SYMPTOM EXPERIENCE AND THEIR EFFECTS ON HEALTH-RELATED QUALITY OF LIFE OVER TIME IN ADULTS WITH PRIMARY BRAIN TUMOR RECEIVING RADIOTHERAPY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY (NURSING)
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2015

Thesis
entitled

SYMPTOM EXPERIENCE AND THEIR EFFECTS ON HEALTH-RELATED QUALITY OF LIFE OVER TIME IN ADULTS WITH PRIMARY BRAIN TUMOR RECEIVING RADIOTHERAPY

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was submitted to the Faculty of Graduate Studies, Mahidol University
for the degree of Doctor of Philosophy (Nursing)
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ACKNOWLEDGEMENTS

This dissertation would not have been possible achievement without enormous support and guidance from many people. First of all, I would like to express my sincere appreciation and gratefulness to those who always supported me throughout not only the way to doctoral studies but also the way to handle my family. My most earnest acknowledgement express to my major advisor, Asst. Prof. Dr. Orapan Thosingha for her generosity, valuable guidance, thoughtful suggestion, kindly support, enthusiastic encouragement, and providing endless consultant throughout the coursework and in the dissertation process. My words cannot express all of my grateful to her.

I would like to express my deep gratitude to Assoc. Prof. Prasert Sarnvivad, M.D. for his thoughtful suggesting, valuable guidance, comments, and enthusiastic work with me on developing a dissertation. I would like to extend my sincere thanks and appreciation to the members of my dissertation committee, Assoc. Prof. Dr. Usavadee Asdornwised for her valuable and creative suggestions and Assoc. Prof. Dr. Chukiat Viwatwongkasem for his knowledgeable guidance in data analysis. I am also especially grateful to Prof. Emeritus Dr. Somchit Hanucharurnkul, the chair of my dissertation defense for her supporting, guiding, and Dr. Somphob Sangkittipaiboon my external examiner, for his time to read my study thoroughly, particularly his valuable comments. They have bigheartedly given their time and proficiency to better my work.

My sincere gratitude conveys to Assoc. Prof. Mantana Dhanachai, M.D. and Assoc. Prof. Vutisiri Veerasarn, M.D. for theirs kindness to be as a project coordinator in clinical setting. I wish to thank the head and staff nurses in the outpatient radiotherapy unit of Ramathibodi Hospital, Siriraj Hospital and the National Cancer Institute of Thailand for their supporting as a resource person for my research.

My deepest gratitude goes to my wonderful family, my mother, my sisters and my brother for their greatest love and support. I wish to thank all my friends, and Ph.D. nursing students' batch 10, my doctoral classmates, for their experience and information sharing, friendship, and support.

Finally, special thanks and sincere appreciation are due to all brain tumor patients and their families who provided time and their willingness to share information. Without their cooperation, this study could not have been successful. It is my sincere hope that they, and other brain tumor patients in the future, benefit from my research.

Natthacha Chiannilkulchai

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ABSTRACT

The purpose of this prospective study was to evaluate patterns, relationships, and factors predicting changes in symptom experiences and adverse effects on health related quality of life (HRQOL) in adults with primary brain tumors (PBT) receiving radiotherapy, using the Symptom Management Model as a conceptual framework. One hundred and twenty adults aged above 18 years were recruited from three tertiary care hospitals. The measurements in this study comprised of the demographic and medical record form, the Mini-Mental State Examination, the M.D Anderson Symptom Inventory-Brain Tumor, and the Functional Assessment of Cancer Therapy-Brain. Data were collected prior to, during, and at the end of radiotherapy. Descriptive statistics, ANOVA, MANOVA, and GEE were used to analyze the data.

The result showed that the majority of patients were meningiomas (60.0%) and pituitary adenoma (16.7%). Radiotherapy included Intensity-modulated radiotherapy (IMRT), X-knife a median fractional dose of 2.0 Gy (range 1.8-6.75) up to a median total dose of 45 Gy (range 20.0-70.0), and a Cyber knife with a median fractional dose of 4.63 Gy (range 4.0-6.75 Gy) up to a mode total dose of 25 Gy (20.0-33.75 Gy). The pattern of symptom occurrence and severity increased in a linear pattern, whereas symptom interference changed in a quadratic pattern. The tumor type had a significant predicted symptom experience at each time point and over time. The type of radiotherapy significantly predicted symptom occurrence and severity during and at the end of treatment and over time. Tumor laterality significantly predicted symptom occurrence at the end of treatment and predicted the symptom severity over time. The interaction between tumor laterality and tumor type significantly predicted symptom occurrence and severity before receiving radiotherapy and predicted symptom occurrence over time. The interaction between tumor location and tumor type significantly predicted symptom severity during treatment and predicted both symptom severity and interference at the end of receiving radiotherapy. The pattern of HRQOL decreased after receiving radiotherapy 8-10 Gy, but it increased at the end of radiotherapy. The symptom severity and interference predicted HRQOL at each time point and over time.

It is recommended that patients with PBT, receiving radiotherapy, should be monitored for their specific symptoms including weakness, sad feelings, irritability and difficulty with concentration from the beginning until the end of radiation therapy. Practice guidelines to manage these symptoms should be developed in order to better improve their quality of life across the treatment trajectory.

KEY WORDS: SYMPTOM EXPERIENCE / HEALTH-RELATED QUALITY OF LIFE / OVERTIME / PRIMARY BRAIN TUMOR / RADIOTHERAPY

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ประสบการณ์การเกิดอาการ และอิทธิพลของการเกิดอาการต่อคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพ ตามระยะเวลาที่เปลี่ยนแปลงไปในผู้ป่วยเนื้องอกสมองปฐมภูมิที่ได้รับการรักษาด้วยรังสีรักษา

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บทคัดย่อ

วัตถุประสงค์ของการศึกษาแบบติดตามไปข้างหน้านี้ เป็นการศึกษารูปแบบ ความสัมพันธ์และปัจจัยที่ทำนายการเปลี่ยนแปลงของอาการและอิทธิพลของการเกิดอาการต่อคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพ ตามระยะเวลาที่เปลี่ยนแปลงไปในผู้ป่วยเนื้องอกสมองปฐมภูมิที่ได้รับการรักษาด้วยรังสีรักษา โดยใช้กรอบแนวคิดการจัดการกับอาการของดอร์ดและคณะ กลุ่มตัวอย่างเป็นผู้ป่วยเนื้องอกสมองปฐมภูมิซึ่งมีอายุ 18 ปีขึ้นไป จำนวน 120 คน ที่มารับการรักษาในโรงพยาบาล 3 แห่ง และมีคุณสมบัติตามเกณฑ์ที่กำหนด เครื่องมือที่ใช้ในการวิจัยได้แก่ แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา แบบทดสอบสภาพสมองเบื้องต้น แบบวัดอาการเนื้องอกสมองของนายแพทย์แอนเดอร์สัน และแบบวัดคุณภาพชีวิตในผู้ป่วยเนื้องอกสมอง เก็บข้อมูล 3 ครั้ง ตั้งแต่ก่อนการรรักษา ระหว่าง และครบการให้รังสีรักษา วิเคราะห์ข้อมูลโดยใช้ สถิติบรรยาย วิเคราะห์ความแปรปรวน วิเคราะห์ความถดถอยเชิงพหุ และจีอีอี

ผลการศึกษาพบว่าส่วนใหญ่ของผู้ป่วยมีเนื้องอกชนิด meningioma 60.0% รองลงมาคือ pituitary adenoma 16.7% ประเภทของรังสีรักษาประกอบด้วย IMRT, X-knife และ cyber knife องค์ประกอบของประสบการณ์ของอาการ ด้านจำนวนของอาการที่เกิด และความรุนแรงของอาการที่เกิด มีรูปแบบการเปลี่ยนแปลงเป็นเส้นตรง ในขณะที่ผลกระทบของอาการมีรูปแบบการเปลี่ยนแปลงเป็นรูปโค้งคว่ำ ปัจจัยที่มีความสัมพันธ์กับองค์ประกอบของประสบการณ์ของอาการ ได้แก่ ชนิดของรังสีรักษา ประเภทของเนื้องอกสมอง ซีกสมองที่เนื้องอกเกิด ตำแหน่งของเนื้องอกสมอง โดยที่ประเภทของเนื้องอกสมองมีอิทธิพลต่อองค์ประกอบของประสบการณ์ของอาการทั้ง 3 ด้านและ 3 ช่วงเวลา ชนิดของรังสีรักษามีอิทธิพลต่อจำนวนของอาการที่เกิดและความรุนแรงของอาการระหว่างและสิ้นสุดการได้รับรังสีรักษา ซีกสมองมีอิทธิพลต่อจำนวนของอาการที่เกิดตามเมื่อสิ้นสุดการรักษาด้วยรังสีรักษาและระยะเวลาที่เปลี่ยนแปลงไป ปัจจัยทำนายร่วมระหว่างซีกสมองและประเภทเนื้องอกสมองมีอิทธิพลต่อจำนวนของอาการที่เกิดและความรุนแรงก่อนได้รับการรักษาด้วยรังสีและตามระยะเวลาที่เปลี่ยนแปลงไป ปัจจัยทำนายร่วมระหว่างตำแหน่งและประเภทของเนื้องงอกสมองมีอิทธิพลต่อความรุนแรงของอาการและผลกระทบของอาการ รูปแบบคุณภาพชีวิตเป็นรูปโค้งหงาย สำหรับประสบการณ์ของอาการในการทำนายคุณภาพชีวิต พบว่า ประสบการณ์ด้านความรุนแรงของอาการที่เกิด และผลกระทบของอาการ เป็นตัวทำนายคุณภาพชีวิตอย่างมีนัยสำคัญทางสถิติ

ผลการศึกษามีข้อเสนอแนะเพื่อให้พยาบาลและบุคลากรทีมสุขภาพอื่นๆ มีความเข้าใจแบบแผนของอาการที่เกิดขึ้น ควรมีการติดตาม เฝ้าระวังและประเมินแบบแผนของอาการในผู้ป่วยเนื้องอกสมองปฐมภูมิที่ได้รับการรักษาด้วยรังสีรักษา การเปลี่ยนแปลงของอาการ กล้ามเนื้ออ่อนแรง อารมณ์เศร้า หงุดหงิด และ มีความลำบากในการรวบรวมสมาธิ ตั้งแต่ก่อนการรักษา จนเสร็จสิ้นการรักษา และนำไปใช้ในการวางแผนพัฒนาแนวปฏิบัติทางคลินิกในการจัดการอาการที่เปลี่ยนแปลงไปในแต่ละช่วงเวลา เพื่อพัฒนาคุณภาพชีวิตของผู้ป่วยให้ดีขึ้น

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CHAPTER I
INTRODUCTION

Background and Significance of the Study

Currently, primary brain tumor (PBT) is a major cause of death and disability worldwide (Ownsworth, Hawkes, Steginga, Walker, & Shum, 2009). According to the report of the Central Brain Tumor Registry of the United States (CBTRUS, 2012), the prevalence of PBT and central nervous system tumors since 2004-2008 by histology and demographic data was 295,986 cases. The overall age-adjusted incidence rate was 19.89 per 100,000 person–years (CBTRUS, 2012). In Thailand, the incidence rate has been under recording even though some institutes have reported an increasing incidence rate (Prasat Neurological Institute, 2012; Thai Society of Therapeutic Radiology and Oncology, 2012). The National Cancer Institute (2012) reported that the ratio of newly diagnosed cancers of the brain and nervous system compared with new other cancers in 2011 was estimated at 1: 67.1 (new cases of brain and nervous system cancer accounted for 45 patients and other cancers 3,019 patients). The data on central nervous system tumors from 2009 to 2011 compiled by the Prasat Neurological Institute (2012) showed an increase of 6.8% (incidence in 2009 accounted for 515 cases and in 2011 accounted for 550 cases). Although the incidence of PBT is relatively low in comparison with tumors in other organs, they deserve a unique position in tumor treatments because they lead to significant interference with daily life and high mortality (Nasseri & Mills, 2009; Taphoorn, Sizoo, & Bottomley, 2010).

PBTs are a heterogeneous group of neoplasms associated with high rates of morbidity and mortality (Armstrong et al., 2006b). Patients with PBT are unique due to the tumor originating within the skull cavity and their progressive neurologic symptoms (Moore & Kim, 2010). PBT that originate from the supportive cells of the brain or glial cells are called gliomas, which are the most common cellular component of the brain and accounted for 80% of PBT (Moore & Kim, 2010).

Patients with PBT may suffer symptoms caused by their tumors and treatments. Experiencing symptom is the main reason that leads people to seek health care. Typical symptoms include persistent headache, seizure, nausea, vomiting, neurocognitive symptoms, and personality changes (Chandana, Movva, Arora, & Singh, 2008). Many factors influence the occurrence of symptoms. The patient's overall conditions as well as symptoms are related to age, health status prior to diagnosis, tumor location, tumor size, tumor growth rate, and treatment regimen (Ballantyne & Rees, 2008). However, for the majority of these neoplasms, the clinical presentation, diagnostic approach, and initial treatment are relatively similar.

Patients with PBT undergoing any adjuvant treatments including surgery, radiation, and chemotherapy are always bothered by multiple symptoms rather than a single symptom (Cahill, LoBiondo-Wood, Bergstrom, & Armstrong, 2012; Tsay, Chang, Yates, Lin, & Liang, 2012). From a literature review of treatment-related symptoms, mainly research in neurosurgery, cognitive dysfunctions are the principal endpoint in PBT (Das et al., 2012; Jakola, Gulati, Gulati, & Solheim, 2012). The most common radiotherapy-related symptoms in the short term were fatigue or leg weakness (Bosma et al., 2009; Brown et al., 2006), while in the long-term were cognitive impairments (Douw et al., 2009; Gleason et al., 2007; Surma-aho et al., 2001). Symptoms mainly related to chemotherapy treatment were psychological, such as depression, and physical symptoms such as fatigue and cognitive impairments (Erharter et al., 2010; Laack et al., 2011; Wellisch, Kaleita, Freeman, & Cloughesy, 2002). Even though many studies described the prevalence of symptom experience due to PBT, the majority of these studies reported that the symptoms are more accurately described as "sign" because they were objective assessments (Molassiotis et al., 2010b).

Dodd et al. (2001a) definitely a symptom as a subjective experience reported by an individual who interprets changes in bio-psychosocial functioning, sensations, or cognitive functioning. The symptom experience consists of one's perception of a symptom, evaluation of the meaning of a symptom and response to a symptom. Perception of symptoms is defined as whether an individual observes a change in the way he or she usually feels or behaves. People evaluate their symptoms by making judgments about the severity, cause, treatability and the effects of

symptoms on their lives. Responses to symptoms include physiological, psychological, socio-cultural and behavioral components (Dodd, et al., 2001). Cancer patients experience a multi-dimension of symptoms during the diverse stages of their disease (Spichiger et al., 2011).

To understand symptom management, comprehensive assessments provide a detailed view of patients. An appropriate care plan in response this assessment is modified from time to time in regular intervals (Lee & Fisch, 2011). A limitation of the research on the prevalence and features of the symptoms is the lack of knowledge and skills of health care providers to design effective symptom management plans (Patrick et al., 2003). Understanding a patient's symptom experience is a prerequisite for an appropriate symptom management strategy (Teunissen et al., 2007). Therefore, study of symptom experience over time provides a picture of the symptom management's effectiveness (Fairclough, 2012; Padilla, Kagawa-Singer, & Ashing-Giwa, 2012). That is urgently needed in PBT cases.

A few studies have investigated symptom experience over time, but they did not result in a consensus on symptom stability (Kim et al., 2009). Some studies reported no change in symptoms over time (Gleason et al., 2007) while other studies indicated symptoms changing over time. Whether symptom prevalence is consistent or changes over time, it is essential both in the clinical setting and for the science of symptom experience research. Therefore, clarifying if symptom experience changes over time is important in clinical practice to develop symptom management strategies. However, there has been limited information on the results of clinical trials.

