have the potential to guide research and provide the basis for effective research and interventions in practice. They may be developed inductively through qualitative research and practice observations, or deductively through logical analysis and synthesis. Middle-range theories address the substantive knowledge of the discipline by explaining and expanding on specific phenomena related to the nursing process. The philosophies guiding the abstract views of human beings, human-environment interaction and health and caring are reflected in each of the paradigms (Smith & Liehr, 2018).

The Theory of Unpleasant Symptoms

The middle-range Theory of Unpleasant Symptoms (TOUS) has served as the theoretical framework in this thesis, as it captures several aspects of the symptoms in focus.

The theory was created in 1995 by Lenz, Suppe, Gift, Pugh, & Milligan (1995), with the purpose of improving understanding of the symptom experience in various clinical situations, as well as diminishing the negative effects of these experienced symptoms. The TOUS was developed inductively from specific to general, and from concrete observation in practice environments to theoretical ideas. It was first published in Advances in Nursing Science in 1995 (Lenz et al., 1995). As the TOUS was developed, it emerged that there were sufficient commonalities among symptoms to warrant not restricting the theory to one symptom. Instead, the TOUS can explain, and guide research and practice regarding, an array of unpleasant symptoms. Two years later, the theory was presented in an updated version, that asserts that while symptoms can occur alone or isolated from one another, more often multiple symptoms are experienced simultaneously or one symptom can lead to another, e. g. anxiety may result in sleep disorder (Lenz, Pugh, Milligan, Gift, & Suppe, 1997) (Figure 2).

The TOUS comprises three overarching concepts: *symptoms, influencing factors* and *performance*. According to the theory, symptoms vary in *intensity*, *distress*,

timing and *quality*. The *intensity* dimension can be described as the severity or the strength of the symptom. The *timing* dimension reflects how the symptoms vary in frequency and duration. The *distress* dimension reflects the degree to which an individual is bothered by the symptom, and refers to the meaning he/she ascribes to it. The last dimension in the TOUS *symptoms* concept is *quality*, which enables inclusion of a personal aspect. This aspect requires a qualitative approach in research and the patients must be able to describe the experience of the symptom (Lenz et al. 1997).

The *influencing factors* have been divided into *physiological factors*, *psychological factors* and *situational factors*. The *physiological factors* involve anatomical, physiological, genetic and treatment-related variables, and are described as influencing the occurrence of symptoms and how they are experienced. The *psychological factors* are described as one of the more complex components of the model, and include both affective and cognitive variables. These variables, e.g. anxiety, sadness and cognitive impairment, may affect the individual response to the symptom and can possibly intensify it. The *situational factors* cover the social and physical environment. Examples of situational factors are marital status, socioeconomic status, lifestyle behaviors and social support. According to the TOUS, the physical environment also influences the experience of symptoms. All of the three influencing factors may interact with each other, as well as affecting the *symptom* experience (Lenz et al. 1997).

The authors have defined the outcome of the first two concepts as *performance*, described as the consequences of the symptom experience. A symptom or a
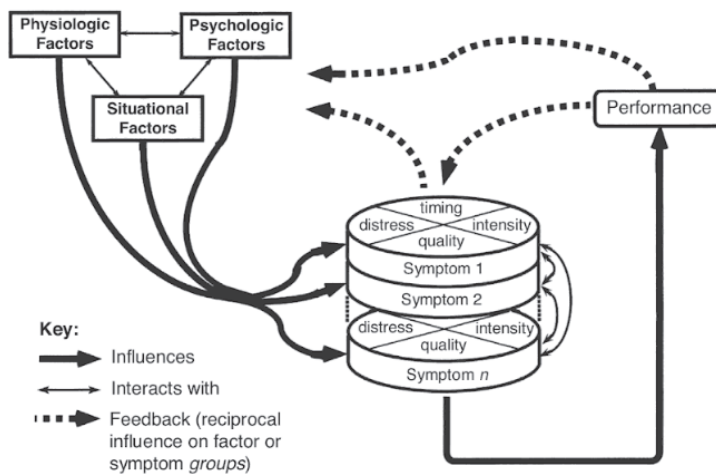

Figure 2. The Theory of Unpleasant Symptoms
Source: Reprinted with permission from Lenz, E. R., Pugh, L.C., Milligan, R. A., Gift, A.G., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: An update. Advances in Nursing Science, 19(3), 17.

symptom cluster may yield a number of different *performance* outcomes (e. g. cognitive impairment, reduced capacity to work or worsened financial situation), and it is assumed that the symptom experience can impact a person´s ability to function. The theory includes feedback loops to indicate that influencing factors can affect the symptom experience, symptoms can affect performance and performance can in turn affect influencing factors and the symptom experience (Lenz et al. 1997).

Illness

Illness is conceptualized as an experience of changes in bodily processes and the appraisal of these processes as serious or requiring treatment (Kleinman, 1988). Moreover, illness is a change in condition or social function experienced by the individual. A person's experience of illness is always subjective. In fact, illness is the disease understood in terms of its meaning for the individual (Benner & Wrubel, 1989), involving not only the biological body but the individual's own existence. This means that individuals' worldviews change when they experience illness (Toombs, 1987). Each illness has its own temporal nature. A common illness trajectory entails a predictable decline in physical health over a period of time spanning weeks, months or years (Lynn & Adamson, 2003). Illness both brings particular meanings to a sick person's lifeworld (e.g. the threat of death, the loss of valued body image or a new way of seeing and living in one's world heretofore taken for granted) and also crystallizes those special meanings in his/her world that constitute and express a particular form of life (Kleinman, 1988). Symptoms are an expression of illness. The symptom experience includes an individual's perception of a symptom, evaluation of the meaning of a symptom and response to a symptom (Dodd et al. 2001).

The symptom experience

Symptom experience is the primary reason that patients seek healthcare, and symptom management is a critical component of oncology nursing care (Rutledge & McGuire, 2004). Symptoms may be an outcome or a consequence of the disease itself or of the associated treatment. The word "symptom" can be traced to its Latin origin synthoma. It was first used in its present sense in the seventeenth century (Rhodes & Watson, 1987). Efforts to describe symptoms have shown that each symptom has an associated constellation of shared dimensions. These commonalities include intensity (strength), timing (duration and frequency), level of perceived distress and quality (Lenz et al., 1997). Several theories have been developed in an attempt to explain the occurrence of symptoms and the relation of symptoms to other factors (Lenz et al., 1997; Leventhal & Johnson, 1983; Rhodes & Watson, 1987). In Leventhal's and Johnson's theory of self-regulation, symptoms are concrete representations of disease experienced by individuals as a component

of cognitive processing. Their work highlights the differentiation between the occurrence of a symptom (a concrete, objective event) and the emotional response to that event. Dodd et al. subsequently defined symptoms as a subjective experience of altered functioning, which cannot be objectively observed (Dodd, Miaskowski, & Paul, 2001). This definition is based on a subjective assessment, and it implies that the symptom can only truly be known and described by the person experiencing it, who should be the only one to report it. In this thesis, the definition by Lenz et al. (1997), according to which symptoms are "perceived indicators of change in normal functioning as experienced by patients", is used. They conceptualized each symptom as a multidimensional experience that can be assessed separately or in combination with other symptoms (Lenz et al., 1997).

Moreover, symptom distress associated with disease-related symptoms or treatment-related side effects is part of the experience of patients with malignant disease. Distress has a multifaceted meaning and is particularly important in nursing practice, education and research, in order to detect disease, promote the speed of recovery, maintain health and enhance HRQoL. The phrase "symptom distress" was originally used in McClorke and Yung´s (1978) definition, applied in development of the Symptom Distress Scale, i.e. "the degree of discomfort from the specific symptom(s) being expressed (and) as perceived by the patient" (p.374). Rhodes and Watson opine that symptom distress is the physical or mental suffering resulting from the experience of symptom occurrence and/or the perception of feeling states (Rhodes & Watson, 1987). According to Lenz et al. (1997), the distress dimension of the symptom experience refers to the degree to which the person is bothered by it. A symptom of a given severity can be incapacitating to some individuals but much less bothersome to others. For this reason, distress is another component of symptoms that can be measured with self-report questionnaires or through narratives.

Symptom clusters

Symptoms seldom occur in isolation in patients with cancer (Rutledge & McGuire, 2004). Clustering of symptoms occurs when patients experience multiple related symptoms concurrently (Xiao, 2010). One discrepancy in the existing definitions is the minimum number of symptoms constituting a cluster. Dodd et al. (2001) and Miaskowski, Dodd and Lee, (2004) suggested that at least three interrelated symptoms (e.g. pain, fatigue and sleep disturbances, or nausea, vomiting and poor appetite) constitute a cluster, whereas Kim et al. (2005) recommended a minimum requirement of only two symptoms. The definition of symptom clusters by Kim et al. indicates that the symptoms must be related to each other, occur together, be a stable group and be relatively independent of other clusters (Kim et al., 2005). A set of multiple symptoms differs from a symptom cluster by only including symptoms that occur simultaneously, whereas symptoms in a symptom cluster

must be related to each other, as well as occurring simultaneously. Symptoms within a cluster are not required to share the same etiology; for instance, pain may be caused by the disease, fatigue by the disease or the treatment and sleep disturbances by chemotherapy or anxiety. Symptom clusters may have an adverse effect on patient outcomes and may have a synergistic effect as a predictor of patient morbidity (Dodd, Janson et al., 2001; Dodd et al., 2001). The National Cancer Institute's Symptom Management and Health-Related Quality of Life Steering Committee (Reeve et al., 2014) identified a core symptom set that should be assessed across oncology trials to better understand treatment efficacy and toxicity and facilitate cross-study comparisons. This symptom set consists of fatigue, insomnia, pain, anorexia, appetite loss, dyspnea, cognitive problems, anxiety (including worry), nausea, depression (including sadness), sensory neuropathy, constipation and diarrhea. This has caused research to shift from a single symptom approach, in order for clinicians to better understand symptom experience and symptom clusters, as well as improving symptom management (Xiao, 2010).

Health-Related Quality of Life

There is no single, universally agreed-upon definition of QoL. QoL is a multi-dimensional outcome indicator that theoretically incorporates all aspects of an individual's life (Bowling, 1995; Ferrans, 1990). QoL can be defined as "a person´s sense of wellbeing that stems from satisfaction or dissatisfaction with areas of life that are important to him/her" (Ferrans, 1990). When defining QoL as it applies to healthcare, the term "health-related" is commonly used to focus on the effects of health, illness and treatment (Ferrans & Hacker, 2000). HRQoL is based on subjective assessment and, according to Osoba et al. (1996) and Aaronson et al. (1993), HRQoL can only truly be known and described by the person experiencing it. It includes the following dimensions: psychological /emotional functioning, physical functioning, social functioning and disease-specific symptoms. A HRQoL study can either be generic or specific to a disease. A generic HRQoL inventory does not include disease-specific questions, and can therefore be used and compared across populations. A disease-specific questionnaire includes disease- and treatment-specific characteristics, and can therefore not be used in other populations. The number of research papers on HRQoL in brain tumor patients is substantial. However, the literature describing HRQoL in relation to PBT in this patient group is more limited.

Quality of Care

QoC is considered to be a multidimensional concept. In the early 1980s, Vuori (1982) stated that it was difficult to define. Vuori recommended that researchers using the concept describe their perspective by clarifying quality for whom,

defined by whom, as well as the aspect of quality to which they are referring. In addition, Donabedian's work (1980) describes the structure, process and outcome model by taking a classic approach to the discussion and assessment of QoC. He emphasized that the interpersonal process is crucial to the outcome of a patient's perception of care quality, and stated that the assessment of quality must rest on a conceptual and operationalized definition of what QoC means (Donabedian, 1980). Researchers have developed the concepts further; Wilde et al. (Wilde, Starrin, Larsson, & Larsson, 1993) conceptualized QoC as multidimensional and a measure of patients' experiences of the quality of the healthcare encounter, entailing both their perceptions of the care received and the importance they attributed to the different aspects of care. Patients' perceptions of what constitutes QoC are formed by their system of norms, expectations and experiences and by their encounters with an existing care structure (Wilde et al., 1993). The WHO considers QoC to be a concern because of the wide variance in care delivered within and between healthcare systems, and it includes four dimensions in its definition: professional management of care, minimal risk of harm to the patient, effectiveness and patient satisfaction (WHO, 1989). Patients' views of what is important in connection with the care they receive may be seen as an aspect of quality, and patient satisfaction has increasingly come to be used as an indicator of this quality. High satisfaction with care is associated with better clinical outcomes, such as improved physical function and HRQoL (Yamamoto et al., 2015). It is important to assess patient-reported satisfaction with care, as it may influence adherence to treatment and therefore affect disease outcome (Hirji et al., 2013). However, an often-mentioned limitation of patient-reported satisfaction with care is that it is influenced by the patient's expectations. The literature concerning patient satisfaction with care is extensive. Previous research of satisfaction with care have shown high overall satisfaction (Al-Mailam, 2005; Fröjd, Swenne, Rubertsson, Gunningberg, & Wadensten, 2011; Grøndahl, Karlsson, Hall-Lord, Appelgren, & Wilde-Larsson, 2011; Thi, Briancon, Empereur, & Guillemin, 2002). Elucidating factors associated with patient satisfaction may be helpful in assessing QoC.