The impact of symptom experience on individual outcomes has become interested in clinical trials. Several findings revealed that people with multiple symptoms had more difficulty in regard to everyday functions (Fan, Filipczak, & Chow, 2007). Patients with multiple symptoms demonstrated a lower functional health status, reduced cognitive functioning, less effective role performance, and lower physical performance capabilities (Madsen & Poulsen, 2011). Suffering from those multiple symptoms has affected patients' quality of life (QOL) (Liu, Page, Solheim, Fox, & Chang, 2009). Although many studies evaluated the impact of symptoms on QOL, only a few reported a correlation between cognitive function and health-related quality of life (HRQOL).

To achieve the highest number of desirable treatment outcomes, the individual's perspective and its influence on symptom prevalence and treatment outcome are now important issues in clinical trials (Armstrong, 2012). The best way is to evaluate the effect of a treatment from a patient's viewpoint is to use HRQOL as a patient-reported outcome (PRO) (Armstrong, 2012; Cleeland & Sloan, 2010; Efficace & Taphoorn, 2012; Mauer, Bottomley, & Taphoorn, 2008). One of the major findings from a workshop on QOL assessment in cancer symptom management trials was the need for further research to determine how HRQOL and symptoms or symptom clusters are related (Buchanan et al., 2007). The U.S. Food and Drug Administration (FDA) strongly recommended the use of a PRO instrument, which provides information from a patient's perspective, to evaluate a patient's symptoms (Armstrong, 2012; Cleeland & Sloan, 2010; Efficace & Taphoorn, 2012).

Despite the most effective treatment options such as surgery, radiotherapy, chemotherapy, combined radio-chemotherapy and other new treatments, greater toxicity and new deficits will emerge (Quinones-Hinojosa, Kosztowski, & Brem, 2011). Previous studies always measured symptom relief, progression-free survival, and/or overall survival from a primary brain tumor as the principal endpoint of treatment (Nieder, Mehta, & Jalali, 2009). These types of studies might not adequately reflect patients' outcomes. In 2010, Cleeland & Sloan proposed that HRQOL is an alternative to effectively reflect on patients' outcomes (Cleeland & Sloan, 2010). Accordingly, HRQOL has become an important endpoint in the brain tumor study.

QOL may depend on aspects of cognitive functioning which are difficult to explore and may have to do both with the disease itself and with the subjective reactions of patients undergoing treatment (Talacchi et al., 2012). Patients' reported outcomes on QOL should be based on both the brain tumor and treatment-related symptoms rather than only on patient satisfaction. This self-report should have good psychometric properties, be able to be finished with the majority of patients with cognitive declines, and be sensitive to changes over time. However, QOL changes do not parallel cognitive changes and thus cannot be used as a proxy for neurocognitive assessment (Meyers, Rock, & Fine, 2012).

Although there are a number of studies related to the prevalence of symptoms, little is known about how patients experience these symptoms and the

impact these symptoms in their daily lives from their own perspectives (Molassiotis et al., 2010b). In Thailand, symptom experiences among patients with PBT from their own perspectives are also unknown, which might lead to ineffective symptom management. Evidence from previous studies (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006; Buchanan et al., 2007) confirmed the need for gaining a better understanding of symptom experience, because this clinical groundwork could provide a scientific foundation for health care providers so that target health outcomes could be effectively achieved (Barsevick et al., 2006).

In response to this need, the Symptom Management Model (SMM) will be used to guide the present study (Dodd, Miaskowski, & Paul, 2001b). The SMM was developed to elaborate on the multifaceted nature of the individual's experience and perception of symptoms by his/her self-report, the impact of symptoms, and the individual's response to symptoms. Symptom management is a dynamic process of individuals' health/illness to the actions that begin with judgment to prevent or delay a negative outcome or minimize the symptom experience. According to the SMM, individuals' health-related outcomes are dependent on their health perceptions, symptom experiences, management capabilities, and on environmental factors. The overall purpose of the present study is to explore the pattern, relationships, and factors predicting changes in symptom experiences over time and to examine the adverse effect of symptom experiences on HRQOL over time in adults with PBT receiving radiotherapy.

Conceptual Framework

Although an individual's symptoms can be measured by various methods, the most valid way of measuring symptoms is to use a self-report (Dodd et al., 2001a). The Symptom Management Model (SMM) recognizes that symptom experiences are related to human consciousness and relies on human cognitions, thus it respects patients as selves (Dodd et al., 2001a). Symptoms are important phenomena and unique feature that reflect individual health status. It is difficult for health care providers to precisely assess symptoms and provide appropriate management

strategies if patients do not describe theirs perceived experience. Accordingly, the information gained from patients experience is crucial evidence in forming the basic knowledge to handle and provide essential management for patients. To understand the phenomena of symptom experience and the HRQOL in adults with PBT, the SMM will be used as the framework in this study. The SMM was developed by the University of California, San Francisco (UCSF) Symptom Management Faculty Group (Larson et al., 1994) and was revised in 2001 (Dodd et al., 2001a). Recently the SMM was renamed as "symptom management theory" (Humphreys et al., 2008).

The SMM based on the interrelationships among three important concepts, including symptom experiences, symptom management strategies, and symptom status outcomes. The concepts are framed within the dimensions of nursing science; person, health/illness, and environment. The model is based on six assumptions; 1) a self-report is the best way to assess the perception of the individual experiencing the symptoms, 2) intervention strategies may be initiated for people who are predicted to be at high risk for a symptom before they actually experience it, 3) a person who cannot communicate verbally may still experience symptoms and their interpretation by the caregiver is assumed accurate, 4) symptom management may be the purpose of the individual, group, family, or the environment levels, 5) symptom management is a dynamic process it is change by individual outcomes and effect their contextual of nursing domains 6) Symptoms are a part of a disease and need to be managed.

Symptom experience is a dynamic process combined with the interaction of an individual's perception, evaluation, and response to symptoms. Perception of symptoms is defined as the individual's interpretation of a change from the usual way that person feels or behaves. Evaluation of symptoms refers to an individual assessment of their symptoms by making judgments about the severity, cause, treatability and the effect of symptoms on their lives. Response to symptoms means a reflection of the change in emotion, sensation, or cognition. The relationships between these three components of the symptom experience are bi-directional (Dodd, et al., 2001).

Symptom management refers to the actions that begin with judgment of the symptom experience from the individual's perspective in order to prevent or delay a negative outcome or minimize the symptom experience. It is a dynamic process

requiring changes in strategy from time to time. A symptom management strategy identifies the need not only to provide an intervention, but also to identify the specifications of *what, when, how much, to whom, and why* of what can be done to treat symptoms (Dodd, et al., 2001).

Symptom outcomes are the consequences of symptom experiences and symptom management strategies, including functional status, emotional status, self-care, cost, quality of life, morbidity, and mortality. Outcomes, as depicted by the bi-directional arrows, can affect the symptom experience and symptom management. To measure outcomes should assess following the implementation of a strategy. This management of symptoms can lead to better or worse outcomes. For example, improvement in symptoms can lead to better functional status, emotional status, and self-care, less cost to individual, or health care system, improve in quality of life, can control morbidity & co-morbidity, decrease mortality rate, and stabilized in symptom status (Dodd et al., 2001a; Humphreys et al., 2008). The SMM model is shown in Figure 1.1

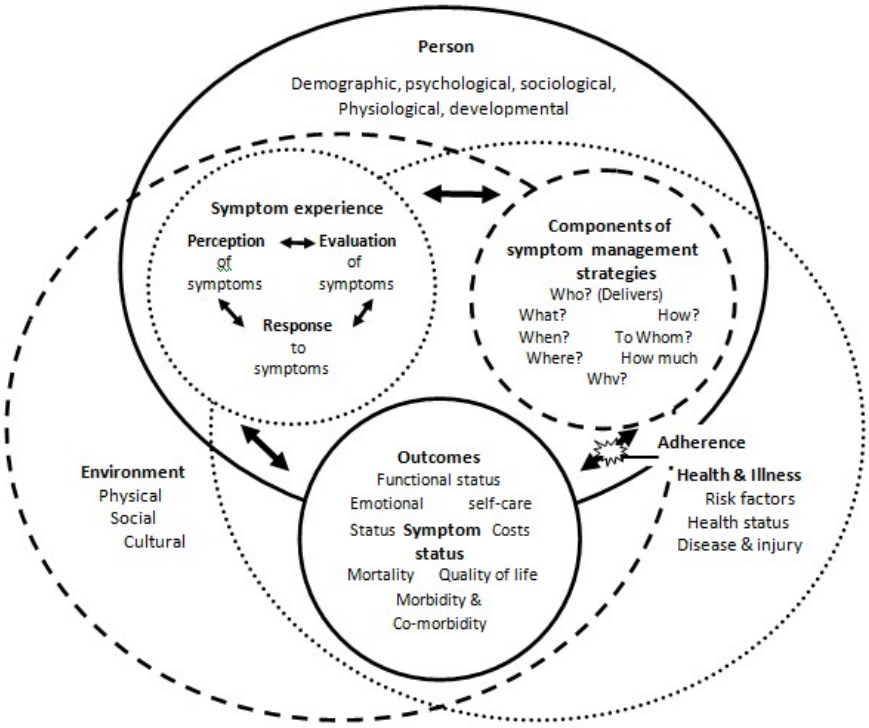

Figure1.1 Symptom Management Model (Dodd et al., 2001a) p. 670

Critique of the Symptom Management Model (SMM)

The SMM is a middle range theory. It can be applied as a guide in various health sciences especially in nursing. Some issues related to SMM that might cause limitations in this study should be noted.

The first concern is the difficulty of evaluating symptom frequency. An individual observing the incidence of his/her symptoms within a timeline can determine their frequency. However, some symptoms might have periodic patterns and there could be very slight changes. The individual might not notice their frequency within a short period, even within a week. This might result in a limitation in measuring the multiple dimensions of symptom experience.

The second concern is how to select an appropriate sample, choosing between a homogeneous sample which provides more disease-specific symptoms but low variance and a heterogeneous sample which provides broader and more common symptoms across diagnosis groups, increasing variance but has more confounding variables (Molassiotis, Wengström, & Kearney, 2010a). Nevertheless, focusing on the same disease and the same type of cancer, but on different treatments or at different stages, the presentations of symptoms will be varied.

The third is the lack of a clear definition for each component of the symptom outcome dimension. Clarification should lead to the determination of what a symptom is, what it is not, and how to separate responses to symptoms based on the outcome. For example, what the differences are between psychological symptoms and emotional status.

A related concern is the lack of comprehensive and integrated change in symptom experience over time, symptoms can be temporary, vary over time, or be chronically present (Portillo & Holzemer, 2007). The SMM does not consider how temporal symptoms are evaluated (Brant, Beck, & Miaskowski, 2010).

The last concern is what scale should be used to assess the symptom experience. There is a variety of different instruments for evaluating symptom experience. Even though some researchers used the same instrument, the ways that they interpreted the results were not the same. For example, Spichiger et al. (2011) used the MSAS to assess cancer-related symptoms. They determined a score for each symptom by using the mean of the summation of symptom frequency, symptom

severity, and symptom distress. Other researchers interpreted each symptom by using a total score from the summation of symptom frequency, symptom severity, and symptom distress for each symptom. In addition, a majority of these studies interpreted each symptom by using a total score from the summation of symptom frequency, symptom severity, and symptom distress. However, some researchers interpreted symptom experience as the summation of symptom occurrence and symptom distress (Fu, McDaniel, & Rhodes, 2007; Ryu, Kim, Choi, Cleland, & Fu, 2012). Fu, McDaniel, and Rhodes (2007) assessed symptom experience in cancer patients using the Symptom Experience Index. They interpreted symptom experience as the summation of symptom occurrence and symptom distress. Their results were confirmed by the study of Ryu, Kim, Choi, Cleland, and Fu (2012). They assessed symptom experience in cancer patients using the Symptom Experience Index and interpreted symptom experience as the summation of symptom occurrence and symptom distress. Therefore, it is difficult to compare studies and conclude which one used the most effective instrument for assessing the symptom experience and evaluating the effectiveness of treatment or intervention in terms of symptom perception, evaluation of symptoms, and response to symptoms.

In conclusion, the SMM has been used with a variety of groups of people with acute and chronic illness. Most studies are on a descriptive level. Identified limitations are mainly concerned with insufficient concept clarification, e.g. different concepts of the outcome dimension. Although the SMM has been utilized to explain the symptoms of many patients with cancer, these studies did not clearly elaborate on the cause of the symptoms; the explanations of symptom experiences and responses were emphasized. Therefore, there is still a limitation in differentiating between symptoms derived from the tumor itself or from the consequences of cancer treatment, including surgical treatment, radiotherapy, chemotherapy, or a combination of treatments. This might lead to some issues in measuring symptom experience in the present study. However, the SMM can be used to guide the present study by creating appropriate operational definitions.

Conceptual Framework of the Study

The Symptom Management Model will be used to describe and provide a better understanding of adults with PBT. This study was modifying the conceptual framework deriving from the SMM consists of two key concepts, including symptom experience and symptom outcomes that affects HRQOL.

Symptom experiences of adults with PBT in this study consist of their perception of symptoms, evaluation of symptoms, and response to symptoms as life interference. These interferences retained to general activity, mood, work, relations with other people, walking, and enjoyment of life.

Health-related quality of life (HRQOL) is a broad and multidimensional concept, which reflects the way that individuals perceive and react to their health status (Lin, Lin, & Fan, 2013; Revicki et al., 2000). HRQOL is defined as a subjective assessment that focuses on the effects of illness and the comprehensive health benefits and side effects of its treatment (Buchanan et al., 2007). All of these reflections are affected by individual experiences, expectations, beliefs, and perceptions (Testa & Simonson, 1996). HRQOL refers to a combination assessment of several health domains including the physical, psychological, social and somatic domains of functioning and well-being (Revicki et al., 2000). However, for other potential domains such as cognitive ability or sexual desire, there is less agreement on what should always be assessed (Buchanan et al., 2007). In clinical research, HRQOL can provide a means of capturing the personal and social context of the disease experience. HRQOL in patients with PBT will be assessed using five dimensions: physical well-being, social/family well-being, emotional well-being, functional well-being, and brain tumor specific concerns.

According to the changeability of symptoms related to the tumor itself and its treatment across the treatment trajectory, the patients may experience the change of symptoms over time. Thus the symptom experience, symptom outcome and theirs predictability were investigated at three time periods before receiving radiotherapy, after receiving radiotherapy 8-10 Gy, and at the end of receiving radiotherapy. The conceptual framework modified for adults with PBT based on the SMM model is shown in Figure 1.2.

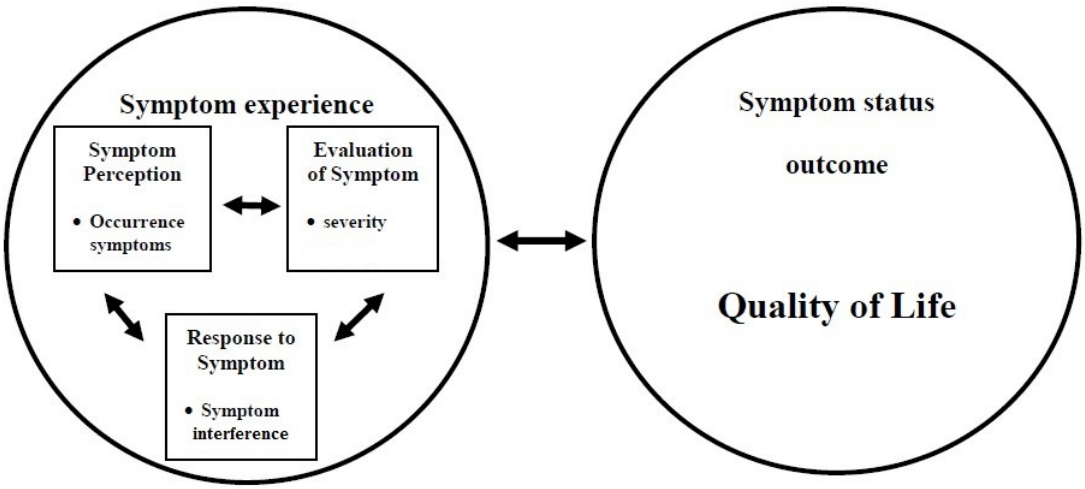

Figure 1.2 Conceptual framework of this study

Research Questions

The research questions to be addressed in this study are as follows:

1. What are the symptom perceptions (occurrence), symptom evaluations (severity), and symptom responses (life interferences) in Thai adults with PBT receives radiotherapy at time 1 (before receiving radiotherapy), time 2 (after receiving radiotherapy 8-10 Gy), and time 3 (at the end of receiving radiotherapy)?

2. What are the patterns of symptom perceptions (occurrence), symptom evaluation (severity), and symptom response (life interferences) in Thai adults with PBT receiving radiotherapy during time 1 to time 2 and during time 2 to time 3?

3. What are the effects of tumor factors (type, laterality, and location) and types of radiotherapy on symptom experiences (occurrence, severity, and life interferences) in Thai adults with PBT receiving radiotherapy at each time point?

4. Do tumor factors (type, laterality, and location) and types of radiotherapy predict changes in the symptom experiences (occurrence, severity, and life interferences) of Thai adults with PBT receiving radiotherapy during time 1 to time 2 and during time 2 to time 3?

5. What are the HRQOL of Thai adults with PBT receiving radiotherapy in each of the three points in time?

6. What are the changes over time in the HRQOL of Thai adults with PBT receiving radiotherapy from time 1 to time 2 and from time 2 to time 3?

7. What are the relationships among symptom experiences (occurrence, severity, and life interferences) and HRQOL at each time point?

8. Do symptom experiences (occurrence, severity, and life interferences) predict changes in HRQOL from time 1 to time 2 and from time 2 to time 3?

Purpose of the Study

The purposes of this study are to:

1. Describe the symptom occurrence, severity, and life interferences experienced by Thai adults with PBT receiving radiotherapy at each time point.

2. Describe the changes over time in symptom occurrence, severity, and life interferences experienced by Thai adults with PBT receiving radiotherapy at time 1 to time 2 and time 2 to time 3**.**

3. Determine the effect of tumor factors (type, laterality, location) and types of radiotherapy on symptom experiences (occurrence, severity, and life interferences) at each time point

4. Determine the predictability of tumor factors (type, laterality, location) and types of radiotherapy on the change of symptom experiences (occurrence, severity, and life interferences) experienced by Thai adults with PBT receiving radiotherapy over time

5. Investigate the HRQOL among Thai adults with PBT receiving radiotherapy at each time point.

6. Investigate the changes over time in the HRQOL among Thai adults with PBT receiving radiotherapy

7. Determine which domains of symptom experiences (occurrence, severity, and life interferences) predicting on HRQOL at each time point

8. Determine which domains of symptom experience (occurrence, severity, and life interferences) predicting on HRQOL over time

Scope of the Study

The scope of this study is to describe the symptom experiences and HRQOL of Thai adults with PBT at three times: 1week before radiotherapy, after receiving radiotherapy 8-10 Gy, and at the end of receiving radiotherapy. It was also evaluate the relationships among tumor factors (type, laterality, and location) and type of radiotherapy on the changes of symptom experiences (occurrence, severity, and life interferences). In addition, to evaluate the adverse effects of symptom experience on HRQOL over time. The subjects were Thai adults diagnosed with PBT who were receiving treatment in the outpatient radiotherapy clinics at the National Cancer Institute in Bangkok, Ramathibodi Hospital, and Siriraj Hospital. This study was conducted during October 2013 to October 2014.

Definition of Terms

Symptom experiences:

Conceptual definition: The interplay of an individual's perception of a change in bio-psychosocial functions, sensation, or cognition as symptoms, the way to interpret the change as an evaluation of symptoms, and reflection on the change as a response to the symptoms (Dodd, et al., 2001).

Operational definition: Adults with PBT reported on the change in their bio-psychosocial functions, sensation or cognition. Change is assessed by recognizing the occurrence of symptoms defined as the perception of symptoms, the evaluation of symptoms as symptom severity, and analyzing the response to symptoms as interferences with life. It will be measured by the MDASI-BT (item 1 to item 28 within the last 24 hours. Each symptom will be rated on an 11- point scales) (Armstrong et al., 2006b).

Perception of symptoms:

Conceptual definition: Perception of symptoms refers the change in the way a person usually feels or behaves, as noticed by that individual. It is a conscious

cognitive interpretation of information gathered by the senses in the context of a particular environment or situation (Dodd, et al., 2001) defined as the occurrence of a symptom.

*Operational definition***:** Perception of symptoms refers to the change that adults with PBT can observe from usual feel or behave. The perception of symptoms was measured by self-reported using the MDASI-BT (item 1 to item 22 within the last 24 hours). The occurrence of a symptom is defined by rating each item more than zero at time 1 (within 1 week before treatment), time 2 (after receiving radiotherapy 8-10 Gy), and time 3 (within 1 week before the treatment is completed).

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Evaluation of symptom:

Conceptual definition: Evaluation of symptom referes to the process of judgment about cause, frequency, and severity of symptoms which intermittence of symptom prevalence and the intensity or strength or amount of symptom being experience (Lenz, Pugh, Milligan, Gift, & Suppe, 1997).

*Operational definition***:** Evaluation of a symptom refers to the judgment of patients with PBT rated their severity of symptoms. The severity of symptoms was measured at three times by using self-reported MDASI-BT (item 1 to item 22 within the last 24 hours). Each symptom can be measured by self-reported on an 11- point scale with 1 meaning the least severity of the symptom to 10 meaning the most severe.

Response to symptoms:

Conceptual definition: Response to a symptom refer to the degree or level of physical or mental upset or suffering that result from the experienced symptom defined as symptom distress (Rhodes & Watson, 1987). It is the degree to which the person is bothered by the symptom (Lenz et al., 1997).

Operational definition: Response to a symptom refers to the interpretation of adults with a PBT rating of how much the symptom interfered with different aspects of a patient's life in the last 24 hours at the three times. The interfere of symptoms was measured by self-reported using MDASI-BT (part II item 23 to 28) on an 11-point scale with 0 meaning no interference to 10 meaning considerable interference.

Health Related Quality of Life (HRQOL)**:**

*Conceptual definition***:** A subjective assessment of the impact of disease and treatment from their own perspective across physical, psychological, emotional, and social domains of daily life (Aaronson, 1988; Revicki et al., 2000; Testa & Simonson, 1996).

*Operational definition***:** HRQOL of adults with PBT will be evaluated by using the Functional Assessment of Cancer Therapy- Brain (FACT-Br). This instrument has a 5-point scale with 0 meaning not at all of 4 meaning very much. The FACT-Br consists of five dimensions: physical well-being, social/family well-being, emotional well-being, functional well-being, and disease specific concerns.

Table 1.1 Summarized concepts and instruments

Variables	Instruments	Assessment
Perception of symptom	MDASI-BT, item 1-item 22	Sum total number of symptoms
Evaluation of symptom	MDASI-BT, item 1-item 22	Sum total of scores of all symptom severity score
Response to symptom	MDASI-BT, item 23-item 28	Sum total of scores on all interferences due to symptoms
Quality of life	FACT-Br	The sum total of scores on all items and mean and standard deviation of each sub-domains of quality of life scores

CHAPTER II
LITERATURE REVIEW

This chapter contains a review of the literature relevant to the scope of the study. The topics are as follows:

1. Overview of primary brain tumors
2. Symptom experiences of patients with primary brain tumors
3. Factors associated with symptom experiences
4. Impact of symptoms on outcomes
5. Impact of symptom management on outcomes
6. Health-related quality of life in adults with primary brain tumors
7. Cognitive decline and self-reports
8. Knowledge gaps identified

2.1 Overview of Primary Brain Tumors

2.1.1 Epidemiology

The worldwide incidence rate in 2008 for brain and central nervous system (CNS) cancers was estimated at 3.5 cases per 100,000 person-years. The incidence estimated by gender was 3.9 cases per 100,000 person-years for males and 3.2 cases per 100,000 person-years for females (Ferlay et al., 2010). The ratios of age-standard rates of incidence between developed and developing regions are 1.76 for males and 1.82 for females (Ferlay et al., 2010). The overall incidence rate has increased in the last two decades, mainly due to improvements in diagnosis (Cahill & Armstrong, 2011).

In Thailand, the incidence rate of primary brain tumor (PBT) cases has been under-estimated. The incidence of CNS tumors in 2011, estimated by the Prasat Neurological Institute (2012), was 550 cases (11.61%) which was one of the five most

common diseases of the brain. The incidence rate from 2010 to 2011 increased by 2.6 %. In addition, the Thai Society of Therapeutic Radiology and Oncology (2012) reported that the number of patients who were treated only with radiation from 2010 to 2012 has increased by 26.7%. The National Cancer Institute (2012) reported that the ratio of new brain and nervous system tumors (45 cases) in 2011 compared with new other cancer organs (3019 cases) was estimated to be 1: 67. However, these three data sets do not provide an estimate of the total incidence rate of primary brain tumors in Thailand.

2.1.2 Classification and Grading

PBT affecting the brain may arise within the brain itself or from nerves and other structures within the skull cavity. PBT are classified according to their cellular origin according to the World Health Organization (WHO) classification of central nervous system tumors. Tumors of neuroepithelial origin represent a significant number of PBT, including astrocytomas, oligodendrogliomas, ependymomas, choroid plexus tumors, neuronal and mixed neuronal-glial tumors, pineal lesions, and embryonal tumors (Louis et al., 2007).

The most common PBT in adults are gliomas, primary central nervous system lymphomas, meningiomas, and pituitary adenomas. Gliomas, which are mostly intra-axial masses in adult patients, accounted for 40 % of PBT and 70 % of adult malignant PBT (Ricard et al., 2012). Gliomas are a complex and heterogeneous group of PBT . There are two major subtypes of gliomas which derive from astrocytes and oligodendrocytes, the latter including pure and mixed oligodendrocytes (Gravendeel & French, 2011). Infiltrative astrocytomas are much more common, representing 75% of all lesions (Morales & Gaskill-Shipley, 2010). Meningiomas are neoplasms of meningothelial cells of the arachnoid layer and occur most frequently along the dural venous sinuses. Meningiomas accounted for 15-25% of all primary intracranial tumors in adults (Mennel et al., 2010). More than 80% of meningiomas are benign in nature (Sandberg & Stone, 2008). Pituitary adenomas accounted for 10-15% of all primary intracranial tumors (Choi & Biagioli, 2008; Lim & Lo, 2011) and are most common /frequent in adults following gliomas and meningiomas. Pituitary adenomas are benign epithelial tumors of the sellar region derived from secretory cells of the

adenohypophysis (Reifenberger, Blümcke, Pietsch, & Paulus, 2010). Primary central nervous system lymphomas (PCNSL) accounted for approximately 5 % of all PBT. More than 95 % of PCNSL are diffuse large B-cell lymphomas (Doucet, Kumthekar, & Raizer, 2013).

Grading of brain tumors, according to the WHO, assigns them to four grades: grades I and II are low-grade benign tumors and grades III and IV are high-grade malignant tumors. Grading is based on the degree of nuclear changes, mitotic activity, endothelial proliferation, and necrosis (Morales & Gaskill-Shipley, 2010). Grading is clinically important because a prognosis becomes worse as tumor grading increases (Bent, Hegi, & Stupp, 2006).

2.1.3 Type and Protocol of Treatment

The tumor type, location, and grade are the key factors used to determine the type of treatment. Treatment is a possible cure for some brain tumors while there may be no recommended course of treatment for other brain tumors.

Surgery

Surgical resection is the initial choice of treatment for brain tumors. Different from a tissue diagnosis, resection aims to reduce symptoms from tumor mass effect or hydrocephalus and to reduce steroid requirements (Nieder et al., 2009; Pouratian, Crowley, Sherman, Jagannathan, & Sheehan, 2009). Surgical approaches in brain tumor treatment include tumor resection (complete removal) or debulking (removing as much as possible), or biopsy (removal of a small fragment of the tumor). The indicated type of surgery depends on the location, the size, the tumor growth rate, and whether or not hydrocephalus is present (Mennel et al., 2010). Most tumors will be treated by resection if possible for safety, but some are primarily unresectable (mostly midline tumors). These tumors will be biopsied to obtain a proper tissue diagnosis before considering conservative or nonsurgical treatments (Ironside & Ironside, 2012). In some cases, surgery may be the single method that is essential, but other cases may require different treatments such as radiation therapy or chemotherapy. Although, open excisional biopsy or resection provides a way of tissue examination or tumor size reduction better than biopsy, a stereotactic or image-guided

biopsy can be a substitute for a craniotomy for the purposes of histological diagnosis. The Image-guided stereotactic provides in which a small deep lesion or tumor located in the eloquent cortex prohibits the use of craniotomy or excisional biopsy. Moreover, this method is suitable for diffusive neural tumors (Tamber & Bernstein, 2009). However, one pitfall of a stereotactic biopsy for tissue diagnosis is the possibility of misdiagnosis or inaccurate tumor grading owing to tumor heterogeneity and diagnosis bias resulting from limited tumor sampling (Sanai & Berger, 2011). Currently, the role of surgical intervention is growing with various novel techniques, e.g. awake surgery (Talacchi, Santini, Savazzi, & Gerosa, 2011), language mapping surgery (Sanai & Berger, 2009), and cytoreductive surgery (Ryken, Frankel, Julien, & Olson, 2008). Controversial issues remain due to the lack of consensus on which is the most effective type of surgery (Ryken et al., 2008).

In conclusion, the majority of studies of brain tumor surgery focused on methods to diagnose the tumor, e.g. tissue biopsy, use of craniotomy or open resection, the advantages and disadvantages of these two methods, and the type of extensive resection associated with prolonged survival. This lack of clarity is confounded by the fact that these types of surgery may reduce or increase symptoms. Therefore, aggressive surgery may be associated with new deficits (Chaichana & McGirt, 2012; Quinones-Hinojosa et al., 2011). At present, surgery followed by radiotherapy has been reported as the principal treatment used to increase overall survival and reduce recuperation time. However, only palliative advantages have been considered (Nieder et al., 2009).

Radiotherapy

It is well recognized that radiotherapy is still the initial standard therapy and a major treatment modality for patients with primary brain tumors (Henriksson, Asklund, & Poulsen, 2011). The current modalities of radiation therapy for treatment of benign and malignant brain tumors are conventional radiotherapy, stereotactic radiosurgery, and stereotactic radiotherapy (Chaichana & McGirt, 2012; Jabbour, Zhang, Arnold, & Wharam, 2009). Conventional radiotherapy is typically fractionated radiation of a lower daily dose, which is assumed to reduce the effects of radiation on normal tissue. Fractionated radiotherapy allows the repair of deoxyribonucleic acid

(DNA) in normal cells, reoxygenation of hypoxic tumor cells, repopulation of tumor cells, and reassortment of tumor cells into more susceptible phases of the cells cycle (Jabbour et al., 2009). Radiation energy of conventional radiotherapy is delivered in two ways. First, radiation beamed from a radiation source to the patient is called 'external beam radiotherapy'. Second, a technique in which a radioactive source is implanted within the patient and provides a high local dose of radiation while minimizing damage to surrounding tissue is called 'brachytherapy' (Chaichana & McGirt, 2012). Fractionated radiotherapy is frequently used for the treatment of benign primary brain tumors, either as a primary treatment or more frequently as an adjunctive therapy (Talacchi et al., 2011). For patients with low-grade gliomas, a total dose of fractionated radiotherapy (45-50.4 gray (Gy) in 25-28 daily fractions of 1.8 Gy) is recommended (Board of the Faculty of Clinical Oncology The Royal College of Radiology, 2006). For malignant gliomas, the standard of care in the adjuvant setting after aggressive operative resection is radiotherapy (Teixidor et al., 2007). A total dose of fractionated radiotherapy for high-grade gliomas (60 Gy delivered in 1.8–2 Gy in 30 daily fractions over 6 weeks) is recommended (Board of the Faculty of Clinical Oncology The Royal College of Radiology, 2006).

Radiosurgery has become one of the primary modalities used for the treatment and management of patients with brain tumors. Stereotactic radiosurgery allows for very high doses of radiation to be delivered in a single treatment to a small volume of tissue with little damage to surrounding tissue. The key requirements for using radiosurgery are the exact target location, using stereotactic techniques; direct superimposition of isodose distribution, accurate knowledge of the dose for a particular pathology, steep dose fall-off immediately outside the target; low doses delivered to the skin, lens, and other critical intracranial structures; and treatment completed in a reasonable amount of time (Chaichana & McGirt, 2012).