RATIONALE

Brain tumor patients may be faced with many demanding challenges, including symptom experience and major changes in their daily life. It is well known that conventional RT causes acute and late symptoms that affect various organs and functions. There is currently no optimal treatment modality regarding both tumor response and decreased negative symptom experience for this group of patients.

The evidence regarding how patients treated with PBT experience symptoms during and after treatment is sparse, despite PBT having been administered for a long time at various institutions worldwide. Knowledge about the symptom management process and how it affects primary brain tumor patients' everyday life is essential to enhance understanding of their experiences and needs. Against that background, investigation of PROs in patients with brain tumors undergoing PBT is crucial. Moreover, when starting up a new healthcare organization, such as the Skandion Clinic, it is important to ensure high QoC in relation to HRQoL so that patients feel their needs have been met.

The increased knowledge generated from this thesis will hopefully contribute to improved support and care for brain tumor patients given PBT.

AIMS

The overall purpose of this research project was to investigate the symptom experience and HRQoL in patients with primary brain tumors that underwent PBT in a recently established clinic.

Specific aims

Study I   The aim of this study was to describe the patient perspective on QoC and its associations with HRQoL in brain tumors patients undergoing PBT in a newly established PBT clinic.

Study II   The aim of this study was to explore symptom clusters that occurred during PBT in patients with primary brain tumors, and investigate associations between demographic variables and comorbidity and symptom clusters in this patient group.

Study III The aim of this study was to investigate HRQoL, including acute side effects, and associations with demographic and medical factors in patients with primary brain tumors treated with PBT or CRT.

Study IV   The aim of this study was to explore the process of symptom management in patients with brain tumors receiving PBT.

METHODS

Design

The studies reported in this thesis had a prospective, longitudinal, multicenter design. Multiple scientific approaches were used to achieve the overall aim. A full understanding of how patients experience their situation, related to their disease and treatment, and how it affects their life required both qualitative and quantitative approaches. The core component was quantitative, with a complementary qualitative component. All four studies included self-reported data with focus on QoC, symptom experience, HRQoL and symptom management. The designs were guided by the aims of the studies. An overview of study designs is shown in Table 1.

The deductive research component (Papers I-III) aimed at evaluating QoC, as well as exploring symptom clusters and experiences and predictors of HRQoL. The respective chosen designs were prospective, longitudinal and descriptive (Paper I), prospective, longitudinal and explorative (Paper II) and prospective, longitudinal and comparative (Paper III).

A qualitative approach was adopted in Study IV. The inductive research component in this study aimed at understanding the major concerns of patients with primary brain tumors given PBT. A Grounded theory (GT) method, as described by Glaser and Straus (1967), was chosen to explore the process of symptom management in this group.

Power calculation

A power analysis, based on a two-sample t-test/Fisher's non-parametric permutation test for CRT vs PBT, yielded an estimate that 175 patients in the PBT group and 50 patients in the CRT group were needed in order to obtain accurate estimates. This was calculated based on a statistical power of 80% and a two-tailed probability of 0.05, assuming that the difference, in change from baseline to three months after treatment, between the two groups would be 1.6, with a standard deviation (SD) of 3.5. The estimations of the mean and SD were adopted from observations concerning the main variable *general fatigue* in the MFI-20 and an estimated 5% dropout of patients over time. A clinically significant difference of 1.6 between the two groups corresponds to 10%. Allocation to the two groups in 7:2 proportions corresponds to 175:50; thus, *n*=225 in total.

Setting

Studies I-III

All seven RT departments at the Swedish university hospitals (in Lund, Göteborg, Linköping, Örebro, Stockholm, Uppsala and Umeå) were involved, together with the Skandion Clinic, in the process of recruiting participants to the studies. The Skandion Clinic is organized according to a model of distributed competence and shared governance, in which all clinical experts collaborate closely with clinicians at the respective local departments (Karlsson et al., 2006). All preparations, including fixation, computed tomography and treatment planning, are undertaken at the local department. The patients' treatment plans and immobilization devices are transferred to the Skandion Clinic, which is responsible for administering the PBT and for clinical evaluations during treatment. After completion of the PBT, the patients are referred back to their local departments for long-term follow up.

Table 1. Overview of the studies in the thesis

	Study I	Study II	Study III	Study IV
Design	Prospective, longitudinal, descriptive, quantitative study	Prospective, longitudinal, explorative, quantitative study	Prospective, longitudinal, comparative quantitative study	Prospective, longitudinal, qualitative study
Data collection	Questionnaires QPP, SCQ, EORTC QLQ-C30	Questionnaires RSAS, SCQ	Questionnaires EORTC QLQ-C30, BN20, SCQ	Individual and repeated interviews
Outcomes	QoC and HRQoL	Symptom cluster and influencing factors	Symptom experience and HRQoL	Symptom management
Participants	(n=186)	(n=187)	(n=255)	(n=22)
Data analysis	Descriptive statistics, comparison between groups, rank correlations.	Descriptive statistics, explorative factor analysis, linear regression analyses	Descriptive statistics, comparison between groups, rank correlations	Constant comparative method with classic GT[*]

QPP=Quality from the Patient's Perspective (B. Wilde et al., 1993)
SCQ=Self-Reported Comorbidity Questionnaire (Sangha, Stucki, Liang, Fossel, & Katz, 2003)
RSAS=Radiotherapy-Related Symptom Assessment Scale
EORTC QLQ-C30= European Organisation for Research and Treatment of Cancer, Quality of Life Instrument (Aaronson et al., 1993)
EORTC BN20= European Organisation for Research and Treatment of Cancer, Diagnosis-Specific Instrument (Taphoorn et al., 2010)
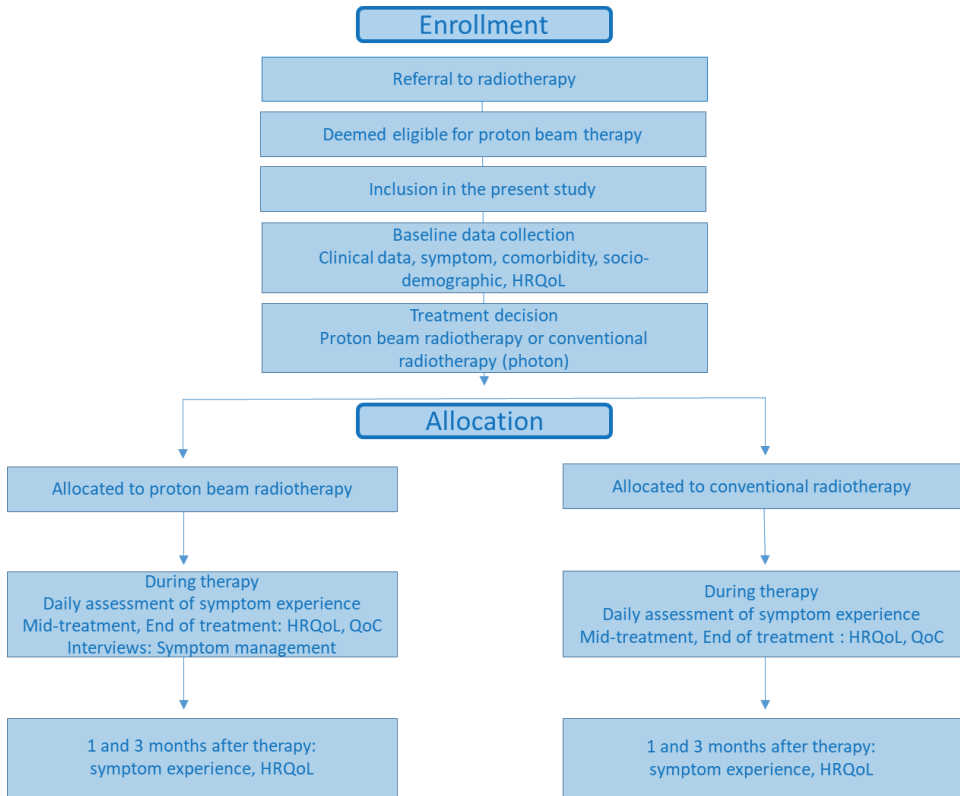[*] GT=Grounded Theory

Figure 3. Flowchart of the study

Study IV
The interviews were conducted at the Skandion Clinic and two local RT departments.

Participants

Studies I-IV
Adult patients (≥18 years) with primary brain tumors who were eligible for either PBT or CRT during 2015–2018 were invited to participate. All patients were managed according to a multicenter prospective PBT protocol for adults with primary CNS tumors (PRO-CNS, 2015). Patients with benign tumors were included in both the PRO-CNS protocol and this project because they had non-resectable tumors with substantial tumor volumes and continuous tumor growth. Patients with benign tumors thus constituted a subgroup with life-threatening tumors requiring the same treatment as malignant brain tumors. Target volumes (including margins) and target doses for these patients were comparable with those for primary malignant brain tumors. The exclusion criterion was inability to understand and communicate in Swedish. Patients with primary brain tumors

who are potentially eligible for PBT or CRT are evaluated during bi-weekly video conferences between the Skandion Clinic and the university hospitals' RT departments. They are subsequently either referred to the Skandion Clinic for PBT or treated with CRT at the local RT department, depending on the dose distribution plan.

Deductive research components

Procedures

Studies I-III

All patient-reported data were collected with online or paper questionnaires, according to the participant´s choice. A link to the online questionnaires was emailed to participants at each assessment. In Study I, data were collected at baseline, after three weeks and at the end of treatment. In Study II, online questionnaires were emailed to participants every day during the treatment period. An email reminder was sent on each day that the questionnaire was not completed. Patients who chose the paper-based format were handed one questionnaire for each treatment day at the start of treatment by an oncology nurse at the Skandion Clinic. A reminder was send by post if the questionnaires were not returned within one week after the end of treatment. In Study III, data were collected before the start of RT, after three weeks, at the end of treatment and at one and three months after completion of RT. Patients choosing paper received the questionnaires and a pre-paid envelope at the RT department or by post after treatment ended. The timing of the data collection was chosen in order to pinpoint the expected maximum increase in symptom experience and its development after treatment.

Data collection

The data collection procedure is shown in Figure 3.

Medical and demographic background data

When it came to the three studies with quantitative designs, medical data regarding the participants' tumors and treatments were collected from their medical records. Demographic data (e.g., marital, age, sex, occupational status and education) were collected with a project-specific questionnaire in all four studies

Questionnaires

In this thesis, five instruments were used, as shown in Table 1.

Comorbidity

The comorbidity questionnaire, completed at the start of treatment, was based, with the addition of two items, on the Self-Administered Comorbidity Questionnaire (SCQ), originally developed by Sangha, Stucki, Liang, Fossel and Katz (2003). The SCQ asks "*Do you have any of the following problems?*" and lists 15 medical problems, i.e. diseases related to the heart, lungs, stomach, liver, kidney, blood (e.g. anemia), connective tissue/muscle and skin, as well as other cancers, high blood pressure, diabetes, depression, arthritis and rheumatoid arthritis. Participants also have the option of adding additional conditions in an open-ended format. For each problem, participants were asked, "*Are you being treated?*" as a proxy for disease severity. To address the consequences of the reported conditions, we added the question, "*Does it limit your daily activities*?" Participants scored a maximum of three points for each medical condition: one for the presence of the problem, another if they were being treated and an additional point if the problem limited functioning (maximum score was thus 45 points). The comorbidity incidence was low. Therefore, in order to include this variable, scores were dichotomized based on SCQ cut-offs: 0–3 or ≥4 points.

Study I

Quality from the patient´s perspective

A modified version of Quality from the Patient's Perspective Questionnaire (QPP) was used to assess patients' views of QoC (Larsson, Larsson, & Munck, 1998; Wilde, Larsson, Larsson, & Starrin, 1994; B. Wilde Larsson & Larsson, 2002). The instrument evaluates four dimensions of patient perceptions of QoC: *medical-technical*, *physical-technical*, *identity-oriented* and *sociocultural atmosphere*. The QPP was developed from interviews using a using a Grounded Theory (GT) approach; a model of QoC was created to reflect a deeper understanding of the phenomenon. The questionnaire has been psychometrically tested (Wilde et al., 1994) and validated with a dimensional analysis using structural equation modeling (Larsson et al., 1998). It has been further adapted to numerous healthcare contexts and has been translated and validated for several languages, e.g. English, French and Norwegian (Wilde-Larsson, Larsson, Wickman Chantereau, & Staël von Holstein, 2005). We used one questionnaire for the baseline assessment and one for the follow-up assessments. The baseline questionnaire comprised 32 questions and the follow-up questionnaire comprised 43 questions. All responses were scored according to the perceived reality (PR) of the QoC (i.e. "*This is what I experienced*": 1 = *do not agree* to 4 = *fully agree*) and the subjective importance (SI) of the care (i.e. *"This is how important it was to me"*: 1 = *of little importance* to 4 = *of greatest importance*). Participants could also choose a "*not applicable*" response alternative. Four additional items covering the experience of waiting to start PBT were included in the baseline questionnaire and these were not repeated in the follow-up questionnaire. One item concerning the PBT experience

was added to the follow-up questionnaire, as well as questions about continuity, collaboration between the units, relatives and access. The scoring options (PR) for these items ranged from 1 (*to a very low extent*) to 5 *(to a very great extent)*. The internal consistency reliability coefficients (Cronbach's alpha) at baseline ranged between 0.83 and 0.89 for the PR subscale and between 0.88 and 0.94 for the SI subscale.

Study I and III

Health-Related Quality of Life
HRQoL was measured using the European Organization for Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ-C30), version 3 (Aaronson et al., 1993). 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 cancer patients (*loss of appetite, insomnia, dyspnea, diarrhea* 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, i.e. estimating the average of the items contributing to each scale, and second, by using linear transformation to standardize the raw scores. This procedure is in accordance with the scoring manual (Fayers, Aaronson, Bjordal, Curran, & Grønvold, 2001). High functioning scores represent better HRQoL, and high symptom scores are related to more severe symptoms.

Study II

Radiotherapy-Related Symptoms Assessment scale
Prior to the start of this study, we designed the Radiotherapy-Related Symptoms Assessment Scale (RSAS) to evaluate symptom experience and symptom distress in patients undergoing RT. Reeves et al. (2014) suggested that a core set of symptoms should be used as a basis for the RSAS. These symptoms—fatigue, insomnia, pain, loss of appetite, dyspnea, cognitive problems, anxiety (including worry), nausea, depression (including sadness), sensory neuropathy, constipation and diarrhea—are recommended to be considered for inclusion in all cancer studies investigating PRO. The RSAS comprises a core symptom set of 13 items: *fatigue, insomnia, pain, loss of appetite, dyspnea, cognitive impairment, worry, anxiety, nausea, sadness, constipation, diarrhea* and *skin reactions*, to fit into the current context. The TOUS was the theoretical basis used to develop the RSAS.

Application of this theory transformed the RSAS from a purely linear to a more interactive questionnaire, and allowed for the simultaneous experience of multiple symptoms. Furthermore, the RSAS was created inspired by the design of the QPP (Wilde et al., 1994). 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*). In the initial evaluation of the reliability, responsiveness and validity of the RSAS, it was found to be a reliable, responsive and valid questionnaire suitable for assessing symptom experience and distress in primary brain tumor patients undergoing PBT. The psychometric properties (test-retest reliability, responsiveness and criterion-related validity) of the RSAS were within the expected range. The stringent validation process helped establish its comparability with the European Organisation for Research and Treatment of Cancer, Quality of Life Instrument (EORTC-QLQ-C30). Each item score is converted to a score ranging from 0–100, analogous to the EORTC-QLQ scoring process (Fayers et al., 2001). The RSAS was developed in accordance with published guidelines from expert advisory bodies (Stucky & Pereira, 2012).

Study III

The EORTC QLQ-C30, version 3 (Aaronson et al., 1993), was used to measure HRQoL.

The diagnosis-specific EORTC QLQ-BN20 was also used. This questionnaire was developed as a site-specific supplement to the QLQ-C30 for use among patients with brain tumors undergoing chemotherapy or RT. It should always be accompanied by the QLQ-C30. It addresses symptoms that are specific to brain tumors or treatment. The questionnaire consists of 20 items, comprising 4 scales (*future uncertainty, visual disorder, motor dysfunction* and *communication deficit*) and 7 single symptom items (*headaches, seizures, drowsiness, itchy skin, hair loss, weakness of legs* and *bladder control*) (Taphoorn et al., 2010). The items in all symptom scales were scored from 1=*not at all* to 4=*very much*. All items and scale scores were linearly transformed into a 0–100 scale, with higher scores reflecting more severe symptoms. The internal consistency reliability coefficients of the multi-item scales ranged from 0.64 to 0.89 (Taphoorn et al., 2010).

Data analysis

Study I

The descriptive statistics frequency, percentage, mean, and SD were used to describe the study sample and the respondents' perceptions of QoC, PR and SI. QoC is considered to be high when PR scores are higher than SI scores, as well as when both are high and in balance. In this study, low values were

defined as below 1.7, medium as 1.7–3.3, and high as 3.4–4.0. Missing values were not imputed and "*not applicable*" responses were treated as missing data. Mean values for the dimensions were only calculated if >50% of the questions had been answered. For between-group comparisons, Fisher's exact test was used for dichotomous variables and the Mantel–Haenszel chi-square test was used for ordered categorical variables. To describe the discrepancy in frequencies, PR scores were dichotomized: *do not agree* and *partly agree were* combined into *do not agree,* and *agree to a large extent* and *fully agree* were combined into *fully agree*. SI scores were dichotomized: *No or of little importance* and *of some importance* were combined into *of low importance*, and *of great importance* and *of the greatest importance* were combined into *of great importance.* As QoC correlates with HRQoL (Arraras et al., 2013; Jayadevappa, Schwartz, Chhatre, Wein, & Malkowicz, 2010), we tested whether QPP scores correlated with scores on the functioning scales, *global health*, the *fatigue* symptom scale and the single symptom *insomnia* in the QLQ-C30. Correlations were rated as low (<0.30), moderate–high (0.30–0.60), or substantial (>0.6) (Revicki, Rentz, Luo, & Wong, 2011). Statistical analyses were performed using the SAS system, version 9.4. Reported p-values are two-tailed, and p<0.05 was considered statistically significant.

Study II

Descriptive statistics were used to analyze frequencies and intensity of participants' daily symptoms during the treatment period. Numbers and percentages are presented for categorical variables and means and SD are presented for continuous variables. The Wilcoxon signed rank test was used to compare changes in symptoms during the treatment period. Symptom clusters based on symptom intensity ratings were analyzed using exploratory factor analysis, which is widely used to identify symptom clusters (Thompson, 2004). All symptoms correlated (minimum of 0.3) with at least one other symptom, suggesting reasonable factorability. The Kaiser-Meyer-Olkin measure and Bartlett's test were performed before proceeding with the factor analysis. Given these indicators, factor analysis with varimax rotation was considered appropriate. Only factor loadings (rotated factors) over 0.4 were calculated. The number of factors selected was based on those with an eigenvalue equal to or higher than 1. Linear regression analyses were used to analyze how medical and demographic data were associated with symptom clusters. Variables that were significant in the univariable analysis (p<0.1) were entered into a backward stepwise multivariable regression model. Beta estimates with 95% confidence intervals, p-values, and r^2 were calculated. Missing values were imputed using the last value carried forward method (Twisk & de Vente, 2002). Statistical analyses were performed using the SAS system, version 9.4. Reported p-values are two-tailed, and p<0.05 was considered statistically significant.

Study III

Descriptive statistics were used to analyze numbers and percentages and are presented for categorical variables, while means and SD are presented for HRQoL and continuous variables. The Wilcoxon Signed Rank test was used to analyze changes over time within treatment groups and the Mann-Whitney U test was applied to analyze differences between treatment groups. Additionally, changes in clinical significance over time were assessed, according to Osoba et al. (1998), based on the observed percentages with decrease or increase of at least five points on the respective subscale or, for single items, at three-month follow-up. Linear regression analyses were used to analyze how demographic and medical data were associated with HRQoL. Dependent QLQ-C30 variables were: *global health/QoL* and *physical, role, emotional, cognitive* and *social functioning*. Selected QLQ-C30 items were: *fatigue, nausea, pain* and *insomnia*. The scales for *future uncertainty*, *visual disorder, motor dysfunction* and *communication deficit*, well-known brain tumor symptoms, were chosen from the QLQ- BN20. Beta estimates with 95% confidence intervals and r^2 were calculated. Missing values were imputed using the last value carried forward method (Twisk & de Vente, 2002). Statistical analyses were performed using the SAS system, version 9.4. Reported p-values are two-tailed, and $p<0.05$ was considered statistically significant.

Inductive research components

Study IV

The aim of this study was to explore symptom management and the effects on everyday life in the target patient population. Through interviewing, participant observations and rich descriptions of the social world, qualitative researchers hope to come close to the actor's perspective and try to capture his or her point of view or lived experience. Classic GT was chosen, as the method's aim is to discover the participants' main concerns and how they resolve them, as well as to explain problematic and relevant patterns of behavior (Glaser & Strauss, 1967; Glaser & Holton, 2005). GT is distinguished from other qualitative methods in that data collection and analysis occur simultaneously through constant comparative conceptualization (Glaser & Strauss, 2009). The goal of classic GT is to generate a theory that accounts for a pattern of behavior and is relevant and significant for those involved. GT attests that people have multiple and variable perspectives and that the researcher´s purpose is to raise these perspectives to an abstract level of conceptualization, to be able to see the underlying or latent pattern (Glaser, 2002).

Participants

A total of 23 adults with primary brain tumors who underwent PBT were asked to participate in interviews addressing their major concerns about their situation

and how they managed their symptoms. One patient declined to participate due to lack of time. Interviews (34), of which 29 were face-to-face and five were telephone interviews, were conducted between September 2015 and June 2016. Ten participants were interviewed during the treatment period and another 12 were interviewed both before and immediately after the treatment period.

Data analysis

During the interviews, participants described the symptoms they experienced before, during and after treatment. Furthermore, they discussed their feelings, intentions and actions, as well as the context and structure of their lives in relation to their experienced symptoms. This provided an overall picture of how they managed their symptoms. Interviews started with the open-ended question, "*Can you please tell me about your situation based on your current illness, including how you manage the symptoms you experience?*" Follow-up questions were asked, such as "*What does it mean to you in your daily life?*" This resulted in a deeper narrative in which participants reflected on their symptom experience and how they managed their symptoms. The interviews were transcribed verbatim and, according to classic GT, consecutively analyzed using the constant comparative method (Glaser & Strauss, 1967; Starrin, Larsson, Dahlgren, & Styrborn, 1991).

The first step was open coding, in which data were examined line by line to identify the patient's described thought patterns, feelings and actions. During this open coding, a set of questions concerning the data are asked, i.e. *What is this data a study of?, What category does this incident indicate?, What is actually happening in the data?, What is the participant's main concern?* and *How do they continually resolve this concern?* The purpose of these questions is to keep the analysist theoretically sensitive and to avoid description when analyzing, collecting and coding data (Glaser, 1998). The initial open codes are then compared with each other, followed by comparing newly generated concepts to new open codes and then comparing concepts to other concepts. Through this process, the core concepts eventually emerge. The core category is central in GT and explains the behavior of the participants in processing or resolving their main concerns. The theory is generated around a core category, which can be any kind of theoretical code such as dimensions, a process or consequences. Throughout the analytic process, conceptual memos were written to capture emergent theorizing at any time and place, often in the shape of text and figures to represent creative ideas. Memos are the theorizing notes of ideas about substantive codes and their theoretically coded relationships as they emerge during coding, collecting and analyzing data, as well as during memoing (Glaser & Holton, 2005).

Sampling is an important process in GT. During the first step of the recruitment process, participants were strategically selected to provide a broad perspective,

with selection based on age, sex, marital status, how far treatment had proceeded and how they managed their symptoms. At this stage of the sampling, a majority of the included participants had malignant tumors. After analyzing the initial interviews, we replaced the strategical sampling with theoretical sampling based on the emerging findings. In this second step, participants with benign tumors were primarily selected, in order to obtain variation in symptom management during the treatment period, as well as to confirm saturation. This theoretical sampling allowed specification of relationships between categories and abstraction to theoretical concepts. Recruitment of new participants and data collection concluded when saturation was reached, which was the point at which the most recent interviews did not appear to make a substantial contribution to the model that had been successively generated from earlier data.

ETHICS

Informed consent was obtained from all participants in the four studies. The studies complied with the World Medical Association´s Declaration of Helsinki ("World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects," 2014), that states that research should contribute to welfare, must aim to benefit and not harm participants, must respect the autonomy of participants and must follow the principles of justice.

All patients in Studies I-IV were contacted by a PCSG member (UL) and invited to participate in the project, contributing patient-reported data with questionnaires. Patients were also invited to participate in Study IV by the same PCSG member (UL). Since talking about one's illness may create memories and thoughts perceived as unpleasant, the participants were informed that they could contact healthcare professionals or the principal investigator if the need arose.

If the patients accepted participation, they received oral and written information about the aims and procedure of the study, including the voluntary nature of participation, confidentiality and freedom to withdraw from the study without explanation. All participants provided written informed consent before data collection started. The principal researcher was not involved in the care of the participants in any of the studies.

The total of all studies included a large number of questionnaires covering symptom experience and effects on daily life. Information about physical and psychological functions might be perceived as an infringement of personal integrity. This is one reason that participants must feel confident about the way the data is processed, and information about the process from data collection to data presentation was thus provided, both orally and in writing.

Confidentiality was ensured by removal, and replacement by codes, of names and personal identity numbers in all collected material. The coding lists were kept separately from the other research material (questionnaires, interviews, etc.). All study data were treated as confidential information and stored in safe archives.

Ethical approval of the studies included in this thesis was obtained from the Ethical Research Committee, University of Gothenburg, Sweden (Dnr:433-15). Approval was also obtained from the medical directors at each participating hospital.