Chemotherapy

Current literature shows that the major role of chemotherapy treatment is as an adjuvant or concurrent treatment of high-grade gliomas although it is used as a first-line treatment of low-grade gliomas when the tumor was not treated by resection or radiotherapy (Tamber & Bernstein, 2009). Malignant tumors are infiltrative and

local therapy alone is not sufficient to eradicate all tumor cells. These tumors therefore tend to recur after surgery or local radiation. Chemotherapy may be a means of treating the cells that escape local therapy (Barker, 2011). However, chemotherapy can be effective only when drugs are sufficient and sensitive to tumor cells (Pouratian et al., 2009).

There are numerous difficulties in attempting to treat PBT with chemotherapy. A variety of histological types of tumor cells of malignant brain tumors are difficult to kill. One of the other main difficulties is the presence of blood-brain barriers, which seem to prevent effective delivery of potentially active chemotherapeutic compounds (Barker, 2011; Emanuele, Santini, Talacchi, Gerosa, & Savazzi, 2012) and severely restrict the amounts of drugs reaching the tumor.

Therefore, the number of chemotherapeutic agents available to treat brain tumors is limited. Only four drugs, temozolomide, carmustine, lomustine, and bevacizumab, have been approved by the U.S. Food and Drug Administration (FDA) for specific use in brain tumor patients (Barker, 2011). The role of chemotherapy in PBT treatment is still evolving. In glioma, chemotherapy has been proposed with enhanced concern due to two perspectives. First, chemotherapy plays a role in the treatment of 1p and 19q chromosome loss. The majority of PBT, which result in the loss of chromosomes 1p and 19q, are oligodendrogliomas. Therefore, assumed as the most of oligodendrogliomas patients are response to chemotherapy. Second, the accessibility of temozolomide which has good penetration in the CNS (Bent et al., 2006). In addition, the treatment modality of chemotherapy alone includes not only a single agent but also a combination of agents with various regimens. Several regimens of temozolomide with other drugs such as procarbazine, marimastas, and cisplatin have been reported with high response rates of patients free from tumor progression at six months (Bent et al., 2006). Lomustine (CCNU) is an integral component of the procarbazine, lomustine, and vincristine (PCV) regimen. Each course of standard PCV chemotherapy consists of lomustine (110 mg/m^2 orally on day 1 with anti-emetics) , procarbazine ; Natulan (60 mg/m^2 orally for 14 days on each cycle, on days 8 through 21) , and vincristine (1.4 mg/m^2 intravenous on days 8 and 29 of each cycle; maximum 2 mg). A full course of therapy will be repeated every 6 weeks (42 days) for a

maximum of six cycles. The efficacy of vincristine has been questioned and so it is left out of the treatment schedule by many physicians (Ironside & Ironside, 2012).

Although the use of chemotherapy alone is an uncommon modality in the treatment of PBT, the majority of treatments consist of a combination of chemotherapy and radiotherapy (Terasaki et al., 2011). For example, a treatment program of radiotherapy with the adjuvant temozolomide for high-grade glioma consists of two phases: radiotherapy combined with temozolomide chemotherapy followed by six cycles of the classic regimen of temozolomide chemotherapy on days 1–5 every 4 weeks (Ironside & Ironside, 2012). Numerous in-vitro and preclinical studies have revealed an interaction between low-dose fractionated radiation therapy and chemotherapy (Diletto et al., 2012). The role of chemotherapy in the treatment of PBT is still developing. Not everyone responds to chemotherapy, however the cost of treatment can be high.

2.2 Symptom Experiences of Patients with Primary Brain Tumors

To provide a better understanding in symptom experiences of adults with PBT, a review of the literature was conducted. The search process included papers found in databases. The inclusion criteria were: (a) studies published between 2000 and 2013 in the English language, (b) studies whose subjects were at least 18 years of age with a PBT, (c) search terms used key words relevant to symptom experience/ symptom perception, symptom evaluation, impact of symptoms in PBT/ glioma/ high-grade glioma/ low-grade glioma. Databases searched were CINAHL, ProQuest, PubMed, ScienceDirect, SpringerLink, and WILEY. Additional sources included reference lists from published studies.

One hundred twenty-three publications were retrieved, and 42 studies met the inclusion criteria. Eight were on symptoms leading to diagnosis; 28 were on treatment-related symptoms, with one from symptoms leading to diagnosis; 7 were on symptom-related tumor location, with two citing the result from other groups; and 3 were on recurrent symptoms with on symptoms leading to diagnosis.

2.2.1 Symptoms Leading to Diagnosis

Eight of 42 studies included symptoms leading to diagnosis. According to Edvardsson, Pahlson, and Ahlstrom (2006), their qualitative study reported that headaches, epileptic seizures, vomiting, and vision changes were the most common symptoms of both acute and late onset patients diagnosed with low-grade glioma. Additionally, Armstrong, Vera-Bolanos, Bekele, Aldape, and Gilbert (2010b) reported that 70% of patients with ependymoma stated that pain was a common symptom. This finding was confirmed by Armstrong, Vera-Bolanos, and Gilbert (2011a) in their study of patients with ependymoma who experienced headaches (52%) as a symptom leading to diagnosis. The reviewed studies used different scales regarding the level of symptoms. Some studies indicated that the headaches had the highest frequency, but others reported seizures or depressive symptoms. Bauman, Fisher, Watling, Cairncross, and Macdonald (2009) found that seizures had a higher prevalence (81%) than headaches (28%) among participants with supratentorial tumors. Similarly, Ruge, Ilmberger, Tonn, and Kreth (2011) evaluated patients with newly diagnosed supratentorial low-grade gliomas before treatment who reported seizures (63.6%) as symptoms leading to diagnosis followed by mild depressive symptoms (27.3%). Simó et al. (2012) evaluated the symptoms at onset of 101 patients with glioblastoma multiforme who experienced seizures (35%). Similarly, the prevalent symptoms of 50 patients with glioblastoma multiforme during their first visit to a neuro-oncology clinic were distress and symptoms related to distress such as memory/ concentration problems and fatigue (28%) (Kvale, Murthy, Taylor, Lee, & Nabors, 2009).

However, Brown et al. (2006) evaluated the baseline characteristics of 194 patients with newly diagnosed high-grade gliomas and reported that one-third of these patients had clinically significant fatigue before treatment.

Some studies included problems with cognitive functions which were presented as symptoms before observation or therapy (Rieken et al., 2013; Ruge et al., 2011; Stanca et al., 2011). For example, Ruge et al. (2011) studied 33 patients with supratentorial gliomas who had significant impairment of the selective and divided attention domain of their cognitive function at the time of diagnosis or prior to

treatment. Miotto et al. (2011) evaluated 27 high-grade gliomas patients before surgery. They found that 88% of these patients had impaired nominal and categorical verbal fluency. Stanca et al. (2011) reported that 45 patients (66%) with menigiomas showed a significant decline in attention domain of their cognitive function, and 105 patients (60%) with gliomas had impaired executive function, memory, or attention. Rieken et al. (2013) evaluated 92 patients with pituitary adenomas who reported visual field deficits (31.5%) as symptoms at the time of diagnosis.

In conclusion, the most common symptoms that led PBT patients to seek health care were headaches or pain, epileptic seizures, vision changes, weakness, and nausea/ vomiting (Armstrong et al., 2010b; Armstrong et al., 2011a; Bauman et al., 2009; Edvardsson et al., 2006; Rieken et al., 2013; Ruge et al., 2011; Simó et al., 2012). In addition, fatigue and depression were the main symptoms at baseline before treatment of high-grade gliomas. Limited information is available on cognitive declines reported at the time of diagnosis and before PBT treatment.

2.2.2 Treatment-related Symptoms

Treatment-related symptoms are defined as specific symptoms associated with therapy designed to treat a tumor or associated signs and symptoms (Armstrong, Cohen, Eriksen, & Cleeland, 2005). Some studies reported on symptoms presented during ongoing diverse treatments in PBT. Fatigue or a subtype of fatigue such as feeling tired, lack of energy, or leg weakness, and sleep disturbance were the symptoms most often experienced (Armstrong, Cron, Bolanos, Gilbert, & Kang, 2010a; Armstrong et al., 2006b; Feuerstein, Hansen, Calvio, Johnson, & Ronquillo, 2007; Fox, Lyon, & Farace, 2007; Gustafsson, Edvardsson, & Ahlström, 2006; Molassiotis et al., 2010b; Pelletier, Verhoef, Khatri, & Hagen, 2002). For example, Feuerstein et al. (2007) evaluated 95 patients with malignant brain tumors who survived for four years after diagnosis and after treatment had higher levels of fatigue, depression, and anxiety-related symptoms and cognitive limitations. Similarity, Fox et al. (2007) studied 73 patients with high-grade gliomas receiving various treatments who had sleep disturbance (100%), fatigue (96%), depression (95%), cognitive impairment (79%), and severe pain (58%). Flechl et al. (2012) evaluated 17 patients with glioblastomas muliforme (long-term survival of about 3 years after initial

treatment) who showed impaired motor function, dysphasia, drowsiness, and fatigue. Nevertheless, some studies revealed hemi-paresis and cognitive problems (limited communication, memory loss) at high levels in PBT patients receiving palliative care (Arber, Faithfull, Plaskota, Lucas, & de Vries, 2010; Faithfull & Lucas, 2005).

The type and protocol of treatment of brain tumors mainly depend on the type and grade of brain tumor, tumor location, tumor size, and the expected benefits of each kind of treatment. From the literature review, brain tumor treatments were grouped into surgery, chemotherapy, radiotherapy, and combinations of treatment, which can all lead to treatment-related symptoms.

Surgery

Surgical intervention cannot reverse the effects of direct tumor invasion on adjacent nervous structures. However, surgery can reduce the severity of symptoms caused by increased intracranial pressure from mass effect such as headaches and vomiting. After the tumor has been removed, the perception of symptoms is changed to recognize some relief (Tamber & Bernstein, 2009). For example, Jakola et al. (2012) studied 54 patients with meningiomas after surgery at different time points who reported less pain and anxiety and increased ability to conduct their usual activities. Das et al. (2012) evaluated the symptom experiences of 111 patients with low-grade gliomas after surgery with and without anticonvulsant drugs (AEDs). The results showed that patients not taking AEDs postoperative had seizures (2.7%) less often than preoperative seizures (14%). However, patients taking AEDs had seizures more than patients not taking AEDs both before resection (71%) and after resection (48%). In addition, Teixidor et al. (2007) evaluated 23 low-grade glioma patients who underwent awake surgery for language deficits (frontal premotor and anterior temporal areas). Verbal working memory assessments significantly improved 3 months after surgery compared with before surgery. This was confirmed by Tsay et al. (2012) who reported that the mean scores of symptom distress and depression after discharge (1 month) were lower than before surgery.

On the other hand, Lepola, Toljamo, Aho, and Louet (2001) interviewed patients with brain tumors who reported being fearful and depressed before surgery and after surgery, had trouble speaking, and had unilateral hemiplegia. The majority of

common symptoms that remained after surgery and before starting other treatments were headaches, seizures, and weakness/ gait abnormalities (Armstrong et al., 2010b; Armstrong et al., 2011a; Budrukkar et al., 2009b; Yuile, Dent, Cook, Biggs, & Little, 2006). Some studies reported both common and cognitive symptoms after surgery such as speech/ coordination problems, vision disturbances, and memory loss (Armstrong et al., 2010b; Budrukkar et al., 2009b; Yuile et al., 2006). For example, Yuile et al. (2006) studied patients with glioblastoma after surgery and before radiotherapy who reported common symptoms such as seizures, loss of consciousness, headaches, and cognitive symptoms such as speech or visual disturbance, and weakness. Similarly, Budrukkar et al. (2009b) evaluated 243 PBT patients who reported that the most common symptoms which remained after surgery and before starting other therapy were headaches, seizures, gait abnormalities, and cognitive symptoms such as memory loss. These results were confirmed by a study of 123 patients with ependymoma after surgery who had pain and nausea/vomiting as common symptoms, and mental changes, problems with coordination, and vision disturbances as cognitive symptoms (Armstrong et al., 2010b). In addition, Armstrong et al. (2011a) analyzed the symptoms of 118 adults with ependymomas who experienced weakness (33%) and seizures (12%) after surgery. From the literature review, there were only two studies that assessed patients with brain tumors after surgery relative to a specific impact on cognitive function (Emanuele et al., 2012; Santini et al., 2012). Emanuele et al. (2012) assessed 14 patients with brain tumors after tumor resection who presented evidence of visuo-spatial deficits (57%) and spatial neglect (43%) compared to pre-operative visuo-spatial deficits of 43% and spatial neglect of 14%. After surgery, patients with glioma had significant deficits in memory, attention, and picture naming (Santini et al., 2012).

In conclusion, the main research finding was that the effects of neurosurgery on cognitive functions were deficits in specific domains after brain tumor resections. Cognitive dysfunctions are the primary endpoint in PBT resection. The studies of surgery-related symptoms focused on symptoms remaining after surgery, which included general symptoms such as headaches, seizures, fatigue, feeling tired, or weak, and cognitive symptoms such as attention, memory, and verbal

communication deficits. Therefore, aggressive surgery may be associated with new deficits (Quinones-Hinojosa et al., 2011).

Radiotherapy

Fractionated radiation therapy of brain tumors may produce adverse effects and characteristic changes in patients in a distinct chronological order depending on total dosage, dose per fraction, total time, volume, host factors, radiation quality, and adjunctive therapy (Butler, Rapp, & Shaw, 2006). Acute effects of an extremely high dose and short period of radiation occurs within hours or days after exposure.

Regarding early complications, patients with brain tumors receiving radiotherapy may experience fatigue or weakness of legs, and emotional problems/ slow mental processing (Bosma et al., 2009; Brown et al., 2006; Mauer et al., 2007; Powell et al., 2011). For example, Brown et al. (2006) evaluated patients with newly diagnosed high-grade gliomas who had radiotherapy. They experienced more fatigue than those who did not have radiation treatment. These results were confirmed by Mauer et al. (2007) who studied patients with anaplastic oligodendrogliomas receiving radiotherapy or radiotherapy with chemotherapy and who reported having worse emotional functioning, communication deficits, future uncertainty, and leg weakness. In the short-term, high-grade glioma survivors showed increased leg weakness from baseline to 4 months during radiotherapy compared to those who were long-term survivors (Bosma et al., 2009). Powell et al. (2011) evaluated 68 PBT patients after surgery and receiving radiotherapy. The results showed that these patients had a somnolence syndrome (drowsiness, clumsiness, lethargy, and slow mental processing) for 3-12 weeks during radiotherapy and lesser effects from this syndrome 6 weeks after completion of radiotherapy.

Long-term or late complications occur in 6 months to even 10 years after radiation treatment. Patients may exhibit a cognitive decline including poor attention and concentration, difficulty with multitasking, and memory deficit (Douw et al., 2009; Gleason et al., 2007; Surma-aho et al., 2001). For example, Surma-aho et al. (2001) reported that 28 of 101 low-grade glioma patients followed up after 7 years had a greater post-surgery memory deficit after early radiotherapy than the group which

did not have radiotherapy. Torres et al. (2003) evaluated 17 adults with PBT in a non-progressive group over a 2-year period who underwent fractionated radiation therapy. They reported no evidence of cognitive decline while the patients with progressive disease had a more substantial decline in memory and attention. Gleason et al. (2007) conducted a longitudinal study of 68 patients with brain tumors who underwent radiation therapy. After radiotherapy, the results showed that 24% of the patients could not remember new things, and 21% could not find the right word. Similarly, Douw et al. (2009) studied 65 long-term survivors of low-grade gliomas followed up after 12 years (mean) who received radiotherapy. They showed a progressive decline in attention functioning, even those who received fraction doses that are regarded as safe (≤2 gray).

In conclusion, the most common early radiotherapy-related symptoms were fatigue or leg weakness. Cognitive impairment was a long-term effect.