RESULTS

Studies I-III

The study population consisted of adults diagnosed with primary brain tumors, benign or malignant, who underwent PBT. In Study I, a total of 216 patients were invited to participate. The response rate was 86% and the final sample comprised 186 participants. In Study II, 187 of 217 (86%) patients agreed to participate, four declined to participate and 26 were non-responders. Study III also included a control population, primary brain tumor patients who underwent CRT, and 255 of 301 (85%) patients, treated with PBT (n=224) or CRT (n=31), agreed to participate. Demographic and clinical baseline data are shown in Table 2.

Table 2. Demographic and clinical baseline data

	Study I n=186 (%)	Study II n=187 (%)	Study III PBT n=224 (%)	Study III CRT n=31 (%)	Study IV n=22 (%)
Women	98 (53)	95 (51)	121 (54)	17 (55)	10 (45)
Men	88 (47)	92 (49)	103 (46)	14 (45)	12 (55)
Mean age years (range)	48 (18-85)	48 (19-80)	48 (19-80)	58 (29-76)	47 (29-75)
Marital-status:					
Married/co-habiting	129 (69)	129 (70)	152 (68)	27 (87)	16 (72)
Single	57 (31)	58 (30)	72 (32)	4 (13)	6 (28)
Education:					
Elementary school	15 (8)	15 (8)	22 (10)	5 (16)	3 (14)
Secondary	86 (46)	86 (49)	105 (47)	18 (58)	11 (50)
University	76 (43)	76 (43)	94 (42)	6 (19)	8 (36)
Missing (education)	-	10 (5)	3 (1)	2 (7)	-
Malignant tumor	100 (54)	101 (54)	129 (58)	12 (39)	14 (63)
Benignant tumor	86 (46)	86 (46)	95 (42)	9 (61)	8 (47)
Comorbidity: SCQ category*					
<=4	-	155 (83)	189 (84)	24 (77)	21 (95)
≥=4	-	30 (16)	29 (13)	7 (23)	1 (5)
Missing		2 (1)	6 (3)		

*SCQ= Self-Administered Comorbidity Questionnaire, PBT=proton beam therapy, CRT=conventional radiotherapy.

In summary, no statistically significant differences between the patients with malignant tumors and benign tumors were found when it came to change from baseline to end of treatment in Studies I and II. Furthermore, no significant differences between the patients with benign and malignant tumors were found when it came to change between baseline and three months after PBT in Study III. However, in the CRT group in Study III, no significant differences were found in change from baseline to three months, except when it came to *fatigue* (Study III). The malignant and benign subgroups in these studies are presented as a homogenous group due to the high degree of similarity between them.

Quality of Care and Health-Related Quality of Life

In Study I, we evaluated QoC and the association with HRQoL. QLQ-C30 *fatigue* scores correlated negatively with the QPP item *support for fatigue* at baseline and at six weeks. Hence, patients who had high levels of fatigue perceived that they did not receive effective support from the healthcare staff. Patients who experienced a high level of global health reported high levels of effective support for fatigue, understanding from the doctor and obtained information about common symptoms.

Further, we found that *global health/QoL* status, *physical functioning*, *role functioning* and *cognitive functioning* significantly declined over time, whereas *emotional functioning* significantly improved from baseline to six weeks from start of treatment. Furthermore, we found that *fatigue, nausea* and *pain* increased after six weeks. There were also significant increases after six weeks in the single items *dyspnea, insomnia, appetite loss, constipation* and *diarrhea*.

However, the main finding concerning QoC was medium levels (mean 2.05–3.21) of PR in the *medical-technical, physical-technical, identity-oriented* and *sociocultural atmosphere* dimensions. PR scores were high (>3.4) for items concerning treatment information, common symptoms and interactions between clinicians and patients. PR scores were low (<1.6) for items about dietician information and support to stop smoking. Improvements were found in PR after six weeks for items about treatment information, self-care, symptoms, doctors' understanding and good information about physical activity.

According to the responses concerning how important the QoC was (SI), the items of greatest importance were related to interactions with doctors and nurses and treatment information, and the *identity-oriented* dimension was also of great importance (mean 3.4). The SI of the other two dimensions was medium (3.07 and 2.75, respectively). As expected, no item was rated as being of low importance (<1.7). The importance of the item "*I received useful information about how long the RT symptoms might last*" underwent a significant increase between baseline and six weeks.

An important finding in this study is the discrepancy between participants' experiences of their care, i.e. the PR, and how important they perceived the care to be, i.e. the SI. SI scores for 55% of the items were significantly higher than the corresponding PR scores. These differences were found in the *medical-technical, identity-oriented* and *context-specific* dimensions. Of these 15 significant items, 60% concerned information or consequences related to fatigue, sleeping problems, worry, anxiety and participation in care decisions.

Symptom clusters

In Study II, we aimed to explore symptom clusters and associations with comorbidity and demographic factors among brain tumor patients undergoing PBT. *Fatigue, insomnia, pain, appetite loss, dyspnea, cognitive impairment, worry, anxiety, sadness nausea, constipation, diarrhea* and *skin reactions* were assessed every treatment day. *Fatigue, pain, loss of appetite, cognitive impairment* and *nausea* increased significantly during the 35-day treatment period, ($p=0.02$ to $p<0.001$), while *worry* decreased ($p<0.001$).

In this study an explorative factor analysis was conducted, identifying three symptom clusters: 1) *Mood,* including worry, anxiety, and sadness; 2) *Reduced Appetite*, including loss of appetite and nausea; and 3) *Reduced Energy*, including fatigue, insomnia, pain and cognitive impairment. These clusters were consistent over time. The *Mood* cluster had the highest factor loading on day 35 (0.71–0.86), followed by the *Reduced Appetite* cluster (0.62–0.84), and the *Reduced Energy* cluster (0.61–0.70). This study also investigated risk factors associated to the symptom clusters. The multivariable analysis indicated that female sex ($p=0.04$) and more comorbidity ($p<0.001$) were associated with worse *Mood* cluster symptoms. Low education level ($p=0.04$) was the only variable significantly associated with worse *Reduced Appetite* cluster symptoms. Finally, in the *Reduced Energy* cluster, we found that female sex ($p=0.01$) and gastric ulcer ($p=0.01$) were significant variables. However, sex and comorbidity contributed to the increased experience of the symptom clusters during the treatment period and were significant risk factors during PBT (Study II). Figure 4 shows the longitudinal profiles of the three symptom clusters.

Symptom experience and Health-Related Quality of Life

In Study III, we assessed the symptom experience and HRQoL at baseline, during treatment and at one and three months after end of treatment during treatment and at one and three months after end of treatment in patients with brain tumors given PBT or CRT. We did not find statistically significant differences between the PBT group and CRT group in any of the subscales or single items in the EORTC QLQ C-30 and QLQ-BN20 questionnaires, when it came to change from baseline to
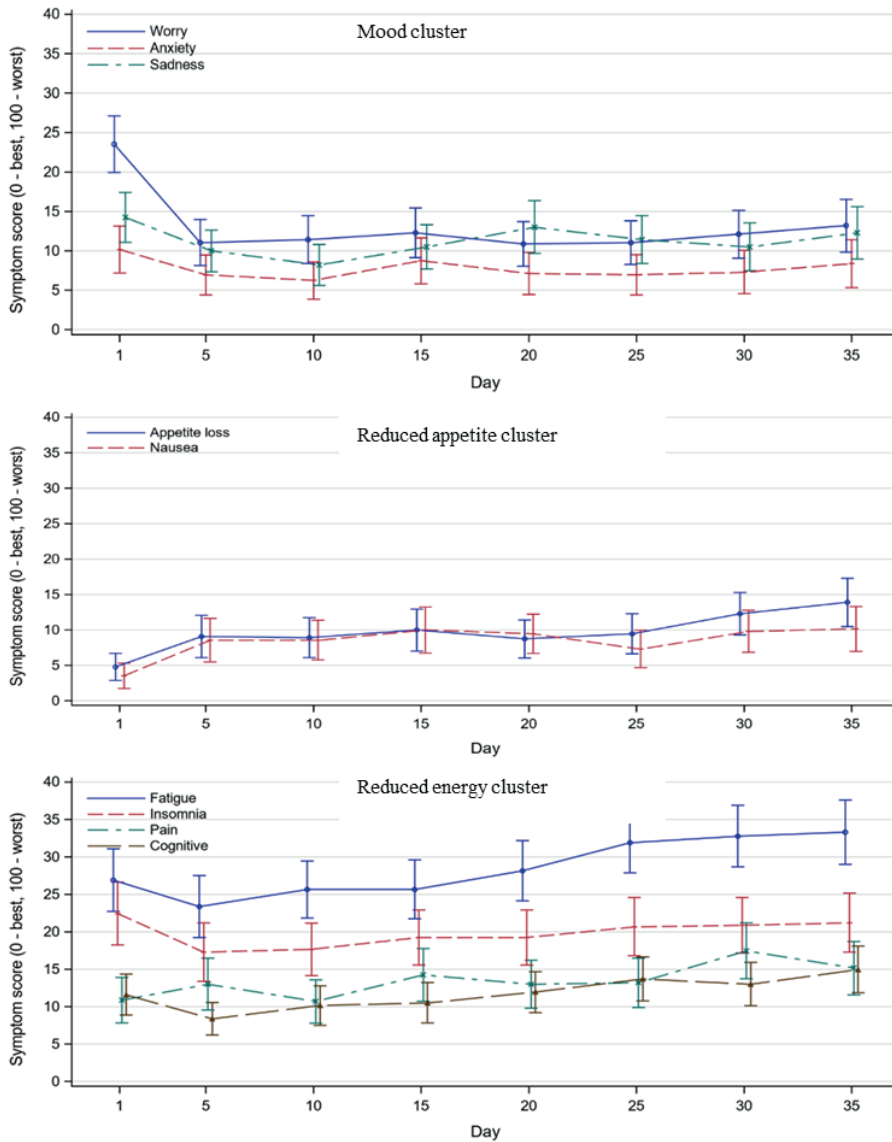
Figure 4. Longitudinal profiles of symptom clusters: *Mood* cluster, *Reduced Appetite and Reduced Energy* cluster in patients undergoing proton beam therapy for five weeks due to brain tumors (n=187)

three months after treatment. In the PBT group, *global health/QoL* significantly decreased between baseline and three months. Moreover, significant decreases were found between baseline and three months in *physical functioning* and *cognitive functioning*. Scores in the symptom scales *fatigue, nausea and vomiting* and *pain* deteriorated significantly between baseline and three months. When it came to the single items, *dyspnea, appetite loss, constipation, drowsiness, itchy*

skin, hair loss, weakness of legs and *bladder control* deteriorated significantly during the study period. The mean summary scores significantly decreased from baseline to three months. Figure 5 shows the differences in means from baseline to
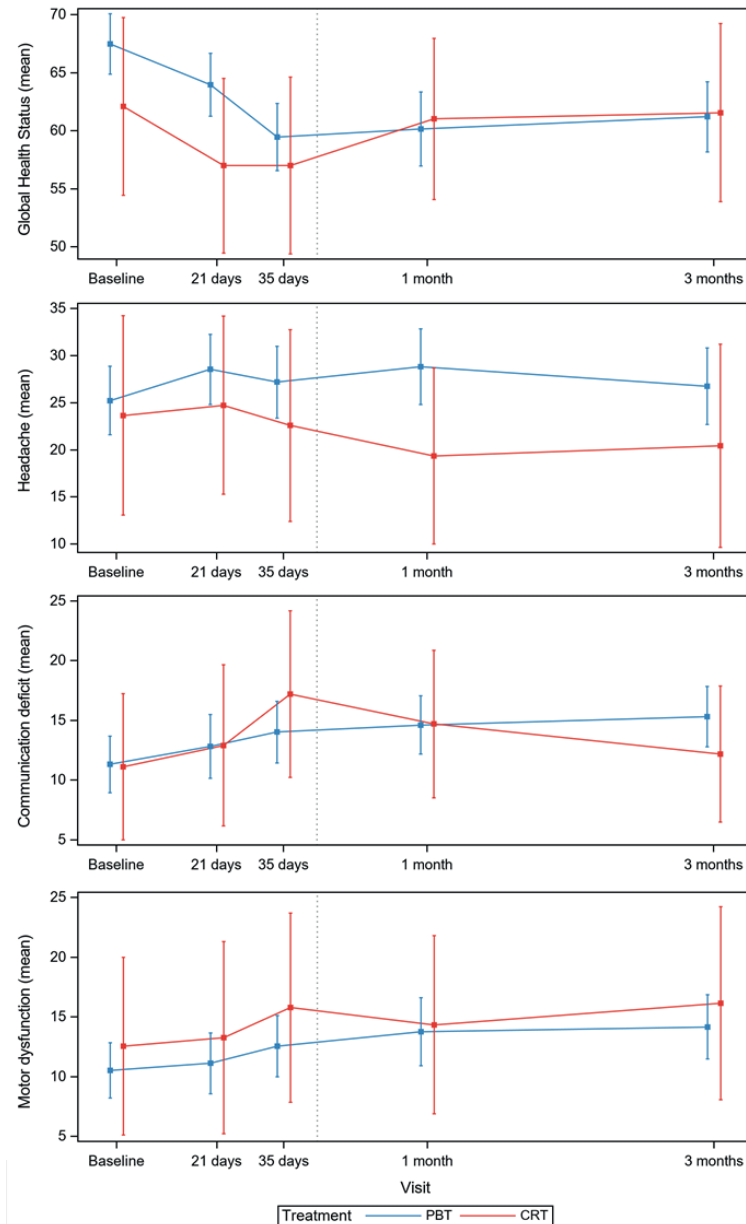
Figure 5. Mean change in common brain tumor symptoms in patients undergoing PBT or CRT, from before start of treatment (baseline, BL) to three months after completion of treatment

three months regarding *global health/QoL* and *headache, communication deficit and motor dysfunction*, which are common brain tumor symptoms.

We also investigated the importance of clinical relevance. The incidences of clinically relevant (a change ≥5 points) differences in *QoL* scores showed that increasing *fatigue* over time was the most common change, reported by114/224 (51%) in the PBT group and 12/31 (39%) in the CRT group. In the PBT group, 108/224 (48%) participants reported clinically significant deterioration in *global health/QoL*, as did 12/31 (39%) in the CRT group. A total of 62/224 (28%) in the PBT group and 9/31 (29%) in the CRT group reported unchanged *global health/ QoL*.

Concomitant chemotherapy combined with RT was associated with deteriorating *emotional function*ing ($p=0.011$) and *cognitive functioning* ($p=0.05$). Women reported lower *cognitive functioning* than men ($p=0.0096$). Higher education was associated with worse *cognitive functioning* ($p=0.010$) and *physical functioning* ($p=0.018$). Women reported more *pain* than men, as did those given chemotherapy, compared to those who were not ($p=0.036$). Chemotherapy after RT was associated with more *communication deficit* ($p=0.030$) and chemotherapy before RT was associated with more *future uncertainty* ($p=0.020$). Moreover, more comorbidity was associated with increased *motor dysfunction* ($p=0.0034$) from baseline to three months (Study III).

Study IV
The process of symptom management

"The Art of Living with Symptoms" is the title of Study IV, illustrating an ongoing process of action and thoughts throughout the treatment period. Despite the presence of symptoms, ranging from severe (e.g. the consequences of epilepsy) to less severe (e.g. low-intensity headaches), and significant restrictions in everyday life, the participants expressed that they lived satisfying lives and that they managed the situation with different strategies based on their own actions and personal resources.

Through constant comparative conceptualization, the core category "*The art of living with symptoms*" emerged and was related to three interconnected symptom management concepts: *Adapting to limited ability, Learning about oneself and Creating new routines*. Each of these sub-processes influenced the others in an ongoing and interactive process. The analysis resulted in a substantive theoretical model with eight categories resting on three concepts and one core concept (Figure 6).
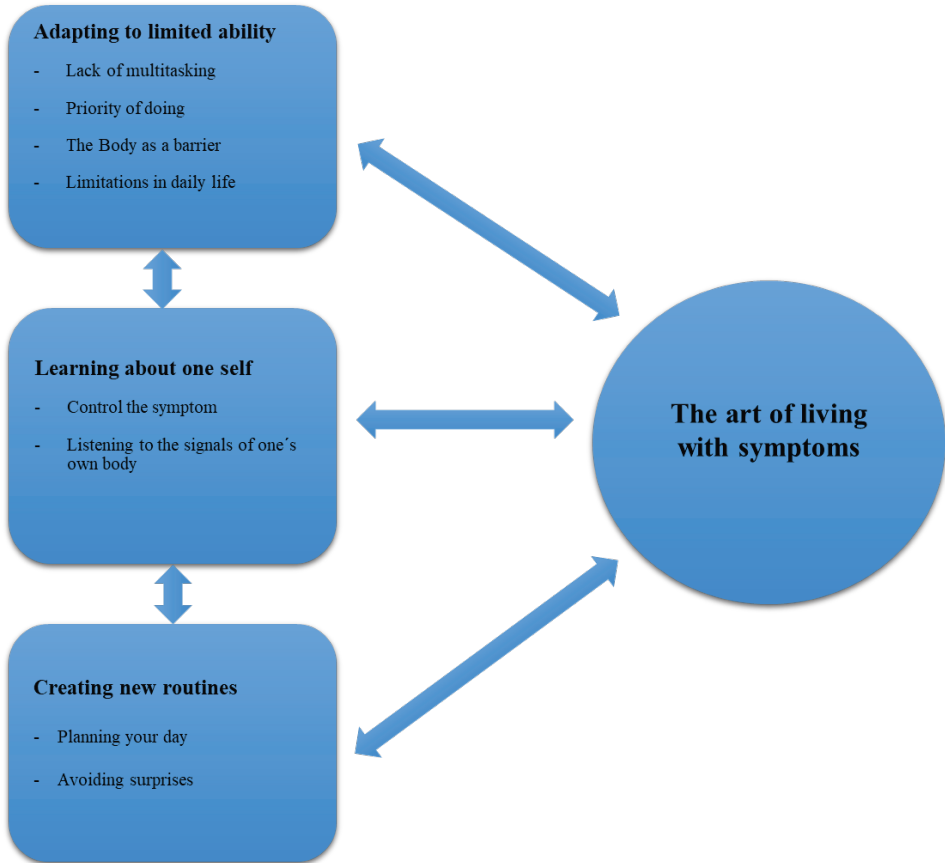
Figure 6. Substantive theoretical model describing the process of symptom management in patients with primary brain tumors given proton beam therapy. The analysis extracted "*The art of living with symptoms*" as a core concept that encompassed three interconnected symptom management concepts: *Adapting to limited ability, Learning about oneself,* and *Creating new routines.*

Results, summary

This thesis provides increased knowledge about patients with primary brain tumors underwent PBT. It contributes to new insights into the subsequent consequences and the effects on patients' everyday life. One finding was that all assessed symptoms experiences were reported at generally low levels. However, research on symptom experience in relation to brain tumors has been conducted for decades, finding that there are major shortcomings in providing high QoC. A need for improvement was identified for 60% of items concerning information or consequences related to high symptom experience. Three symptom clusters emerged in the explorative factor analysis: *Mood*, *Reduced Appetite* and *Reduced Energy*. This was interesting and this was the first published article worldwide concerning the population in this thesis. The qualitative study showed that these

patients need support to mobilize their personal resources and find symptom management strategies, and thus maintain daily life. The substantive theoretical model developed in this study may be used to increase caregivers' understanding of a patient's individual resources in managing symptoms, as well as for initiating discussion about his/her symptom experience and symptom management.

DISCUSSION

The image on the cover of this thesis symbolizes the balancing act of living with symptoms in the case of primary brain tumor patients. I interpret it as the big black stone representing the time of life when the brain tumor became a fact, while the stones on the other side symbolize the person acquiring tools along the way, in the form of experiences and strategies.

The main purpose of this thesis was to investigate the experience of symptoms and HRQoL in patients with primary brain tumors who underwent PBT at a recently established clinic. The introduction section provided an overview of the research field of symptom experience in patients with primary brain tumors. Publications in this research field have in common the finding that people with brain tumors experience several concurrent symptoms and have special needs that require qualified care (Afseth, Neubeck, Karatzias, & Grant, 2019; Catt et al., 2008a; Janda, Eakin, Bailey, Walker, & Troy, 2006; Janda et al., 2008; Renovanz et al., 2017).

The grading of CNS tumors is fluid and not comparable to that of other tumors (Ford et al., 2012), yet most of the research about brain tumors distinguishes between different tumor types. In this thesis, however, both malignant tumors and benign tumors requiring RT were included. Symptoms and outcomes in patients with benign CNS tumors are often overlooked, as these tumors are not categorized as cancer and, in many cases, not followed up. However, the influence on QoL related to the symptoms may be just as severe as that related to malignant tumors, and some benign tumors are incurable. RT does not eradicate a benign tumor but removes its capability for growth. The follow-up of benign CNS tumor patients may be just as long as for malignant tumors, and this close surveillance may also influence QoL (Zamanipoor Najafabadi et al., 2016). I will discuss these two subgroups as one homogeneous group, despite the fact that there were minor differences in HRQoL between the subgroups in Study I.

The assumption underlying this research project was that PBT would be associated with less negative PROs in the short-term perspective, due to lower integral doses than those administered in CRT. However, no significant differences between the PBT and CRT groups were found in Study III, when it came in symptom change from baseline to three months after treatment. We thus failed to find evidence concerning this assumption. This was unexpected and indicates the importance of studying this group in long-term follow-up studies.

In order to take into account the growing body of symptom experience research, it is increasingly important to understand this knowledge in a more connected

fashion (Cashion, Gill, Hawes, Henderson, & Saligan, 2016). Furthermore, it will remain important to understand symptoms in a multidimensional, contextual way (Corwin et al., 2014). Heretofore, symptoms have typically been studied in relation to specific conditions or pathophysiological processes. Nursing researchers must regard symptoms in the context of a person's life, since a person's context adds complexity to his/her experience and interpretation of symptoms.

The Theory of Unpleasant Symptoms

Based on the research questions and focus on the multidimensional aspect of symptoms, the middle-range TOUS was used to explore and elucidate the results, guide the concept development, analyze the process and interpret the data in this thesis. We included the major TOUS concepts and all of the four studies are contextualized in the model. The TOUS emphasizes three major aspects: the *symptoms*, the *influencing factors* that give rise to or affect the nature of the *symptom experience* and the consequences of the *symptom experience*, i.e. the *performance*.
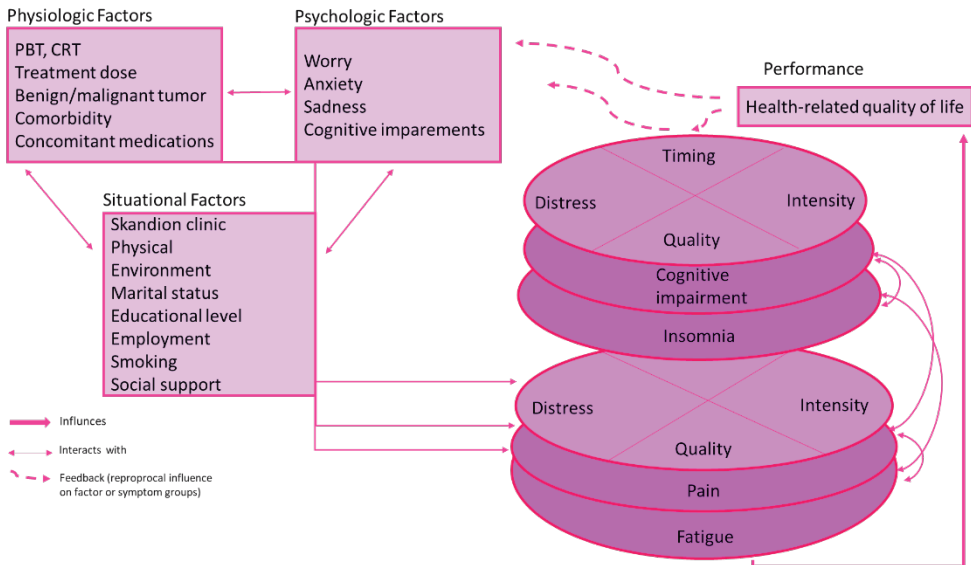
Figure 7. Adjusted model of the Theory of Unpleasant Symptoms, Lenz et al. 1997

Symptoms

Intensity dimension

Symptoms is the central TOUS concept and is also the starting point in the process of all symptom research. Figure 7 shows how the model may be practically useful. There is no simple explanation for the varying degrees of symptom experience in the three quantitative studies (or in the qualitative study). In Study I, there were no significant differences between the malignant and benign subgroups in functioning scale scores, except *cognitive functioning*. No significant differences whatsoever were found between these two subgroups in Studies II and III. This inconsistency may be respectively explained by the fact that symptoms were assessed with another questionnaire (Study II) and that more participants were included (Study III).

In Studies I and II, the participants reported an increase in the majority of the assessed symptoms during the treatment period, although the intensity was generally low. Nonetheless, they reported a relatively substantial decline in HRQoL (Study I) from baseline to the end of treatment (range 68.5-60.7, $p=<0.0001$). As mentioned in a literature review, this group of patients experiences symptoms such as personality changes, epileptic seizures, cognitive impairments and headache, all of which may markedly affect HRQoL (Englot et al., 2016; Flechl et al., 2017; Jzerman-Korevaar et al., 2018). Study III showed that the symptom experience was at its worst at the end of treatment, but also that it was still significantly higher three months after treatment, compared with baseline levels. This finding is consistent with that of Bitterlich and Vordermark (2017), who analyzed HRQoL in patients with brain tumors before and after CRT. Concurring with the literature, we found that participants who underwent PBT experienced a similar degree of symptoms as those treated with CRT during the treatment period and up to three months after the end of treatment.