Chemotherapy

Wellisch et al. (2002) evaluated 25 of 89 patients with primary malignant brain tumors receiving chemotherapy who experienced a major depressive disorder. In addition, Erharter et al. (2010) used a cross-sectional design to evaluate 110 PBT patients undergoing chemotherapy. Fatigue was found to be the highest prevalent symptom in this group. Molassiotis et al. (2010b) interviewed 9 patients with PBT who reported fatigue, memory loss, and inability to drive four times during the interviews. This result was confirmed by Sutton (2012) who conducted a qualitative study of patients with brain tumors receiving chemotherapy and had experienced a complex symptom profile relating to fatigue, mobility, and consequent reduction in independence. However, interviews of high-grade gliomas patients undergoing treatment showed that they experienced feelings of uncertainty, loss of independence, problems with vision, loss of balance, inability to drive, and difficulty with communication (Halkett, Lobb, Oldham, & Nowak, 2010). Furthermore, the incidence of neurotoxicity (motor weakness, cognitive dysfunction, and seizures) was high in 30 (83%) patients with primary central nervous system lymphoma receiving chemotherapy or chemotherapy combined radiotherapy (Laack et al., 2011).

Zucchella, Bartolo, Di Lorenzo, Villani, and Pace (2013) evaluated 102 PBT patients receiving chemotherapy. They reported significantly impaired cognitive functioning.

In conclusion, chemotherapy-related symptoms were mainly depressive symptoms and cognitive dysfunctions.

2.2.3 Recurrent Symptoms

Regarding symptoms of patients with recurrent high-grade gliomas, the results showed that more than 50% (488 patients) reported severe general symptoms and cognitive symptoms as fatigue, future uncertainty, motor dysfunction, drowsiness, headaches, visual problems, and communication deficits (Osoba, Brada, Prados, & Yung, 2000). For example, Meyers, Hess, Yung, and Levin (2000) studied the symptoms of recurrent GBM patients after surgery. They reported that patients experienced reduced executive functioning. Armstrong et al. (2011b) evaluated ependymoma patients with a variety of treatments in the recurrent state. They focused only on physical symptoms and reported that 25% of the patients who experienced numbness or tingling and headaches. In conclusion, the symptoms found in PBT patients in a recurrent state were inconsistent and may come from different measurements and purposes.

2.2.4 Measurement of Symptom Experiences

From the extensive literature review, varieties of instruments are used to measure symptom prevalence in PBT patients. However, most clinicians identify symptoms from medical records/ chart reviews (Arber et al., 2010; Armstrong et al., 2010b; Bauman et al., 2009; Das et al., 2012; Faithfull & Lucas, 2005; Gathinji et al., 2009; Hamilton & Kernick, 2007; Simó et al., 2012; Yuile et al., 2006). Self-report questionnaires, cognitive function assessments, and interviews are also used.

Self-report questionnaires use a multi-item scale to measure multiple symptoms. For example, general cancer instruments includes the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire; EORTC QLQ-C30 (Gustafsson et al., 2006), the MD Anderson Symptom Inventory; MDASI (Tsay et al., 2012). For specific brain tumor instruments presented in the EORTC QLQ-C30 with Brain Cancer Module; BCM 20 (Bosma et

al., 2009; Budrukkar et al., 2009b; Erharter et al., 2010; Osoba et al., 2000; Ruge et al., 2011), the Functional Assessment of Cancer General (FACT-G) with the Functional Assessment of Cancer Therapy–Brain; FACT-Br (Fox et al., 2007; Gleason et al., 2007; Pelletier et al., 2002); and the MDASI with Brain Tumor Module; MDASI-BT (Armstrong et al., 2006a; Armstrong et al., 2010a; Armstrong et al., 2011a). These questionnaires, except the MDASI-BT, measure both symptoms and quality of life.

Some instruments are limited and measure a single symptom or a single symptom and its related symptoms such as the Beck Depression Inventory (BDI) for depression (Hahn et al., 2003), the General Sleep Disturbance Scale (GSDS) for depressive sleep disturbance (Fox et al., 2007), the MDASI-BT for fatigue (Armstrong et al., 2010a), the distress thermometer adapted by the National Comprehensive Cancer Network for distress (Kvale et al., 2009), and the Crown-Crisp Experiential Index (CCEI) for anxiety (Mainio et al., 2003). Various instruments are used to measure a single symptom or related symptoms. For example, in 6 studies examining fatigue or fatigue and fatigue-related symptoms, 6 different instruments were used: the BDI I and FACT-Br (Pelletier et al., 2002), The Brief Fatigue Inventory (BFI) (Fox et al., 2007), the Symptom Distress Scale (SDS) (Brown et al., 2006), the Multidimensional Fatigue Symptom Inventory Short Form (MFSI-SF) (Feuerstein et al., 2007), and the Checklist of Individual Strength (CIS) (Struik et al., 2009).

Among the instruments used for assessing cognitive symptoms, the most popular instrument is the Neuropsychological Test Battery which is composed of multiple instruments to measure the sub-domains of cognitive function (Douw et al., 2009; Hahn et al., 2003; Meyers et al., 2000; Miotto et al., 2011; Ruge et al., 2011; Santini et al., 2012; Wellisch et al., 2002). The Cognitive Functioning of the Medical Outcomes Scales (COGMOS) (Fox et al., 2007), the Functional Independence Measure scale (FIM), the Cognitive Symptom Checklist (CSC) (Feuerstein et al., 2007), the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA) (Stanca et al., 2011), and the Western Aphasia Battery Japanese version (WAB-J) (Maeda et al., 2009) are used to assess cognitive functions.

In conclusion, the most widely used questionnaires specifically for brain tumor symptoms are the EORTC QLQ-C30 with BCM 20, the FACT-G with FACT-Br, and the MDASI-BT including core and brain tumor items. Both the EORTC QLQ-

C30 with BCM 20 and the FACT-G with FACT-Br have been mostly used to measure health-related quality of life, but the MDASI-BT measures multiple brain tumor symptoms the same as the EORTC QLQ-C30 with BCM 20. However, the MDASI-BT might be useful in describing symptom occurrence throughout the disease trajectory and be suitable to evaluate interventions planned for symptom management. Accordingly, the MDASI-BT will be used to measure the symptom experiences of patients with PBT in the present study.

2.3 Factors Associated with Symptom Experiences

Symptoms may be a result of the tumor itself or of the related treatments. A brain tumor itself produces symptoms depending on size, location, and rate of tumor growth rather than on histological type. Brain tumors produce symptoms by three mechanisms. First, tumor cell infiltration arises beside nerve fiber tracts in both the white matter and the cortex. Low-grade astrocytomas and oligodendrogliomas perform in this style, which often create seizures. Second, tumor cells grow into a mass, displacing but not destroying the neighboring brain tissue. Metastatic brain tumors typically grow this way. Some patients present symptoms and signs of an intracranial mass, which often resolve after treatment. Third, a combination of tumor cell infiltration and growth as a mass destroys the surrounding neuropil. Malignant gliomas perform in this way which produce symptoms and signs that may not improve after treatment (Quinones-Hinojosa et al., 2011). Even though types and regimens of treatment have been found to be related to symptom experiences, they are not included in this section, they are in section 2.

2.3.1 Tumor Size

Brain tumors produce generalized symptoms because of their expanded mass effect. Generalized symptoms are determined by tumor size and manifestations of increased intracranial pressure. An expanded tumor volume and the associated edema can lead to headaches, mental changes, generalized convulsions, nausea, vomiting, and reduced consciousness**.** A tumor may obstruct and narrow the

cerebrospinal fluid path way as its mass enlarges by inducing increased intracranial pressure, and as a consequence, produce various herniation syndromes and sudden headaches (Quinones-Hinojosa et al., 2011).

2.3.2 Tumor Location

The various locations of brain tumors can cause different symptom experiences of patients. Focal symptoms occur as a direct effect of a tumor's growth into the surrounding neuropil depending on which locations in the nervous system are impaired. Focal symptoms include focal seizures, weakness, sensory abnormalities, speech disturbances, and visual defects. Four studies reported on tumor location-associated cognitive functions (Maeda et al., 2009; Mattavelli et al., 2012; Miotto et al., 2011; Stanca et al., 2011)

2.3.3 Tumor laterality

Right side tumors, Mainio et al. (2003) evaluated the level of anxiety of PBT patients before surgery. They reported that right hemisphere patients had significantly higher mean anxiety scores than those with tumors on the left side. Brown et al. (2006) studied the characteristics of 194 newly diagnosed high-grade gliomas patients at base line. They found that right side brain tumors caused more fatigue than those on the left side. Emanuele et al. (2012) assessed 14 patients with right hemisphere tumors after tumor resection compared with before resection. They reported that the incidence of post-operative visuo-spatial deficits (57%) and spatial neglect (43%) were higher than pre-operative incidences, 43% and 14% respectively.

Left side tumors, Hahn et al. (2003) identified the characteristics of 68 adults with newly diagnosed primary malignant brain tumors. The results showed that tumors in the left hemisphere caused more depressive symptoms, increased memory loss, poorer verbal fluency and verbal learning than tumors in the right hemisphere. In the cross-sectional study of Maeda et al. (2009), it was found that frontal and temporal tumors on the left side resulted in aphasia while right side frontal tumors had normal patterns. Miotto et al. (2011) studied patients with left side low-grade gliomas before surgery that they found the patients had delayed verbal memory recall, nominal verbal fluency, processing speed, and impaired decision-making. Mattavelli et al. (2012)

evaluated 22 patients with left frontal low-grade glioma and they reported that left frontal tumor related to impaired decision making. Santini et al. (2012) evaluated 22 left hemisphere glioma patients before surgery who had cognitive impairment (59%), language impairment (50%), depression (45%), and anxiety (23%). After surgery, these patients had significant deficits in memory, attention, and picture naming. The study of patients with left hemisphere gliomas before operation reported that 50% of these patients had language impairment (Stanca et al., 2011). Patients with left hemisphere lesions had a significantly higher percentage of cognitive deficits compared to patients with right side lesions (Zucchella et al., 2013). These studies represented the association between patients' symptoms and tumor location must be considered.

2.3.4 Tumor Growth Rate

The rate of tumor growth indicates the tumor grade (how rapidly they are growing). Benign brain tumors are slow-growing tumors. Current studies have established that before any anaplastic transformation low-grade gliomas display a continuous, constant growth, with a mean tumor diameter growing on average about 4 mm per year (Emmanuel Mandonnet et al., 2003). However, some benign brain tumors may change over time to become malignant. Malignant tumors are quickly growing tumors that invade or infiltrate and destroy normal brain tissue. High-grade gliomas, fast growing tumors have early symptom onset. For example Yuile et al. (2006) found acute onset symptoms in 133 patients with glioblastoma multiforme which were seizures, loss of consciousness, speech and visual disturbance. Slow growing, small-sized tumors may remain asymptomatic for many years, especially if they are located in cerebral mute areas such as the frontal lobe. In these cases, brain neoplasms can be an incidental finding of computed tomography (CT) or magnetic resonance (Mrugala) imaging. The rate of progression varies from onset to progressive mental deterioration. Thus, patients with low-grade glioma may have seizures for months to years, developing progressive neurological signs only late in the course of the disease. By contrast, malignant gliomas may result in headaches and other neurological signs over a few weeks.

2.4 Impact of Symptoms on Outcomes

Many studies have reported on the effects of symptoms on various outcomes. Even though the effects of symptoms have been found to be related to health outcomes, they are not included in this section; they are in section 2 and 6.

2.4.1 Survival

Three articles revealed that multiple symptoms predict survival (Armstrong et al., 2010b; Mauer et al., 2007; Yuile et al., 2006). Yuile et al. (2006) determined that acute onset symptoms such as seizures, loss of conciousness, speech and visual disturbances corresponded with longer survival than less acute on set symptoms such as headaches, weakness, memory loss, and confusion. This result was confirmed by Bauman et al. (2009) in a study of adult supratentorial low-grade glioma patients who had seizures as a primary and significant symptom which was used to predict survival.

Mainio et al. (2005) studied 75 PBT patients with pre-operative depression who had significantly shorter survival times compared with nondepressed patients. This result was confirmed by Gathinji et al. (2009) who reported that 52 malignant brain astrocytoma patients with pre-operative depresson had shorter survival times after surgery. Increased fatigue was an independent predictor of lower overall survival of patients with newly disgnosed high-grade gliomas (Brown et al., 2006). Patients with anaplastic oligodendrogliomas receiving radiotherapy or radiotherapy with chemotherapy experienced emotional dysfunction, communication deficits, future uncertainty, and leg weakness. These symptoms were significant predictors of their survival (Mauer et al., 2007).

Meyers et al. (2000) evaluated 58 patients with recurrent malignant glioma before post-surgical treatment after accounting for four prognotic variables (age, Karnosfsky performance status score, history, and time since diagnosis). The result showed that cognitive function specially verbal memory was a prognotic factor strongly predicted survival in these patients. This result was confirmed by Bosma et al. (2009) who studied long-term and short-term high-grade gliomas survivors after surgery and before radiotherapy who found that the patients with impaired mental

functioning had a shorter median survival time than patients with normal mental functioning.

2.4.2 Functional Status

Fox et al. (2007) evaluated high-grade gliomas patients who experienced depression, fatigue, sleep disturbance, pain, and cognitive impairment. These symptoms were significantly correlated with their functional status.

2.4.3 Work

Feuerstein et al. (2007) explored the symptoms of brain tumor patients including depressive symptoms, fatigue, and cognitive limitations, all of which were found to cause work limitations. Flechl et al. (2012) evaluated the long-term survival of glioblastoma multiforme patients who had impaired motor function which affected their work status.

In conclusion, the impact of symptoms on most outcomes focused on survival estimates (both progression-free survival and overall survival), and the effects of symptoms on patient functioning. Although these outcomes provide evidence of symptom influence on patients' daily functioning, they do not entirely reflect the effect of symptoms on patient HRQOL. There is a limited number of studies that evaluated the effects of cognitive functioning on HRQOL.

2.5 Impact of Symptom Management on Outcomes

2.5.1 Survival

Surgical treatment has an impact on outcome. A number of studies evaluated the impact of surgery on survival rates and most stated that more extensive resection was associated with prolonged survival. For example, the study of Yuile et al. (2006), a retrospective study of 133 glioblastoma maltiforme patients, reported that patients who undergo extensive brain tumor resection have significantly prolonged survival compared with biopsy alone. This was confirmed by Bauman et al. (2009) who evaluated 145 adults with supratentorial low-grade gliomas (median follow-up of

105 months). They reported that the extent of surgery was a significant factor in extending progression-free survival. In these studies, it is difficult to distinguish between biopsy and resection or the extent of resection on survival (Pang, Wan, Lee, Khu, & Ng, 2007). Today, surgery followed with radiotherapy has been reported as the principal treatment which increased overall survival and the time to progression, but deals with only palliative advantage (Nieder et al., 2009).

Radiotherapy effects on patients with PBT may be caused by radiation alone or in combination with different factors including patient-related factors, tumor related-factors, and treatment-related factors. The results of current studies of radiotherapy effects can be divided in two different types of studies: focus on early or late post-operative radiotherapy effects and impact of radiotherapy alone or radiotherapy plus chemotherapy.

First, the studies focused on post-operative radiotherapy effects can divided in two different perspectives: one group of researchers did not believe in post-operative early radiotherapy while the other group believed in early post-operative radiotherapy. Karim et al. (2002) reported on the effects of radiotherapy of 311 adults with low-grade gliomas. The irradiated group received 54 Gy for 6 weeks after surgery and showed significant improvement in time to progression but not overall survival time compared with those who did not receive any treatment after surgery until their tumors showed progression. Similarly, the van den Bent et al. (2005) study of 243 low-grade gliomas patients who received early radiotherapy after surgery had longer-progression free survival (5.4 years) than those who received late radiotherapy (3.7 years). In a study of patients with high-grade gliomas, those who delayed receiving radiotherapy after surgery reported a decrease in survival time (Irwin, Hunn, Purdie, & Hamilton, 2007). On the other hand, Noel et al. (2012) evaluated 400 adults with glioblastoma. They did not find a significant difference between the time interval before radiation therapy and survival rate.

Second, the studies focused on radiotherapy versus radiotherapy plus chemotherapy to predict survival (Mauer et al., 2007; Shaw et al., 2012). The study of Mauer et al. (2007) analyzed treatment-related factors to predict the survival rate of 288 patients newly diagnosed with anaplastic oligodendroglioma or oligoastrocytoma who were undergoing radiotherapy alone or radiotherapy plus chemotherapy. The data

showed the median survival time was 40.3 months for the radiotherapy plus chemotherapy group compared with 30.6 months for the radiotherapy group. Shaw et al. (2012) evaluated primary and secondary endpoints between radiotherapy and radiotherapy plus chemotherapy that included procarbazine, lumustine, and vincristine. The results showed that radiotherapy combined with chemotherapy did not improve overall survival when compared with radiotherapy alone.

Chemotherapy affects outcome. Laack et al. (2011) assessed the toxicity of chemotherapy compared with chemotherapy plus radiotherapy on patients with primary central nervous system lymphoma. Those who received chemotherapy combined with radiotherapy had a higher survival rate, but more toxic than those who underwent chemotherapy alone.

2.5.2 Quality of Life

Surgical treatment in all regions of the brain has an impact on the QOL. One study stated that long-term high-grade glioma survivors after surgery reported improvement in HRQOL, whereas short-term survivors show a lower level and hardly improvement in HRQOL (Bosma et al., 2009). Post-operative radiotherapy on patients with nonfunctioning pituitary adenoma was not associated with reduced QOL when compared with surgery alone (van Beek et al., 2007).

Chemotherapy influences outcome. Erharter et al. (2010) assessed the QOL of 110 patients with PBT receiving chemotherapy but did not consider how the QOL of patients who underwent chemotherapy was affected. Brown et al. (2006) evaluated the QOL of patients with newly diagnosed high-grade gliomas were undergoing chemotherapy, chemotherapy plus radiotherapy, and radiotherapy. The results showed no significant differences in the completion rates of the QOL forms among the three studies.

In interpreting these findings, most clinical studies of symptom treatment on outcomes have used tumor response and/or progression-free survival as their primary endpoint. Only two studies examined the effects of treatment on QOL. Currently, the most desired clinical outcome of neurosurgery is to preserve motor, cognitive, and complex associative functions in order to maintain the patient's QOL (Talacchi et al., 2012). The present review found only two studies that evaluated

radiotherapy and radiotherapy combined with chemotherapy using HRQOL as an outcome (Taphoorn et al., 2005) Therefore, the data on the effects of treatment on quality of life is limited.

2.6 Health-Related Quality of Life of Adults with Primary Brain Tumors

2.6.1 Definition of Health-Related Quality of Life (HRQOL)

Over the past 30 years, quality of life has become an increasingly important outcome in health care (Ferrans, Zerwic, Wilbur, & Larson, 2005). The concept of QOL has been used in a variety of constructs and is difficult to define and measure (Ferrans & Ferrell, 1990; Osoba et al., 2000). Therefore, quality of life appears as an umbrella term that covers a variety of concepts.

In the health care system, research cannot assess the overall aspects of QOL so the term "health-related quality of life" was introduced to solve this problem. The term HRQOL was narrowed to focus on the effect of disease and treatment on quality of life (Ferrans et al., 2005). HRQOL has become increasingly important in health care and clinical investigations. HRQOL is one type of patient-reported outcomes (PROs) that are currently significant outcome measures in cancer clinical trials (Efficace & Taphoorn, 2012). The U.S. Food and Drug Administration (FDA) proposed using HRQOL as an outcome which is, in essence, an assessment in a clinical trial because HRQOL is the only way to obtain evidence-based data on the effect of a treatment from the patient's perspective (Patrick et al., 2007). Accordingly, HRQOL outcomes have the potential to provide valuable data to completely evaluate treatment effectiveness (Efficace & Taphoorn, 2012).

The terms QOL, health status, functional status, and HRQOL are frequently used interchangeably to refer to the same concept (Guyatt, Feeny, & Patrick, 1993; Revicki et al., 2000; Wilson & Cleary, 1995) although they are different. Leidy (1994) stated that functional capacity refers to the entire domain of functioning, which is unique and different from QOL. Revicki et al. (2000) stated that

functional status, health status, QOL, and HRQOL are often used interchangeably, but these terms have different dimensions, perceptions and scope so QOL has meaning beyond an individual's health status. QOL is a broad concept covering all aspects of human life whereas HRQOL focuses on the consequences of an illness and on the impacts of treatment on QOL (Guyatt et al., 2007). HRQOL is a subset of QOL outcomes (Lam, 2010). Various conceptual definitions may lead to misunderstandings in patient–provider communication and threaten the validity of instruments assessing self-reported health or QOL (Fagerlind, Ring, Brülde, Feltelius, & Lindblad, 2010).

Revicki et al. (2000) defined HRQOL as ''the subjective assessment of the impact of disease and treatment across the physical, psychological, social and somatic domains of functioning and well-being'' (p. 888).

Testa and Simonson (1996) defined HRQOL as the "physical, psychological and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions" (p. 835).

HRQOL is defined as "a personal self-assessed ability to function in the physical, psychological, emotional, and social domains of day-to-day life" (Aaronson, 1988).

Therefore, HRQOL may be defined as a subjective assessment of the impacts of disease and treatment on a person's experience, beliefs, expectations and perceptions across the physical, psychological, emotional, and social domains of daily life.

Although HRQOL is an integrative guide that combines objective functioning and subjective well-being, HRQOL is a judgment outcome based on psychological capacity more than on physical ability so individuals may concurrently assess all aspects to formulate an overall judgment. Therefore, a HRQOL rating should be judged by patients directly (Lin et al., 2013) and considered as an illustration of health outcomes instead of providing pathological information or to report on the state of a disease (Lydick & Epstein, 1993). There may be a misconception that objective assessments are more valid than subjective assessments. Although professional ratings are assumed to be "gold standards", they provide more limited information than patients who view their lives by themselves regarding disease and treatment (Fairclough, 2010).

2.6.2 Measurement of Health-Related Quality of Life

At present, no single "gold standard" instrument exists to measure HRQOL (Sizoo & Taphoorn, 2011; Taphoorn et al., 2010). From the literature review, the EORTC-BN 20 is the most commonly instrument used to measure HRQOL (Flechl et al., 2012; Mauer et al., 2007; Osoba et al., 2000) or QOL (Budrukkar et al., 2009a; Erharter et al., 2010) in brain tumor cases. The FACT-Br assessment is also widely used to measure HRQOL in brain tumor cases (Pelletier et al., 2002; Tsay et al., 2012) or QOL (Brown et al., 2006; Gleason et al., 2007; Meyers et al., 2000). Boini, Briancon, Guillemin, Galan, and Hercberg (2004) suggested strengthening the psychological domain in HRQOL assessment because it is important to evaluate human beings who perceive the value of life from a psychological perspective to cope with and to adjust to a life-threatening event such as having cancer. The present study will use the FACT-Br to measure HRQOL in adults with PBT because the FACT-Br is a self-report designed to measure multiple dimensions of HRQOL in brain tumor cases. Compared with the EORTC-BN20 questionnaires, the FACT-Br modules are more focused on psychosocial aspects and less focused on symptoms (Taphoorn et al., 2010).

2.6.3 Symptom Experiences and Health-Related Quality of Life

From the review, 3 of 58 studies considered the psychological symptoms affecting quality of life (Kvale et al., 2009; Mainio, Hakko, Niemelä, Koivukangas, & Räsänen, 2006; Pelletier et al., 2002). Pelletier et al. (2002) reported on patients with PBT during ongoing care. The results showed that depressive symptoms were the primary independent predictor of quality of life. This was confirmed by Mainio et al. (2006) who evaluated the effects of symptom distress on the QOL of 77 patients with PBT after controlling for age and gender. The results showed an increase in the level of depressive symptoms was significantly associated with a decrease in the quality of life of patients before surgery, and 3 months and 1 year after surgery. A study of 50 glioblastomas multiforme patients showed that distress is associated with the social well-being and emotional well-being subdomains of quality of life (Kvale et al., 2009).

Six studies concluded that fatigue was the most common symptom that impacted on quality of life (Flechl et al., 2012; Fox et al., 2007; Gustafsson et al.,

2006; Molassiotis et al., 2010b; Osoba et al., 2000; Sutton, 2013). Osoba et al. (2000) evaluated patients with recurrent high-grade gliomas who had a high symptom deficit and burden (fatigue, uncertainty about the future, motor deficits, drowsiness, headaches, and communication deficits). For more than 50% of these patients, this burden had a significant impact on quality of life. There was a significant association between fatigue and quality of life in a study of 39 low-grade gliomas patients (Gustafsson et al., 2006). Similarly, a study of patients with high-grade gliomas who received different treatments experienced depression, fatigue, sleep disturbance, and cognitive impairment which were significantly correlated with quality of life (Fox et al., 2007). Molassiotis et al. (2010b) conducted a study of PBT patients who described being tired as the most severe of their multiple symptoms, one that negatively affected their quality of life. Long-term survival patients with glioblastoma multiforme reported drowsiness, fatigue, and uncertainty about the future which correlated with a decreased quality of life (Flechl et al., 2012). Moreover, Sutton (2012) studied brain tumor patients who received chemotherapy and experienced a complex symptom profile including fatigue, mobility, and a consequent reduction in independence that impacted negatively on quality of life.

Only one qualitative study of 19 patients with high-grade gliomas reported that seizures were the symptoms that impacted the most on their quality of life (Halkett et al., 2010). A prospective study of 33 patients with supratentorial gliomas who presenced of seizure and had other symptoms for more than 20 weeks prior to treatment were negatively affected relative to quality of life, while cognitive functions were not impact (Ruge et al., 2011).

In conclusion, the most common symptoms that influence QOL are psychological symptoms such as depressive symptoms, symptom distress, future uncertainty, and some physical symptoms such as fatigue, headache, and seizures. A few studies focused on neurocognitive functioning symptoms. Although cognitive disability is burdensome, symptoms, which implied a cognitive impairment, correlated with decreasing quality of life. There was only one study which evaluated cognitive function and HRQOL in gliomas patients (Giovagnoli, Silvani, & Colombo, 2005). In addition, the term QOL from the review literature did not correspond to HRQOL; only a few studies used QOL interchangeably with HRQOL.

2.7 Cognitive Decline and Self-Reports

Recently, there has been increasing emphasis on patient-reported outcomes in cancer therapy. In the United States, patient-reported outcomes are increasing in value as supporting evidence reflecting the results of novel treatments. Methods for assessing patient-reported outcomes are in the process of development. It is well-acknowledged that cognitive impairment results in behavioral, emotional, and intellectual difficulties, which occur in the majority of patients with brain tumors. Cognitive function is an essential factor in the QOL. QOL data are difficult to collect on cancer patients because they may be unwilling to complete the questionnaire when they feeling sick (Henriksson et al., 2011). Furthermore, when brain tumor patients are unable to complete a self-report due to cognitive decline, clinicians try to overcome this challenge by using a proxy to assess a patient's quality of life (Efficace & Taphoorn, 2012; Henriksson et al., 2011). From the literature review, some cancer studies looked at the degree of agreement between a patient self-rating and a proxy's rating. For example, Armstrong et al. (2012) analyzed the congruence of symptom reporting by 115 patients with PBT and by 115 caregivers. The results showed that the reports of caregivers were highly congruent with self-reports of the patients. Similarly, Steinmann et al. (2013) evaluated 166 patients with brain metastases who reported on their QOL before and after radiotherapy compared with 141 proxy ratings of patients' QOL. The results showed a high correlation and parallel changes over time for both approaches.

Barker (2011) suggested that HRQOL and cognitive function have been difficult endpoints in brain tumor treatment trials for several reasons. First, the reliability of a proxy rating as a replacement for a patient-reported outcome is poor, particularly from patients with cognitive deficits. Many patients had difficulty in completing the assessment instrument themselves because of their cognitive decline. This resulted in missing data, a frequent problem in data analysis. To help prevent this problem, patients who were cognitively deficient were excluded and caregivers were asked to rate them. Second, difficulty in interpreting minor clinical changes in HRQOL caused by some supportive medications that are commonly used in brain tumor treatment can interfere with the interpretation of an outcome (Barker, 2011). Similarly, Meyers et al. (2012) stated that quality of life changes are not equivalent to

cognitive changes. Thus, they cannot be used as a proxy rating in a patient's neurocognitive assessment. However, a neurocognitive assessment needs to include a patient's report of symptoms, an objective assessment of these symptoms, and an assessment of patient functioning. Patient-reported outcomes indicative of QOL should focus on brain tumor and management symptoms rather than patient satisfaction. If the assessment instrument has good psychometric properties, the majority of patients with cognitive impairments should be able to complete it. Also, the instrument should be sensitive to changes over time (Meyers et al., 2012).

Although patient ratings are the main source of individual HRQOLs, proxy ratings tend to be less reliable. However, a proxy can obtain useful information by observation when caring for the patient (Cheng et al., 2010).

2.8 Knowledge Gaps Identified

The knowledge gaps identified from the literature review remain and deserve additional research in order to understand the symptom experiences of adults with PBT receiving radiotherapy over time. Although brain tumor treatment medical records contain remarks about the occurrence of symptoms, there are a limited number of studies presenting symptom experiences of specific self-reports. Most recent studies discussed the impact of PBT symptoms on survival, both progressive survival and overall survival. They did not consider the impact of symptoms experiences on the HRQOL of adults with PBT receiving radiotherapy before, during, and after completing radiotherapy. It will be difficult to plan symptom management programs to handle symptom experiences with limited information, mostly from medical records, not input from the patient. Therefore, to evaluate the symptom experiences of adults with PBT over time, specific instruments such as the MDASI-BT to assess brain tumor symptoms and the FACT-BR to assess HRQOL should be used. In addition, longitudinal studies are needed to describe the trajectories the of the symptom experience of adults with PBT as they undergo radiotherapy

CHAPTER III
METHODOLOGY

Patients with PBT experience both neurological and cognitive symptoms that severely influence their quality of life. This study targeted to evaluate the patterns, relationship, and factors predicting changes in symptom experience and adverse effect on HRQOL in adults with PBT receiving radiotherapy in Thailand. The symptom management model (SMM) (Dodd et al., 2001a) and HRQOL concept was used as the conceptual framework of this study. This chapter contains the research design, population and sampling, sample size, settings, instruments, protection of human rights, data collection procedures, and data analysis.

Research Design

A longitudinal repeated-measures design was used in this study. This design was applied to evaluate the symptom experience dimensions (perception of symptoms, evaluation of symptoms, and response to symptoms) and HRQOL as the overall symptom outcomes of adults with PBT receiving radiotherapy. The study also examined the predicting factors between tumor factors (type, laterality, and location) and types of radiotherapy influencing on symptom experience.

Population and Sampling

Population

The target populations of this study were patients with PBT who were receiving radiation therapy at the outpatient clinics of three tertiary hospitals in Bangkok. Samples were selected from consecutive sampling. The sampling frame

included all of the patients with PBT receiving radiation therapy with the following inclusion criteria: 1) Diagnosed with PBT according to the World Health Organization (WHO) grading system with four grades or tumor histological confirmation, 2) age above 18 years, 3) currently receiving radiotherapy. Patients were excluded if they: 1) have a brain tumor from a secondary source of cancer, and 2) have other cancer.

Sample Size

The sample size was based on the statistical analysis used in longitudinal repeated-measures design.

1) Hedeker, Gibbons, and Waternaux (1999) provided the following formula to estimate the sample size for a longitudinal repeated-measure design with two equal groups:

$$N = \frac{(N_{-1}+1)\,(Z_{\alpha/2}+Z_{\beta})^2\,(\sum_{j=1}^{n} 1/r_j + 2\sum_{j<j'}^{n} \rho^{(j-j')}/\sqrt{r_j r_{j'}})}{(\sum_{j=1}^{n} d_j)^2}$$

N = the sample size

N_{-1} = the ratio of sample size per group ($N_{-1}=1$)

$Z_{\alpha/2}$ = (1- $\alpha/2$) percentile of standard normal distribution at α = .05 for two- sided test ($Z_{\alpha/2} = 1.96$)

Z_{β} = (1- β) percentile of standard normal distribution of power of medium effect size equal.8 ($Z_{\beta} = .842$)

r_j = the attrition rate is expected to be 10% at each time point and assumed to be the same for both groups ($r_1 = 1$, $r_2 = .9$, $r_3 = .81$)

d_j = the group difference is expected to be .5 standard deviation at each time point ($d_j = .5$ for all j)

ρ = the first-order autocorrelation parameter between time points

(Each of the correlations between two time points of the three repeated measures are assumed to be .5)

The most common treatment regimens for adults with PBT were radiotherapy or radiotherapy after surgery or radiotherapy with chemotherapy.