One of the most important, yet challenging, developments has been the burgeoning empirical literature revealing the complexity and pervasiveness of symptom clusters. Experiencing multiple concurrent symptoms, as opposed to single symptoms, has more negative effect on patient outcome (Dodd et al., 2001; Gift, Jablonski, Stommel, & Given, 2004). The symptom clusters identified in Study II remained relatively stable during the treatment period. It is possible that two or more symptoms occurring at the same time may act as catalysts (Lenz et al., 1997). For example, when it comes to the *Reduced Energy* cluster, cognitive impairment seems considerably worse when one is fatigued, is in pain or has problems sleeping (Study II). Symptom cluster research is still limited and scientists are just beginning to understand how to investigate symptom clusters by developing new frameworks, methods and approaches (Miaskowski et al., 2017). Moreover, research aimed at identifying the mechanisms underlying

symptom clusters is essential for developing targeted interventions. It is important for practicing nurses to understand that multiple symptoms can be experienced together and can interact with each other. A middle-range theory can be useful for this purpose. The TOUS has demonstrated good social and theoretical significance (Lee, Vincent, & Finnegan, 2017) and has been used to guide nursing research in various populations with diverse health conditions in different countries.

Another interesting finding was that during the study period, from baseline to three months after the end of treatment, there were certain adverse events subsequent to RT (Study III). In particular, fatigue increased markedly in both the PBT and the CRT groups, which might have been a direct acute effect of the RT. A review by Taphoorn et al. demonstrated that HRQoL decreased in patients with brain tumors suffering from fatigue (Taphoorn, Sizoo, & Bottomley, 2010), concurring with a review by Liu et al. (2009), reporting that CRT adversely affected QoL by leading to a short-term increase in fatigue. It is unclear whether the decrease in functioning scale scores in patients with brain tumors is due to the treatment or to the tumor itself. A study of long-term survivors of low-grade glioma suggested that deterioration in QoL was not due to previous CRT or chemotherapy, but to tumor relapses (Okita et al., 2015). The research in this thesis did not investigate long-term effects, which are very interesting because of the risk of related irreversible impairments. This is one of several current remaining unanswered questions highlighting the need for further research, including long-term follow-up of PBT-related symptom experience in patients with primary brain tumors.

Time dimension
Time is one of the four *symptoms* dimensions outlined in the TOUS. It includes the frequency with which an intermittent symptom occurs, how long it persists and whether it has become chronic. In the analysis of symptoms reported by the participants, while the mean symptom severity had decreased three months after the end of PBT, there was a tendency for some patients to report an unaltered degree of severity for some symptoms. In accordance with these findings, previous studies have demonstrated that most patients maintain their global QoL. Fatigue has always been reported to be prominent in those studies during the first months after diagnosis (Bitterlich & Vordermark, 2017; Flechl et al., 2017). In the absence of evidence, it may be speculated that improved symptom management, adaptation to symptoms over time and/or termination of treatment played a role in counteracting fatigue.

Distress dimension
The *distress* dimension of the TOUS *symptom*s concept was investigated in Study II. The RSAS questionnaire includes a *distress* dimension which was unfortunately

not analyzed in Study II. A future study with more focus on distress is therefore suggested.

Quality dimension

The last dimension in the TOUS *symptoms* concept is *quality*. Symptoms can vary in quality or in how they manifest. *Quality* is often reflected by the vocabulary used to describe what the symptom feels like. By including this dimension, the TOUS contains a personal aspect, as the same symptom will be described differently by different people (Lee et al., 2017; Lenz et al., 1997). This aspect requires a qualitative approach, if it is the focus of research, and participants must be able to describe the experience of the symptom. During the analysis in the qualitative study (Study IV), understanding how patients managed to live a satisfactory life, despite the symptoms and limitations they experienced, presented a challenge. Their narratives included the quality of the symptoms and symptom management. Although they expressed their experiences individually, the common factor for all participants was the increasing intensity of symptoms over time and the impact on their daily lives. The participants described how they used their own strategies to maintain everyday life in the new conditions related to the illness. Most of the participants in Study IV stated that they had had no specific symptoms before being diagnosed. An initial symptom of a tumor may be an acute epileptic seizure or slowly deteriorating eyesight, entailing either abrupt or more gradual adaptation to being diagnosed and experiencing symptoms.

The response shift theory, by Spranger and Schwartz (1999), may contribute to understanding this complex area. Response shift has also been suggested by other authors and has been documented in various cancer populations (Mechteld, Oort, & Mirjam, 2005; Oort, Visser, & Sprangers, 2005; Sharpe, Butow, Smith, McConnell, & Clarke, 2005). Spranger and Schwartz interpreted response shift as an important mediator in the adaptation process when HRQoL is threatened, involving changing internal standards, values and the conceptualization of QoL. When the participants in Study IV were confronted with a life-threatening or chronic disease, they also faced the need to adapt to their illness. According to the response shift model, all individuals differ in terms of the areas of their life that they value most, as well as in their expectations of achievements across life domains. Those whose expectations are met within the areas that they deem most important are those who are most likely to report a good QoL. When individuals experience a change in circumstances, such as a serious health threat, the areas that seem important to them are likely to be subject to change. Similarly, the level of achievement in a particular domain of life is likely to decrease. Response shift occurs as part of the adjustment to illness when individuals manage to shift their priorities and expectations in line with their changed circumstances. Therefore, one explanation for the majority of participants in this study achieving a satisfactory

HRQoL might be that they had the resources to change their internal standards (Sprangers & Schwartz, 1999).

Influencing factors

The *influencing factors* in the TOUS are described as influencing both each other and the symptoms. For example, the presence of physiological pathology (causal to the symptom[s]) may trigger a *psychological* response, such as cognitive impairment, that heightens the perception of the symptom experience (Gift, Stommel, Jablonski, & Given, 2003). Similarly, *psychological factors* and the symptom experience may be worsened or mediated by *situational factors*, such as a strong or weak support system (Study I), as reported by Armstrong et al. (2010). This became very clear in Study I, in which we evaluated QoC. The patients who experienced a high level of global health reported a high level of QoC. Furthermore, patients who reported high levels of symptoms perceived that they did not receive effective support from the healthcare staff. Moreover, staying at a hotel, often alone and far from family, friends and a familiar healthcare system, during PBT may have been an extra challenge for the patients who were already dealing with a complex situation. Systematic assessment and support with adequate interventions are crucial under these circumstances.

In the process of identifying potential influencing factors, the TOUS provides a framework that helps determine the extent of the overlaps between the symptoms at a level of abstraction compatible with nursing diagnoses and interventions. In all four studies, the model was helpful to understand the importance of the influencing factors, and to explore the interactions between e.g. comorbidity, demographic factors and symptom experience. When it came to *physiological factors*, the regression analysis showed that PBT, comorbidity and concomitant medications affected the symptom experience negatively as well as situational factors, such as education level (Study II). Moreover, more comorbidity was associated with increased motor dysfunction from baseline to three months (Study III). Thus, the combination and interaction of multiple influencing factors impact the symptom experience differently from any given influencing factor alone. These results concur with those of Gijsen et al. (2001) and Søgaard, Thomsen, Bossen, Sørensen, & Nørgaard (2013), who found that comorbidity in general is associated with mortality, HRQoL and healthcare. Therefore it is important to consider which influencing factors affected the individual, in order to understand his/her experience.

Performance

Performance, or *consequence*, is the outcome or impact of the symptom experience. The consequences of symptom experience in our studies were HRQoL, a statistically significant clinical outcome in patients with primary brain

tumors (Study I and III). Understanding HRQoL patterns is important for patient information and shared decision-making. Patients need to know what their HRQoL outcome may be during and after PBT (Steinmann et al., 2009). The process as described above, including symptom experience (single or multiple symptoms) and influencing factors, provides a number of different performance outcomes, such as altered functional and cognitive abilities (Study III). *Performance* includes a variety of effects leading to patients with more numerous or severe symptoms tending to have worse health status, lower cognitive functioning and lower HRQoL as we found in Study III. It seems plausible that performance outcomes such as HRQoL influence the experience of unpleasant symptoms.

The TOUS has been a helpful tool in identifying the element of the individual symptoms, understanding interactions among symptoms and distinguishing the different influencing factors of a symptom leading to poorer HRQoL. The TOUS may guide and enable nurses to design interventions taking the multidimensional and interactive nature of symptoms, influencing factors and consequences into account, thereby individualizing them.

Quality of Care

The evaluation of QoC, in the PBT patients we studied, indicated that multiple care domains required improvement. The participants reported a lower QoC in relation to fatigue, insomnia and worry/anxiety. They felt that they did not receive adequate support with symptom management (Study I). Previous research has demonstrated high levels of unmet needs in tumor patients. These include lack of support in managing anxiety, depression and fatigue, as well as lack of information (Barg et al., 2007; Halkett, Lobb, Oldham, & Nowak, 2010; Harrison, Young, Price, Butow, & Solomon, 2009; Janda et al., 2008; Lee, 2017; Puts, Papoutsis, Springall, & Tourangeau, 2012). Numerous studies have found that patients with brain tumor have needs that differ from patients with other cancer diagnoses, and that needs change over time during disease progression (Catt et al., 2008a; Halkett et al., 2010). For instance, patients often do not communicate psychological concerns to their clinicians (Wen & Gustafson, 2004) and there is evidence that healthcare professionals may not detect emotional distress (Mitchell, Hussain, Grainger, & Symonds, 2011). Failure to detect needs is problematic for all tumor patients, but possibly more significant in patients with brain tumors, a group with one of the highest rates of symptoms (Hartung et al., 2017). In combination with their significant and unique needs, this necessitates targeted mechanisms to deliver appropriate supportive care. Participants in Study II reported that their worries increased before being discharged from the Skandion Clinic. We conclude that it is important to ensure that patients feel safe and secure during the transition to the local department.

Our research concurs with a review by Lee et al. (2017) that presents important implications for developing targeted research and targeted interventions. Indeed, there is an urgent need to create evidence-based guidelines for symptom management in order to provide high QoC for patients with primary brain tumors suffering from low HRQoL. Patients' perceptions of their abilities to cope with symptoms may vary. Without effective interventions to alter (restrain or produce) their own actions to cope with symptoms, they may withdraw from potential treatments. Symptom assessment and management is a hallmark of nursing intervention, with the goals of exposing triggers, reducing severity and limiting impact. However, if finding the cause is the only focus in symptom management, the patient may have to live with a symptom, without any hope that it will be alleviated. Accordingly, from a nursing perspective, managing symptoms requires an understanding of the patient's experience of the symptom as well of symptom experience outcomes and consequences. As we have shown, interconnections between symptoms create symptoms clusters (Study II) and symptoms have a significant impact on HRQoL (Study III). A multidimensional assessment of symptom experience in patients with primary brain tumors undergoing PBT might contribute to more comprehensive assessments of symptom experience (Catt, Chalmers, & Fallowfield, 2008b; Ford et al., 2012; Janda et al., 2006; Parvataneni et al., 2011). Such assessments require advanced nursing knowledge to improve clinical practice.

METHODOLOGICAL CONSIDERATIONS

Assessing symptom experience and HRQoL presents various methodological challenges. In order to gain a broad and deeper understanding of the research questions, both quantitative and qualitative methods were used. Consideration should always be given to the study's aim when the method is chosen (Polit & Beck, 2012). Each of the methods contributed to addressing the issues of symptom experience related to PBT. The research design is the overall plan for obtaining answers to the research question and identifying strategies to minimize bias. Research design indicates which questionnaires will be used, how often the data will be collected and what types of comparison will be made. When choosing the setting and sample for a qualitative study, it is important to consider the potential richness of the information it will generate. In this thesis, with a prospective and longitudinal design, the participants contributed with numerous experiences. GT was applied, with a focus on how individuals interact with the phenomenon of symptom management.

The main difficulty in these studies has been to confirm that there were no difference in the results between the participants with malignant and benign tumors. There were, of course, both advantages and disadvantages to including both subgroups. Studying the benign subgroup was intentional, as these patients may be neglected since their tumors are not categorized as cancer. Different brain tumors have different prognoses, but it is generally only patients with a relatively good prognosis (mean expected survival >5 years) that are considered candidates for PBT. Patients who were referred for either PBT or CRT were thus already a selected population. This may be an explanation for the difficulty in recruiting participants to the CRT group. The disadvantage of including both benign and malignant tumors is that the group is not representative and that the results cannot be generalized.

At the start of the data collection, we gave paper questionnaires to the participants. After one year, we entered into a collaboration with a company that delivered electronic questionnaires. However, it was still possible to choose paper questionnaires, as several participants stated that disease-related visual or cognitive disorders made it difficult to read on a screen. While collecting data both electronically and on paper might have been a limitation, previous research suggests that there is little or no difference in reliability between the methods (Alfonsson, Maathz, & Hursti, 2014; Wilde-Larsson, 2006).

In quantitative studies, validity and reliability are often discussed. Validity refers to whether an instrument measures what it is intended to measure, and reliability is the extent to which a variable or a set of variables is consistent with what it is

supposed to measure when measuring is repeated (Polit & Beck, 2008; Straub, 1989; Streiner, Norman, & Cairney, 2015). Questionnaires used in this thesis are well established and have been used extensively before. They have been robustly tested, validated and translated (Aaronson et al., 1993; Bottomley et al., 2005; Koller et al., 2012; Sangha et al., 2003; Taphoorn et al., 2010; Wilde et al., 1994). The RSAS (Study II) was the exception. It was developed and validated as a generic questionnaire with the intention that the items could easily be replaced with other, diagnosis-specific, items. This might have been a limitation. However, a qualitative pilot study was conducted to test the cognitive understanding of the RSAS (Patrick et al., 2007) and examine participants' thoughts when answering the questionnaire. A total of 10 patients (four women and six men) participated in the pilot study. Participants were selected to ensure variety in age and sex, an important aspect of content validity (Streiner et al., 2015). This initial analysis showed that they 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 RSAS was meant to evaluate self-reported symptoms, and depression is a psychiatric diagnosis. We also added skin reactions, as the RSAS was intended for RT patients. This resulted in 13 items in the final version of the RSAS. The psychometric properties (criterion-related validity, test-retest reliability, and responsiveness) of the questionnaire were within the expected range.