Supposing a two-group study will be used participants before treatment to determine as the group one and participants after treatment as the group two. For sample size determination according to this formula, the two-group study has equal sample sizes (N_{-1}=1) with three time measures are needed (n=3). The group difference is expected to be .5 standard deviations at each time point (d_j=.5 for all j). Assume the statistical power of this study is equal to .8 (Z_β = .842) for a two-tailed alpha .05 hypothesis test ($\mathbf{Z}_{\alpha/2}$ = 1.96). The attrition rate is expected to be 10% at each time point after time 1 and is assumed to be the same for both groups (r_1 = 1, r_2 = .9, r_3 = .81)

$$N = (1+1)\,(1.96+.842)^2\,(1/1+1/.9+1/.81) + 2(.5)\,(1/\sqrt{.9}+1/\sqrt{.81}+1/\sqrt{.729})$$

$$N = 46.6 \approx 47$$

The sample size calculated is approximately 47 × 2 = 94 subjects in two groups. The attrition rates ranged from 3 to 27.5 % were reported in previous studies (Brown et al., 2006; Budrukkar et al., 2009a; Emanuele et al., 2012; Gleason et al., 2007; Hahn et al., 2003; Meyers et al., 2000). So the 10% attrition was acceptable in this study. Ten percent of the total number in the sample will be added due to expected attrition at two time points. Therefore, at least 19 extra subjects were needed. Accordingly, the projected sample size would need to enroll 113 patients. The proportional sample size in each hospital were calculated as follows:

The record of patients with brain tumor receiving radiotherapy in 2012, the data from Ramathibodi Hospital was 299 patients, Siriraj Hospital was 87 patients, and the National Cancer Institute was 54 patients (Thai Society of Therapeutic Radiology and Oncology, 2012).

Ramathibodi Hospital $= \frac{299 \times 113}{440} = 77$

Siriraj Hospital $= \frac{87 \times 113}{440} = 22$

The National Cancer Institute $= \frac{54 \times 113}{440} = 14$

2) The other approach for calculating sample size in a longitudinal study was based on comparing the rates of change in the outcome variables of the two groups over the study period. Diggle, Heagerty, Liang, and Zeger (2002) provided a sample size formula to compare the time-averaged responses and the rates of change in studies with continuous outcomes, assuming a compound symmetry correlation among observations from the same subject and no missing data. Their formula is as follows:

$$N = \frac{2\,(Z_{\alpha/2} + Z_{\beta})^2\,(1 + (n-1)\rho)}{n\,[(\mu_1 - \mu_2)/\sigma]^2}$$

N = number of subjects in each of two groups

$Z_{\alpha/2}$ = (1- α/2) percentile of standard normal distribution at α = .05 for two- sided test ($Z_{\alpha/2}$ = 1.96)

Z_{β} = (1- β) percentile of standard normal distribution of power of medium effect size equal.8 (Z_{β} = .842)

$(\mu 1 - \mu 2)/\sigma$ = effect size = (.5)

n = the number of time points = 3

ρ = the assumed correlation of the repeated measures = (.5)

$$N = \frac{2\,(1.96 + .842)^2\,(1 + (3-1) \times (.5))}{3 \times (.5)^2} = \frac{31.404}{.75} = 41.87$$

The sample size calculated was approximately 42 × 2 = 84 subjects in two groups. Ten percent of the total number in the sample will be added due to expected attrition at two time points. Therefore, at least 17 extra subjects were needed. Accordingly, the researcher would need to enroll 101 patients.

As a matter of judgment, the sample size of adults with PBT were based on the formula of Hedeker et al. (1999). This sample size was assumed adequate to detect statistically significant in a longitudinal repeated-measures design.

A strategy to minimize non-response rate/ attrition rate:

One of the serious problems in many studies is subject retention. Often, subject attrition cannot be avoided. This applied to subjects with PBT. Moreover, PBT patients have reduced cognitive functioning, which is a dominant characteristic of their disease. This is one reason why there are few research studies in this area. To minimize the non-response rate, participants who agree to participate in this study was asked to sign consent forms. In addition, use of short-time-completion instruments was motivated subjects to finish their self-assessments. Another way to track and retain participants is to obtain their contact information, including the names, addresses, and telephone numbers of two or three people with whom the participants were close.

Settings

Data was collected at the radiological outpatient clinics of three tertiary care hospitals in the metropolitan area of Bangkok, Thailand. These clinics are where most patients with PBT usually have access to standard treatment protocols with similar regimens. Two sites were university hospitals, Ramathibodi Hospital and Siriraj Hospital. The other was the National Cancer Institute of the Ministry of Public Health.

Instruments

This study used four instruments: the Demographic and Medical Record Form (DMRF), the Mini-Mental State Examination (MMSE), the M.D. Anderson Symptom Inventory-Brain Tumor (MDASI-BT), and the Functional Assessment of Cancer Therapy-Brain (FACT-Br).

The Demographic and Medical Record Form; DMRF

The Demographic and Medical Record Form; DMRF was developed by the researcher to collect the demographic characteristics that separate into two parts. The first part is the general information including age, gender, marital status, religion,

education level, occupation, income, financial status, expense, living arrangement, and family caregiver. The second part is the information of patients from the medical record, including type of primary brain tumor, stage of disease, type of treatment before receiving radiotherapy, type of radiotherapy, total dose, dose/fraction, treatment combines with radiotherapy, co-morbidity, and medical receiving during radiotherapy.

The Mini-Mental State Examination (MMSE)

Description

The Mini-Mental State Examination (MMSE) was developed by Marshall Folstein in 1975 as a brief screening tool to provide a quantitative measurement of cognitive impairment and to assess cognitive change over time (Folstein, Folstein, & McHugh, 1975). The MMSE is the most commonly used instrument for screening cognitive function. It contains 11 questions, which are grouped into seven categories, each category representing a different cognitive domain or function: orientation to time, orientation to place, registration of three words, attention and calculation, recall of three words, language, and visual construction. Administration takes about 5 to 10 minutes (Tombaugh & McIntyre, 1992)

Validity

Folstein et al. (1975) reported the concurrent validity determined by the association score between the MMSE and the Wechsler Adult Intelligence Scale, using verbal and performance subscale, the correlation of the MMSE with verbal score was equal to 0.776, and the MMSE with the performance score was equal to 0.660. Another way to evaluate validity is to detect how well the MMSE can identify personally between normal and cognitive impairment correctly (sensitivity). Specificity refers to an ability to classify those individuals who previously diagnosed as cognitively intact. For example, Anthony, LeResche, Niaz, Korff, and Folstein (1982) reported the MMSE can detect dementia and delirium among patients on a general medical ward with sensitivity 87% and specificity 82%.

A Thai version of the MMSE was translated by the Institute of Geriatric Medicine, Ministry of Public Health (2000) which was used in Thai elderly people.

The report on score less than 17, sensitivity was 56.5% and specificity was 93.8. Scores less than 22, sensitivity was 92.0% and specificity was 92.6.

Scoring

Each area tested has a designated point value: orientation to time (5 points), orientation to place (5 points), registration of three words (3 points), attention and calculation (5 points), recall of three words (3 points), language (8 points), and visual construction (1 point). Scores range from 0 to 30 with the maximum possible score on the MMSE being 30/30. A score is recorded using a denominator of 30 unless the patient is unable to complete the entire test because of a physical handicap (e.g. blindness). In this case, the value of the items not able to be completed is subtracted from 30 and the resulting number used as the denominator for the test score. Levels of impairment have also been classified as no cognitive impairment (24-30), mild cognitive impairment (18-24), and severe cognitive impairment (0-17) (Tombaugh & McIntyre, 1992).

Reliability

Folstein et al. (1975) reported test-retest reliability of depressed patients on 24 hours by the same examiner and the two examiner, the correlation by the Pearson coefficient was 0.887 and 0.827. The reliability of 23 stable geriatric patients on average 28 days, the correlation was equal to 0.988. Anthony et al. (1982) reported test-retest reliability of 58 patients with cognitive intact, the correlation was 0.85, of 12 dementia patients, the correlation was 0.90, and of 7 delirium patients, test-retest reliability on 24 hour period was 0.56. Dick et al. (1984) reported test-retest reliability of 15 neurological patients on 24 hour interval tested by different observers, the correlation coefficient was 0.95 while test-retest reliability of 44 neurological patients on mean interval 31 days tested by the same observer, the correlation coefficient was 0.92. Molly and Standish (1997) reported an intraclass correlation of 48 older adults was 0.69.

The researcher conducted a pilot study to evaluate cognitive status using MMSE in 17 Thai adults with primary brain tumor. The cognitive status for the pilot and main study at each time point are shown in Table 3.1

Table 3.1 The cognitive status of the pilot and main study at each time point

Cognitive Function		Pilot study (N=17)		Main study (N=120) Time 1		Time 2		Time 3	
		N	%	N	%	N	%	N	%
Normal	(27-30)	7	41.2	63	52.5	74	61.7	71	59.2
Mild	(21-26)	5	29.4	46	38.3	35	29.2	40	33.3
Moderate	(11-20)	4	23.5	10	8.3	10	8.3	8	6.7
Sever	(0-10)	1	5.9	1	.8	1	.8	1	.8
Total		17	100.0	120	100.00	120	100.0	120	100.0

The MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT)

Description

The MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT) has been developed to measure multiple symptoms and the impact of symptoms on the outcomes of PBT patients. The MDASI-BT is a self-report instrument developed to measure both neurologic and cancer-related symptoms. The constructs of this instrument consist of symptom severity and symptom interference or symptom distress. The MDASI-BT is a paper-pencil instrument that takes less than ten minutes to complete. It includes 22 symptoms and 6 questions on the interference of symptoms with daily activities. Patients are asked about the presence of a particular symptom in the last 24 hours because the reliability of symptom recall is a concern. Waiting longer than this and if a symptom is present, the severity of this symptom will be weighed. Neuro-cognitive symptoms included in the instrument are those commonly reported by brain tumor patients (Armstrong et al., 2006b).

Validity

Construct validity was assessed using confirmatory factor analysis. The construction was reported to be appropriate because the standard deviation of the residual was 0.05, which is less than the standard error of a correlation coefficient, which was 0.07 (Armstrong et al., 2006b). Known-group validity was evaluated by detecting group differences due to disease severity and performance status (Armstrong

et al., 2009). They reported a content validity index (CVI) > 0.8 for all items together (Armstrong et al., 2005).

Scoring

Scores on the MDASI-BT for symptom occurrence are "0 = No" and "1= Yes". Symptom severity is measured by ranking from "0 = not present" to "10 = as bad as you can imagine". Symptom interference is measured by ranking from "0 = did not interfere" to 10 = interfere completely". The scores of symptom experience will be summed and averaged on the 22 items together as representing symptom severity while the scores on symptom interference will be summed and average on six items. The average symptom interference score can be used to represent overall *symptom distress* (Armstrong et al., 2006b).

Reliability

The reliability (internal consistency) of this instrument was evaluated in a study of 201 patients with PBT. Symptoms were defined in six major subscales: an affective factor, a cognitive factor, a focal neurologic deficit factor, treatment-related symptoms, generalized / disease status symptom, and gastrointestinal-related factor, and interference scale. The internal consistency (the coefficient alphas) for these subgroups was 0.87, 0.82, 0.72, 0.81, 0.69, 0.67, and 0.91 respectively, indicating a high level of reliability of these subgroups (Armstrong et al., 2006b). The reliability of this instrument was confirmed by a study of 124 patients with brain metastases. Cronbach' s alpha for all scales was between 0.74 and 0.94 except for the neurologic subscale factor which was 0.58 (Armstrong et al., 2009).

The researcher conducted a pilot test for reliability of The MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT) in 17 Thai adults with primary brain tumor. The Cronbach's alpha coefficients for the pilot and main study at each time point are shown in Table 3.1

Table 3.2 Reliability tests of the modified MDASI-BT in a pilot study and the main study at each time point

Subscale	Cronbach's alpha coefficients			
	Pilot study (N=17)	Main study (N=120)		
		Time 1	Time 2	Time 3
Symptom occurrence	.761	.763	.779	.763
Symptom severity	.847	.751	.772	.788
Symptom interference	.635	.790	.794	.808
Total	.879	.833	.836	.851

The Functional Assessment of Cancer Therapy-Brain (FACT-Br)

Description

The Functional Assessment of Cancer Therapy-Brain (FACT-Br) is a subscale of quality of life instrument that is commonly used to assess symptoms or problems associated with brain malignancies. The FACT-Br is a self-report questionnaire developed by Weitzner et al. (1995). It consists of a 23-item questionnaire is specific brain tumor items usually used along with 27 core general items (FACT-G) across four dimensions: 1) physical well-being, 2) social/ family well-being, 3) emotional well-being, 4) functional well-being. The FACT-Br can be completed by the patient or with the assistance of the examiner within 5-10 minutes and does not require pre-certification.

Validity

The FACT-Br was evaluated for validity by Weitzner et al. (1995) using 101 patients with PBT . In the validation phase, FACT-G subscale and total scores as well as the brain subscale scores were evaluated for both convergent and divergent validity. Convergent validity was assessed by investigating the associations between scores on the FACT-G subscales, total score, brain subscale, and the scales of other similar instruments completed at the same time. Relatively high correlation coefficients were expected in these comparisons (a high correlation is **r** = 0.5, with 25% of the variance of one measure being explained by the other measures) Divergent validity was assessed by investigating the associations between scores on the FACT-G

subscales, total score, brain subscale, and unrelated instruments completed at the same time. Low correlation coefficients were expected in these comparisons (a low correlation is **r** < 0.3, with <9% of the variance of one measure being explained by the other measures). Regarding the brain subscale, divergent validity was considered more important because the purpose of the brain subscale differs from that of the FACT-G.

Scoring

Scores on the FACT-Br are from "0 = not at all" to "4 = very much". Negative items are reverse scored. To obtain a score, the sum of the item scores is multiplied by the number of items in the subscale and then is divided by the number of items answered. The scores on each subscale are summed and averaged. The FACT-G has an overall score (0-108) that includes the scores on the 4 subscales indicating participants' physical well-being (range 0-28), social/family well-being (range 0-28), emotional well-being (range 0-24), and functional well-being (range 0-28). The FACT-Br also has an overall summary score (0-92). A higher score indicates a better quality of life.

Reliability

Test-retest reliability was computed using 46 patients who had PBT. The coefficient alphas for all subscales ranged from 0.66 to 0.84 ($p < 0.001$). The test-retest reliability for the whole FACT-Br (FACT-G and brain subscale) was high (0.78, $p < 0.001$) (Weitzner et al., 1995). Reliability of the FACT-Br was confirmed for a translated version in Brazilian Portuguese (Gazzotti et al., 2011) using 30 patients with brain tumors on three separate occasions by two researchers to determine inter-observer reliability. The intra-class correlation coefficients from intra-observer reliability on different subscales (15 day interval) ranged from 0.87 to 0.95. Likewise, the intra-class coefficients from inter-observer reliability on different subscales ranged from 0.87 to 0.95.

The researcher conducted a pilot test for reliability of The FACT-Br in 18 Thai adults with primary brain tumor. The Cronbach's alpha coefficients for the pilot and main study at each time point are shown in Table 3.2

Table 3.3 Reliability tests of the FACT-Br in a pilot study and the main study at each time point

Subscale	Cronbach's alpha coefficients			
	Pilot study	Main study (N=120)		
	(N=17)	Time 1	Time 2	Time 3
Physical well-being	.709	.723	.790	.725
Social/family well-being	.740	.764	.685	.741
Emotional well-being	.542	.811	.800	.789
Functional well-being	.912	.865	.867	.876
Brain tumor subscale	.807	.880	.856	.860
Total	.885	.925	.924	.927

Protection of Human Rights

The research proposal study was submitted to the Institutional Review Board (IRB) of Mahidol University, Ramathibodi and Siriraj Hospital and the relevant IRB at the National Cancer Institute.