The main purpose of calculating power is to help the researcher determine the smallest sample size suitable to detect the effect of a given test at the desired level of significance (Cohen, 1988). Power was calculated based on responses to the MFI-20 *general fatigue* variable among patients with brain tumors given PBT in another research project with which we are affiliated. This variable was chosen because fatigue is the most frequently reported symptom in cancer patients undergoing RT (Ahlberg, Ekman, Gaston-Johansson, & Mock, 2003). To detect differences between the PBT and CRT groups, 175 and 50 participants needed to be allocated to the respective group. A researcher should be aware of the two types of errors, type I and type II, that can arise in statistical tests (Polit & Beck, 2012). While we did attempt to avoid both types of errors, we failed to reach the inclusion goal of 50 patients in the CRT group, as mentioned earlier. This increased the risk of type II errors in Study III (Polit & Beck, 2012).

The questionnaires had different designs. In Study I, we used the QPP, in which participants could choose a "*not applicable*" response alternative. This can be interpreted differently and might have been misleading. Furthermore, criticism has been leveled at the instrument's validity (Beattie, Murphy, Atherton, & Lauder, 2015). Missing values were not imputed and the "*not applicable*" responses were treated as missing data. Mean values for the dimensions were only calculated if >50% of the questions had been answered. In Studies II and III, on the other hand,

missing values were imputed using the last value carried forward method (Twisk & de Vente, 2002). In Study II, when the participants filled out the questionnaire every day, 4.0% of the values for the nine analyzed items were imputed on day 15, 7.5% on day 25, and 28.9% on day 35. Reasons for the high level of missing values on day 35 may be related to response bias or survey bias (Rolstad, Adler, & Rydén, 2011). It is important to know which patients dropped out of the studies, and whether they differ from those that remained. Previous research has demonstrated that those who drop out differ from participants in that they suffer more (Allison, 2001). Missing data should therefore be considered to differ from non-missing data and dropout over time must be expected in follow-up studies.

In Study IV, GT was applied, with the purpose of developing a substantive theory describing the process of how participants expressed their symptoms. The study presents the abstracted core concept and an interpretation of how participants managed their symptoms. GT methodology and other qualitative research methods have been discounted by some researchers as nothing other than 'nice stories' (Urquhart, 2012), while others wonder how readers can determine that the emerging theory is not a result of an author's 'self-delusion' and therefore unreliable and invalid (Carcary, 2009). In order to guarantee the trustworthiness of qualitative studies, several issues need consideration. Four factors have been suggested for establishing trustworthiness of qualitative research: credibility, transferability, dependability and confirmability (Brown, Stevens, Troiano, & Schneider, 2002; Lincoln & Guba, 1986; Rolfe, 2006).

Credibility refers to confidence in the data, whether the results are based on faithful descriptions and to what extent the collected data accurately reflects the multiple realities of the phenomenon. In our study, credibility was established through individual interviews that were transcribed verbatim and by the emerging concepts and categories, or respondent validation. To ensure credibility, the principal researcher was supervised by a more experienced GT researcher, and they started the analysis process and created the concepts together, using classic GT. During the inductive phase, memos and regular discussion were undertaken. The memos provided a trustworthy data source for the analysis, as they were obtained by regular entries in a reflective research diary.

Confirmability tests the 'objectivity' of research (Brown et al., 2002). Pre-understanding can never be totally avoided and always has some influence on the analysis. Classic GT indicates that the researcher should include existing pre-understanding in parentheses, thus raising consciousness about pre-understanding and controlling its influence as far as possible. In this study, the researchers' pre-understanding was constantly noted in memos and discussed with co-authors throughout the entire analysis process.

Dependability refers to the confirmation that the data represents the changing conditions of the phenomenon under study (Brown et al. 2002) and it should be consistent across time (Morrow, 2005). This is done by another individual who audits and confirms that the GT procedures are followed, and verifies that they are applied correctly (Brown et al. 2002). Peer researchers, student advisors or colleagues can examine the detailed chronology of research activities and processes or audit trials to determine the reliability of the findings (Morrow, 2005). In this study, face-to-face interviews were conducted by an PCSG member (UL) and another experienced oncology nurses, enabling inclusion of participants from all parts of Sweden. To ensure dependability, the same interview guide was used by the two interviewers and the interview techniques were discussed by them, according to recommendations put forward by Morse et al. about stepwise verification strategies (Morse, Barrett, Mayan, Olson, & Spiers, 2002).

Transferability refers to the applicability of one set of findings to another setting (Brown et al., 2002). The Skandion Clinic was a recently established facility implementing a new care strategy requiring that patients living far from the clinic stay at the patient hotel. These circumstances may limit the transferability of the findings to patients treated in ordinary Swedish cancer care facilities.

The TOUS has permeated the entire thesis, with the intention of gaining deeper knowledge and understanding of all the dimensions of the symptoms, as well as examining the complex interactions of multiple symptoms, their influencing factors and their performance/outcomes. Furthermore, we aimed at generating suggestions for nurses concerning how the theory can be used practically to support patients in the process of symptom management. Nevertheless, an intervention component was identified as a limitation. There may be several possible explanations for this, e.g. that the intervention component is not clearly explained in the theory and that the theory is more useful for observing concepts and their relationships than for developing interventions. This has also been noted and discussed in an article by Lee et al. (2017), who performed an analysis and evaluation of the TOUS.

CONCLUSIONS

The overall purpose of this thesis was to investigate the experience of symptoms and HRQoL in patients with malignant or benign primary brain tumors who underwent PBT in a recently established clinic. We also investigated whether there were any differences between PBT and CRT patients. The main findings can be summarized as follows:

- A need for improvement was identified in items related to experience of QoC, particularly concerning information or consequences associated to symptoms. Deteriorating symptom experience during the treatment period indicates increased importance of focusing on symptom support.

- Better HRQoL correlated with a higher degree of perceived support concerning the experienced symptoms.

- Three symptom clusters were formed related to PBT: *Mood, Reduced Appetite*, and *Reduced Energy*. Comorbidity, female sex and low education levels may negatively affect the respective symptom clusters.

- No statistically significant differences were found between the PBT and CRT groups in any of the functioning scales or single items in the QLQ C-30, when it came to change from baseline to three months after treatment.

- Patients with primay brain tumors given PBT have needs that change during, as well as up to three months after the end of, treatment.

- A substantive theoretical model was developed to explain symptom management. When participants found new rhythms and routines, they reported that it was important to establish a balance in order to avoid symptoms becoming overwhelming.

- The TOUS highlights the multidimensionality of symptoms in primary brain tumor patients who have undergone PBT.

CLINICAL IMPLICATIONS

There is a need to develop evidence-based guidelines for symptom management, in order to provide high QoC for patients experiencing low HRQoL associated to PBT. Our findings, reported in this thesis, emphasize the importance of tailored symptom care for primary brain tumor patients. When starting up a new healthcare organization, it is important to ensure high QoC so that patients feel that their needs have been met. One suggestion is to implement person-centered care (PCC). PCC can be understood as a model that could be well suited to confronting the specific challenges patients with primary brain tumor may experience. PCC highlights the importance of knowing the person behind the patient – as a human being with reason, will, feelings and needs – in order to engage him/her as an active partner in his/her care and treatment. Giving the patient the opportunity to present her-/ himself as a person in the form of an illness narrative is the starting point for building a collaborative, egalitarian provider (care and treatment expert)-patient (person expert) partnership that encourages and empowers patients to actively take part in finding solutions to their experienced symptoms and other obstacles. Working in partnership with the patient and shared decision-making can also stabilize the relationship between the healthcare professional and the patient. In other words, the patient becomes more than a disease (Ekman et al. 2011). This is borne out by our results, for instance when participants experienced symptoms differently and symptom management was described as a process consisting of actions, thoughts and emotions.

FUTURE PERSPECTIVES

This thesis has discussed QoC and the multiple dimensions of symptoms, including the symptom experience and its predictors, change over time in both symptoms and HRQoL, as well as symptom management during and after PBT and CRT in patients with primary brain tumors. Several questions have been answered but new issues, requiring answers, have also arisen.

Firstly, further studies exploring symptom clusters are warranted, investigating symptom patterns across the illness trajectory and comparing symptom clusters related to PBT and CRT in patients with different cancer diagnoses.

Secondly, the studies in this thesis did not investigate long-term effects, which are very interesting because of the risk of related irreversible impairments. Research taking these variables (affecting HRQoL) into account with a long-term perspective is thus warranted.

Thirdly, the patients we studied have a wide range of prognoses and functional implications of their disease and treatments. A need for improvement was identified related to QoC. This would be an appropriate area for further research, in order to implement tailored care for patients with brain tumors given PBT or CRT. The TOUS should be used when planning such research, to ensure that all interactions and feedback effects on the symptom experience are included.

Finally, patients with brain tumors needs for support and care, including for disabling effects, have been recognized as considerable and shortcomings have been identified. Increased information about symptoms and symptom management would improve care and must be developed in close collaboration with other healthcare professionals. Increased understanding within this area will inform new hypotheses for future research, and identify practice issues that healthcare professionals should address in more depth.

ACKNOWLEDGEMENTS

Last and foremost, I thank my family. My dear mother, *Anita*, you kept your promise. Everyone should have a mother like you. My sister *Jane,* for your love and words of encouragement.

Daniel and Elin, you are the ones who matter most. I love you more than words can describe.

APPENDIX

SAHLGRENSKA AKADEMIN
PROTONCARE

GÖTEBORGS UNIVERSITET

PATNR
INITIALER

Frågeformulär för studien:
Behandling med protonterapi för patienter med cancersjukdom - en undersökning av patientrapporterade biverkningar och hälsorelaterad livskvalitet på kort och lång sikt samt upplevelse och tillfredställelse av vården

IFYLLES AV PATIENTEN (med kryss där inget annat anges)

Civil status   Gift/Sambo [ ]   Ensamboende [ ]

Antal barn i hemmet [ ]

Ålder på barn/en [ ]

Utbildning (ange högsta)   Grundskola [ ]

Gymnasium/Yrkesskola [ ]

Högskola/Universitet [ ]

Sysselsättning   Yrkesarbetande   25% [ ]   50% [ ]
                                        75% [ ]   100% [ ]

Sjukskriven   25% [ ]   50% [ ]
                75% [ ]   100% [ ]

Åderspensionär [ ]

Annat   _____

Datum för ifyllande [ ]

1 (1)

Enkät för självskattning av annan sjukdom

Följande är en lista över vanliga sjukdomar. Sätt ett kryss för varje sjukdom som du har (ja eller nej). Om du har sjukdomen så svara vidare på frågorna om behandling och aktivitet. Om du inte har sjukdomen så gå vidare till nästa.

Sjukdom	Har du sjukdomen?		Om ja, begränsar det dina aktiviteter?		Om ja, får du behandling för det?	
	JA	NEJ	JA	NEJ	JA	NEJ
Hjärtsjukdom						
Högt blodtryck						
Lungsjukdom						
Diabetes						
Magsår eller magsjukdom						
Tarmsjukdom						
Leversjukdom						
Njursjukdom						
Anemi eller annan blodsjukdom						
Depression						
Artros						
Ledgikt eller rematoid artrit						
Sjukdom i bindväv eller muskulatur						
Hudbesvär						
Annan cancersjukdom						
Annat:						

Enkät för självskattning av annan ohälsa. Modifierad utifrån The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Sangha O[1], Stucki G, Liang MH, Fossel AH, Katz JN. Arthritis Rheum. 2003 Apr 15;49(2):156-63.

Baseline

PAT NR

INITIALER

Modifierad K U P P - Kvalitet Ur Patientens Perspektiv
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Markera på varje rad hur länge du fick vänta, samt hur du upplevde väntetiden. På de rader där det frågas om saker som inte ingått i din vård kryssar du "Ej aktuellt".

	Ej aktuellt	Hur länge fick du vänta?						Hur upplevde du väntetiden?				
		0-7 dagar	1 vecka – 1 månad	1-3 månader	3-6 månader	Mer än 6 månader	Vet ej	Mycket lätt	Lätt	Varken lätt eller svår	Svår	Mycket svår
1. ... före första besöket på sjukhuset?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
2. ... besked/diagnos (från ditt första besök på mottagning eller sjukhuset)?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
3. ... på strålbehandling (från besked om behandling)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

4. Hur upplevde du perioden före definitiv diagnos?

☐ Mycket lätt
☐ Lätt
☐ Varken lätt eller svår
☐ Svår
☐ Mycket svår
☐ Vet ej

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under **A** (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under **B** (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**

	A SÅ HÄR VAR DET FÖR MIG				**B** SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG				
	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt

Under min behandlingsperiod för tumör-/cancersjukdom...

5. ... fick jag bra information om planeringen av de olika stegen i min fortsatta vård	☐	☐	☐	☐	○	○	○	○	☐
6. ... hade jag bra möjlighet att samråda om beslut när det gällde min vård	☐	☐	☐	☐	○	○	○	○	☐
7. ... styrdes min vård av mina behov snarare än av personalens rutiner	☐	☐	☐	☐	○	○	○	○	☐

Under min behandlingsperiod för tumör-/cancersjukdom fick jag bra information om...

8. ... hur förberedelserna skulle gå till (skal, masktillverkning, simulator, datortomografi)	☐	☐	☐	☐	○	○	○	○	☐
9. ... hur strålbehandlingen skulle gå till	☐	☐	☐	☐	○	○	○	○	☐
10. ... vilka vanligt förekommande biverkningar jag kunde förvänta mig av strålbehandlingen	☐	☐	☐	☐	○	○	○	○	☐
11. ... resultatet av undersökningar och behandlingar	☐	☐	☐	☐	○	○	○	○	☐
12. ... egenvård; "hur jag bäst bör sköta min hälsa", t ex kost och motion	☐	☐	☐	☐	○	○	○	○	☐
13. ... om vilken läkare som var ansvarig för min vård/behandling	☐	☐	☐	☐	○	○	○	○	☐
14. ... om vilken sjuksköterska som var ansvarig för min omvårdnad	☐	☐	☐	☐	○	○	○	○	☐
15. ... om hur jag kan förebygga och lindra besvär från strålbehandlingen	☐	☐	☐	☐	○	○	○	○	☐
16. ... om hur länge besvären från strålbehandlingen kan finnas kvar	☐	☐	☐	☐	○	○	○	○	☐
17. ... om hur fysisk aktivitet kan öka mitt välbefinnande	☐	☐	☐	☐	○	○	○	○	☐
18. ... hur jag kan förändra min kost vid behov	☐	☐	☐	☐	○	○	○	○	☐
19. ... hur jag kan får hjälp av en dietist vid behov	☐	☐	☐	☐	○	○	○	○	☐
20. ... hur rökning kan påverka min strålbehandling	☐	☐	☐	☐	○	○	○	○	☐

	A SÅ HÄR VAR DET FÖR MIG				**B** SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG				
	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
21. ... hur jag kan få hjälp med att sluta röka	☐	☐	☐	☐	○	○	○	○	☐
22. ... vart jag kan vända mig med frågor om min onkologiska behandling	☐	☐	☐	☐	○	○	○	○	☐

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under **A** (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under **B** (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**

Under min behandlingsperiod för tumör-/cancersjukdom fick jag...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
23. ... effektiv hjälp med trötthet/kraftlöshet när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
24. ... effektiv hjälp med mina sömnproblem när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
25. ... effektiv hjälp vid oro och ångest när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
26. ... undersökningar och behandlingar genomförda inom acceptabel väntetid	☐	☐	☐	☐	○	○	○	○	☐

Läkarna...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
27. ... verkade förstå hur jag upplevde min situation	☐	☐	☐	☐	○	○	○	○	☐
28. ... bemötte mig med respekt	☐	☐	☐	☐	○	○	○	○	☐
29. ... visade engagemang; "brydde sig om mig"	☐	☐	☐	☐	○	○	○	○	☐

Sjuksköterskorna ...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
30. ... verkade förstå hur jag upplevde min situation	☐	☐	☐	☐	○	○	○	○	☐
31. ... bemötte mig med respekt	☐	☐	☐	☐	○	○	○	○	☐
32. ... visade engagemang; "brydde sig om mig"	☐	☐	☐	☐	○	○	○	○	☐

PAT NR

INITIALER

KUPP

KVALITET UR PATIENTENS PERSPEKTIV

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1. Hur upplevde du strålbehandlingsperioden?

☐ Mycket lätt
☐ Lätt
☐ Varken lätt eller svår
☐ Svår
☐ Mycket svår
☐ Vet ej

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under **A** (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under **B** (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**

	A — SÅ HÄR VAR DET FÖR MIG				B — SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG				Ej aktuellt
	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	

Under min behandlingsperiod för tumör-/cancersjukdom…

		A helt	A stor del	A delvis	A inte alls	B största	B stor	B ganska stor	B liten/ingen	Ej aktuellt
2.	… fick jag bra information om planeringen av de olika stegen i min fortsatta vård	☐	☐	☐	☐	○	○	○	○	☐
3.	… hade jag bra möjlighet att samråda om beslut när det gällde min vård	☐	☐	☐	☐	○	○	○	○	☐
4.	… styrdes min vård av mina behov snarare än av personalens rutiner	☐	☐	☐	☐	○	○	○	○	☐

Under min behandlingsperiod för tumör-/cancersjukdom fick jag bra information om…

		A helt	A stor del	A delvis	A inte alls	B största	B stor	B ganska stor	B liten/ingen	Ej aktuellt
5.	… hur förberedelserna skulle gå till (skal, masktillverkning, simulator, datortomografi)	☐	☐	☐	☐	○	○	○	○	☐
6.	… hur strålbehandlingen skulle gå till	☐	☐	☐	☐	○	○	○	○	☐
7.	… vilka vanligt förekommande biverkningar jag kunde förvänta mig av strålbehandlingen	☐	☐	☐	☐	○	○	○	○	☐
8.	… resultatet av undersökningar och behandlingar	☐	☐	☐	☐	○	○	○	○	☐
9.	… egenvård; "hur jag bäst bör sköta min hälsa", t ex kost och motion	☐	☐	☐	☐	○	○	○	○	☐

Under min behandlingsperiod för tumör-/cancersjukdom fick jag bra information…

		A helt	A stor del	A delvis	A inte alls	B största	B stor	B ganska stor	B liten/ingen	Ej aktuellt
10.	… om vilken läkare som var ansvarig för min vård/behandling	☐	☐	☐	☐	○	○	○	○	☐
11.	… om vilken sjuksköterska som var ansvarig för min omvårdnad	☐	☐	☐	☐	○	○	○	○	☐
12.	… om hur jag kan förebygga och lindra besvär från strålbehandlingen	☐	☐	☐	☐	○	○	○	○	☐
13.	… om hur länge besvären från strålbehandlingen kan finnas kvar	☐	☐	☐	☐	○	○	○	○	☐
14.	… om hur fysisk aktivitet kan öka mitt välbefinnande	☐	☐	☐	☐	○	○	○	○	☐

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under **A** (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under **B** (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**

A
SÅ HÄR VAR DET FÖR MIG

B
SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG

	A: Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	B: Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt

Under min behandlingsperiod för tumör-/cancersjukdom fick jag bra information om...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
15. ... hur jag kan förändra min kost vid behov	☐	☐	☐	☐	○	○	○	○	☐
16. ... hur jag kan får hjälp av en dietist vid behov	☐	☐	☐	☐	○	○	○	○	☐
17. ... hur rökning kan påverka min strålbehandling	☐	☐	☐	☐	○	○	○	○	☐
18. ... hur jag kan få hjälp med att sluta röka	☐	☐	☐	☐	○	○	○	○	☐
19. ... vart jag kan vända mig med frågor om min onkologiska behandling	☐	☐	☐	☐	○	○	○	○	☐

Under min behandlingsperiod för tumör-/cancersjukdom fick jag...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
20. ... effektiv hjälp med trötthet/kraftlöshet när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
21. ... effektiv hjälp med mina sömnproblem när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
22. ... effektiv hjälp vid oro och ångest när jag behövde	☐	☐	☐	☐	○	○	○	○	☐
23. ... undersökningar och behandlingar genomförda inom acceptabel väntetid	☐	☐	☐	☐	○	○	○	○	☐

Läkarna...

	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	Ej aktuellt
24. ... verkade förstå hur jag upplevde min situation	☐	☐	☐	☐	○	○	○	○	☐
25. ... bemötte mig med respekt	☐	☐	☐	☐	○	○	○	○	☐
26. ... visade engagemang; " brydde sig om mig"	☐	☐	☐	☐	○	○	○	○	☐
27. Jag fick oftast träffa samma läkare under behandlingsperioden	☐	☐	☐	☐	○	○	○	○	☐

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under **A** (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under **B** (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**

Sjuksköterskorna ...

	A — SÅ HÄR VAR DET FÖR MIG				B — SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG				Ej aktuellt
	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	
28. ... verkade förstå hur jag upplevde min situation	☐	☐	☐	☐	○	○	○	○	☐
29. ... bemötte mig med respekt	☐	☐	☐	☐	○	○	○	○	☐
30. ... visade engagemang; " brydde sig om mig"	☐	☐	☐	☐	○	○	○	○	☐
31. Jag fick oftast träffa samma sjuksköterska under behandlingsperioden	☐	☐	☐	☐	○	○	○	○	☐

Jag upplever att...

	A — SÅ HÄR VAR DET FÖR MIG				B — SÅ HÄR BETYDELSEFULLT VAR DET FÖR MIG				Ej aktuellt
	Instämmer helt	Instämmer till stor del	Instämmer delvis	Instämmer inte alls	Av allra största betydelse	Av stor betydelse	Av ganska stor betydelse	Av liten eller ingen betydelse	
32. ... personalen i kassan bemötte mig med respekt	☐	☐	☐	☐	○	○	○	○	☐
33. ... samarbetet mellan sjukhusets olika enheter fungerade bra	☐	☐	☐	☐	○	○	○	○	☐
34. ... jag fick tala med vårdpersonal i enrum vid de tillfällen som jag önskade	☐	☐	☐	☐	○	○	○	○	☐
35. ... mina närstående bemöttes på ett bra sätt	☐	☐	☐	☐	○	○	○	○	☐
36. ... under min tid på sjukhuset hade personalen jag träffade den kompetens som var nödvändig för min vård	☐	☐	☐	☐	○	○	○	○	☐
37. ... det var lätt att komma fram på telefon till sjukhusets enheter	☐	☐	☐	☐	○	○	○	○	☐
38. ... det var lätt att få besökstid hos läkaren	☐	☐	☐	☐	○	○	○	○	☐
39. ... det var lätt att få besökstid hos sjuksköterskan	☐	☐	☐	☐	○	○	○	○	☐

40. Har du följt de råd och anvisningar som du fått av vårdpersonalen?

☐ Ja, helt och hållet
☐ Ja, delvis
☐ Nej
☐ Vet ej
☐ Har inte fått råd och anvisningar av vårdpersonalen

41. Om du inte har följt råd och anvisningar –
Varför har du inte följt råden och anvisningarna?

_____

_____

_____

_____

42. Kände du dig trygg och säker med den vård du erhöll på sjukhuset under din behandlingsperiod för tumör-/cancersjukdom?

☐ Ja, helt och hållet
☐ Ja, delvis
☐ Nej

43. Om du inte kände dig trygg och säker med den vård du fick –
Varför kände du dig otrygghet?

_____

_____

Modifierad KUPP 2014 IMPROVEIT och Bodil Wilde Larsson

44. Det här var jag särskilt nöjd med:

45. Förslag till förbättringar:

46. Så här skulle jag vilja bli omhändertagen som patient med tumör/cancer:

Modifierad KUPP 2014 IMPROVEIT och Bodil Wilde Larsson
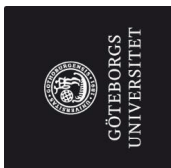
SAHLGRENSKA AKADEMIN
ProtonCare Daglig symtomskattning

GÖTEBORGS UNIVERSITET

Datum för ifyllandet: _____

Markera ditt svar med **två kryss på varje rad.**
1) sätt ett kryss under A (☐☐☐☐) som graderar upplevelsen.
2) sätt ett kryss under B (○○○○) som graderar betydelsen.
Eller sätt ett kryss under **Ej aktuellt.**
Eller sätt ett kryss under **Ej aktuellt**

Har du under det senaste dygnet

	A SÅ HÄR VAR DET FÖR MIG				B SÅ HÄR VAR BESVÄRANDE VAR DET FÖR MIG				Ej aktuellt
	Inte alls	Lite	En hel del	Mycket	Av litet eller inget besvär	Av ganska stort besvär	Av stort besvär	Av allra största besvär	
1. varit trött/kraftlös?	☐	☐	☐	☐	○	○	○	○	☐
2. haft svårt att sova?	☐	☐	☐	☐	○	○	○	○	☐
3. haft ont?	☐	☐	☐	☐	○	○	○	○	☐
4. känt aptitlöshet?	☐	☐	☐	☐	○	○	○	○	☐
5. haft andningssvårigheter?	☐	☐	☐	☐	○	○	○	○	☐
6. haft problem att tänka klart eller minnas?	☐	☐	☐	☐	○	○	○	○	☐
7. känt dig orolig?	☐	☐	☐	☐	○	○	○	○	☐
8. haft ångest?	☐	☐	☐	☐	○	○	○	○	☐
9. mått illa?	☐	☐	☐	☐	○	○	○	○	☐
10. känt dig ledsen?	☐	☐	☐	☐	○	○	○	○	☐
11. varit förstoppad?	☐	☐	☐	☐	○	○	○	○	☐
12. haft diarré?	☐	☐	☐	☐	○	○	○	○	☐
13. haft besvär från huden inom det strålbehandlande området	☐	☐	☐	☐	○	○	○	○	☐

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