Essential information for consent included the purpose of the study, the research activities and the utility of the study outcome, the opportunity to answer any questions that a potential participant may have, assurance of privacy, protect confidentiality, and the option to withdraw at any point in the study with no effect on their treatment or hospital services.

Data Collection Procedures

Data collection procedures are summarized following approval of the Human Subject Committee from Ramathibodi Hospital, Siriraj Hospital, and the National Cancer Institute, as follows:

1. The researcher contacted the head nurse and staff nurses at the outpatient radiological clinics to set up a time to provide them with information about the purpose of the study and data collection. The goal is to establish a working relationship with the staff nurses to identify and facilitate patient recruitment. The researcher will review patient schedules for radiotherapy once a week to identify

tentative or potential subjects. If there are any new patients before radiation treatment, the researcher plans to meet with them to provide information about the study.

2. The researcher will meet with the selected potential participants and give them a chance to ask questions to clarify their understanding of the study. If a patient agrees to participate, his/her informal informed consent will be required after a verbal explanation by the researcher or research assistants. A formal written consent form is then required to be signed.

3. After the informed consent process, the researcher explained to all participants about the questionnaires and how to fill them out.

4. Participants then were test asked to complete the demographic questionnaire, test Neuro-cognitive function (MMSE), and complete self-report on their symptom experiences (MDASI-BT), and what they have done regarding their daily living activities (FACT-Br) initially at the radiological outpatient clinics before radiotherapy (Time 1). After receiving radiotherapy 8-10 Gy (Time 2) participants were tested cognitive status using the MMSE, asked to complete the MDASI-BT and the FACT-Br. At the completion of radiotherapy (Time 3) the participants were tested cognitive status using the MMSE, asked to complete the MDASI-BT and FACT-Br the same as time 2. For time 2 and time 3 the researcher plans to coordinate data collection with patients at each clinic. If any of the participants are unable to complete the questionnaires at the hospital, they were asked to complete them within a day after going back home. In this case, prepaid return envelopes were provided for their convenience. The data collection instruments and time schedules are shown in Table 3.2 and Figure 3.1.

Table 3.4 Data Collection Instruments and Time Schedules

Instrument	Content	Time1	Time2	Time3
DMRF	Demographic features	X		
MMSE	Cognitive function	X	X	X
MDASI-BT	Brain tumor symptoms	X	X	X
FACT-Br	Quality of life	X	X	X

In addition, some participants prefer the researcher or a research assistant to read the questionnaires for them even though they do not have a literacy problem. This option will allow them to complete the questionnaires.

5. Telephone calls were made to participants who complete the questionnaires at home. This is to make sure these participants will complete the questionnaires and allows them to ask for more information if the questionnaires are difficult to complete.

6. After data collection is completed, the data were examined for outliers and missing values. Questionnaires with outliers or many missing value cases were not being used.

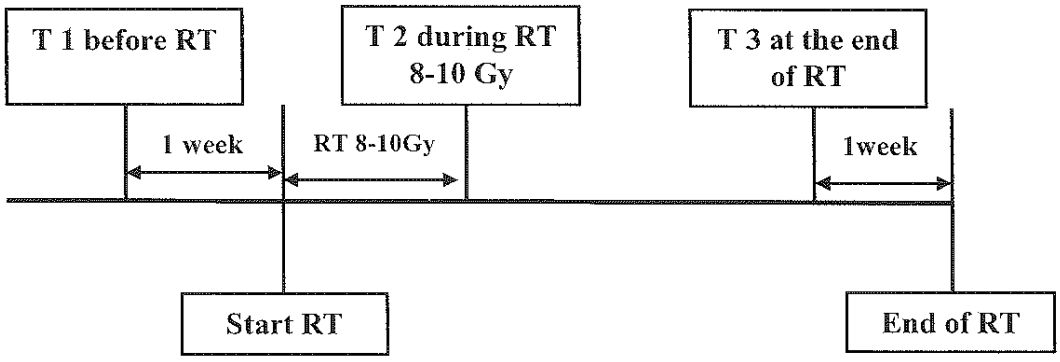


Figure 3.1 Data Collection at Three Time Points

Data Analysis

Data from the four questionnaires will be analyzed using the Statistical Package for Social Science (SPSS) program, version 21. The level of significance will be set at .05. The objectives and analytical methods to be used are as follows:

Objective 1: To describe the symptom occurrence, severity, and life interferences experienced by Thai adults with primary brain tumor receiving radiotherapy at time 1 (1 week before RT), time 2 (after receiving RT 8-10 Gy), and time 3 (at the end of RT). Descriptive statistics were used to analyze overall symptom

experiences dimensions listed on the MDASI-BT in terms of occurrence, severity, and life interferences due to symptoms. These symptom experiences were analyzed in terms of means and standard deviations. In addition, patient demographic data on a nominal scale was described by using frequencies and percentages and interval data will be analyzed by using means and standard deviations.

Objective 2: To analyze the changes over time in symptom occurrences, severity, and life interferences experienced by Thai adults with PBT receiving radiotherapy during time 1 to time 2 and time 2 to time 3. Repeated-measure ANOVA was used to analyze changes over time of their symptom occurrences, severity, and life interferences.

Objective 3: To determine the effect of tumor factors (type, laterality, location) and types of radiotherapy on symptom experiences (occurrence, severity, and life interferences) at each time point. Data were analyzed using means and standard deviations. MANOVA was used to analyze the correlations between each predicting factor, including tumor type, tumor laterality, tumor location and types of radiotherapy on symptom experiences.

Objective 4: To determine the effect of tumor factors (type, location, laterality) and types of radiotherapy on the changes of symptom experience (occurrence, severity, and life interferences) over time. Generalized Estimating Equations (GEEs) analysis were used.

Generalized Estimating Equations (GEEs) is an extension of general a linear model to accommodate correlated data (Ghisletta & Spini, 2004). GEEs analysis is a research method which often used to analyze longitudinal or repeated measures cluster data and other correlated response data for both continuous and discrete outcomes. This technique is suitable for analysis of longitudinal relationship between a continuous outcome variable and several time-dependent and time-independent covariates (Twisk, 2004). GEEs approach uses quasi-likelihood models to relax the constraint of numerous assumptions of traditional regression models by adjusting variance- covariance matrix with working within-cluster correlation structure in the quasi-score equations. Therefore, a GEEs model will be designed and used to analyze the severity of symptom experiences over time, and to determine symptom experience (occurrence, severity, and interfered life) on the changes of HRQOL**.**

Objective 5: To investigate the pattern of HRQOL over time perceived by Thai adults with PBT receiving radiotherapy. Repeated-measure ANOVA analysis will be used to determine the change.

Objective 6: To describe the HRQOL and subdomains of HRQOL in Thai adults with PBT receiving radiotherapy at each time point and over time. Descriptive statistics were used to analyze overall HRQOL. The nature and number of HRQOL items were analyzed in terms of a total score on the FACT-Br. Repeated-measure ANOVA was applied to assess change over time on subdomains of HRQOL.

Objective 7: To determine which domains of symptom experiences (occurrence, severity, and life interferences) predicting on HRQOL at each time point. Descriptive statistics will include the mean and standard deviation. Multiple regression analysis was used to analyze the correlations between each symptom experience and HRQOL.

Objective 8: To determine which domains of symptom experience (occurrence, severity, and life interferences) were predicting on HRQOL over time. GEE was used to evaluate this objective.

CHAPTER IV
RESULT

The results from data analysis are reported in two main parts. The first part shows demographic and clinical characteristics of the patients. The second part shows the results according to the purpose of the study.

Part 1 Demographic Characteristics of the Patients

The one hundred and thirty adults were initially approached to join in to this study. One refused to participate since she felt uneasy to talk about her symptoms. Four patients who had other type of cancers and five who used to receive radiotherapy before this study were excluded. Finally, one hundred and twenty patients with PBT agreed and signed the consent form to join in this study. Those comprised 14 patients from Siriraj Hospital, 12 patients from the National Cancer Institute, and 94 from Ramathibodi Hospital.

The patients' age ranged from 22-78 years with the average of 48.6 years (SD = 10.08 year). The majority of the patients were female (80.8 %), Buddhist (98.3%) lived with the couple (75.8%) in their own home (76.7%)and obtained the primary school education (40.8%). The health care expenses were covered by national health insurance (47.5%), and governmental welfare (26.7%). The participants' monthly income ranged from 2,500 to 60,000 baht in which 26.7% received income less than 10,000 baht per month and three participants have income more than 120,000 baht per month. About 22% of the participants refused to report their income and 22.5% reported that they had no income, but received financial support from their families. Most of the participants perceived that they had sufficient monthly income (56.7%). The demographic' characteristic of participants is shown in Table 4.1

Table 4.1 Demographic Characteristics of the Participants (n = 120)

Characteristic	Total		Rama		Siriraj		NCI	
	N	%	N	%	N	%	N	%
Age (years)								
Age 21-30 years	5	4.2	3	3.2	1	7.1	1	8.3
Age 31-40 years	18	15.0	12	12.9	2	14.3	4	33.3
Age 41-50 years	48	40.0	40	43.0	6	42.9	2	16.7
Age 51-60 years	36	30.0	27	29.0	5	35.7	3	25.0
Age 61-70 years	11	9.2	10	10.8	0	0	1	8.3
Age 71-80 years	2	1.7	1	1.1	0	0	1	8.3
Range	22-78		23-73		22-56		30-78	
Mean	48.63		49.14		45.50		48.31	
SD	10.080		9.575		9.485		13.913	
Gender								
Female	97	80.8	80	14.9	11	78.6	6	50
Male	23	19.2	14	85.1	3	21.4	6	50
Marital status								
Single	16	13.3	13	14.0	2	14.3	1	7.7
Marriage	91	75.8	70	75.3	10	71.4	11	84.6
Widowed / Divorced / Separated	13	10.8	10	10.8	2	14.3	1	7.7
Religious								
Buddhist	118	98.3	91	97.8	14	100.0	13	100.0
Islam	2	1.7	2	2.2	0	0	0	0
Education								
No formal education	3	2.5	3	3.2	0	0	0	0
Primary school	49	40.8	35	37.6	8	57.1	6	57.1
Secondary School	25	20.8	21	22.3	2	14.3	2	16.6
Diploma / Certificate	6	5.0	4	4.3	0	0	2	16.7
Bachelor degree	29	24.2	24	25.5	4	28.6	1	8.3
Higher than Bachelor degree	6	5.0	6	6.4	0	0	0	0
Not mention	2	1.7	1	1.1	0	0	1	8.3
Occupation								
Housewife / unemployed	27	22.5	21	22.6	3	21.4	3	23.1
Private company employee	24	20.0	18	19.4	2	14.3	4	30.8
Farmer	25	20.8	19	20.4	4	28.6	2	15.4
Governmental employee	20	16.7	19	20.4	1	7.1	0	0
Business owner	12	10.0	8	8.6	2	14.3	2	15.4
Other	12	10.0	8	8.6	2	14.3	2	15.4

Table 4.1 Demographic Characteristics of the Participants (n = 120) (cont.)

Characteristic	Total		Rama		Siriraj		NCI	
	N	%	N	%	N	%	N	%
Income								
No income	27	22.5	21	22.6	3	21.4	3	23.1
Refused to report about income	27	22.5	20	21.5	5	35.7	2	15.4
< Or = 10000 Baht	32	26.7	24	25.8	2	14.3	6	46.2
10001-20000 Baht	14	11.7	12	12.9	3	21.4	2	15.4
20001-30000 Baht	6	5.0	3	3.2	1	7.1	0	0
30001-40000 Baht	6	5.0	5	5.4	3	21.4	0	0
40001-50000 Baht	3	2.5	3	3.2	0	0	0	0
> 50001 Baht	5	4.2	5	5.4	0	0	0	0
Range	2500-400000		2500-400000		4250-40000		3000-18000	
Mean	25790.90		28619.62		22541.67		9487.50	
SD	51677.48		57587.76		14354.81		4821.21	
Financial status								
Sufficient with savings	68	56.7	56	60.2	56	60.2	4	30.8
Sufficient with no savings	20	16.7	14	15.1	14	15.1	6	46.2
Insufficient	28	23.3	19	20.4	19	20.4	3	23.1
Other	4	3.3	4	4.3	4	4.3	0	0
Expense								
National health insurance	57	47.5	40	43.0	10	71.4	7	53.8
Government welfare	32	26.7	30	32.3	2	14.3	0	0
Social security worker	17	14.2	10	10.8	1	7.1	6	46.2
Out of pocket	12	10.0	11	11.8	1	7.1	0	0
Other	2	1.7	2	2.2	0	0	0	0
Living arrangement								
Own Home	92	76.7	73	78.5	13	92.9	6	46.2
Live with relative / friend	17	14.2	14	15.1	1	7.1	2	15.4
Rent	7	5.8	3	3.2	0	0	4	30.8
Other	4	3.3	3	3.2	0	0	1	7.7
Family caregiver								
Spouse	50	41.7	39	41.9	4	28.6	7	53.8
Daughter	19	15.8	13	14.0	4	28.6	2	15.4
Brother or sister	19	15.8	15	16.1	1	7.1	3	23.1
Other: relatives	6	5.0	5	5.4	1	7.1	0	0
Mother	4	3.3	4	4.3	0	0	0	0
Son	4	3.3	3	3.2	1	7.1	0	0
No family caregiver	18	15.0	14	15.1	3	21.4	1	7.7

In regard to the participants' clinical characteristic, most patients were diagnosed with the histology and MRI, only 9.2% were diagnosed without histological verification. Seventy two (60%) patients had meningiomas, 20 (16.7%) had pituitary adenoma and 14 (11.7%) had schwannoma. Prior to radiotherapy 110 patients had received tumor resection for the first modality treatment, and 70.8% of these patients were histologically diagnosed as WHO grade I, however only 10 patients did not receive surgery as the first treatment. For the histological classification, meningothelial and transitional meningiomas were found from 7.5% to 10.8%. Most of tumor located at Sellar region, cavernous sinus, sphenoid wing and frontal lobe. After receiving tumor resection, 75 (62.5%) patients received radiotherapy for residual tumor and 29 (24.2%) patients received it for tumor recurrence. Of these, 45 (37.5%) received Intensity-modulated RT with a fractional dose of 1.8- 2.5 Gy up to an accumulated median dose (54 Gy) delivered in 25-34 fractions in 5-7 weeks. Forty patients (33.3%) received treatment on Cyber-knife RT with a fractional dose of 4-6.75 Gy up to an accumulated mode dose (25 Gy) delivered in 5 fractions in 1 week. Thirty-five (29.2%) obtained X-knife RT with a fraction dose of 1.8- 3 Gy up to an accumulated median dose (45 Gy) delivered in 25-30 fractions in 5-7 weeks. The participants' characteristics are shown in Table 4.2.

Table 4.2 Clinical Characteristic of the Participants (n = 120)

Characteristic	N	%
Type		
Meningiomas	72	60.0
Pituitary adenoma	20	16.7
Schwannoma	14	11.7
HGG	8	6.7
LGG	4	3.3
Other: Pineocytoma, Endolymphatic sac tumor	2	1.7
Histology		
Meningiomas (transitional)	13	10.8
Meningiomas (no specific type)	9	7.5
Meningiomas (meningothelial)	9	7.5
Meningiomas (microcystic)	8	6.7
Meningiomas (atypical)	8	6.7
Meningiomas (hyperostosisbone)	7	5.8
Meningiomas (angiomatous)	3	2.5
Meningiomas (chordoid)	2	1.7
Meningiomas (fibroblasts)	3	2.5
Meningiomas (lymphoplasmacyte-rich)	1	.8
Meningiomas (secretory)	1	.8
Pituitary adenoma	20	16.7
Schwannoma	11	9.2
Glioblastoma multiforme	6	5.0
Astrocytoma	3	2.5
Oligoastrocytoma	3	2.5
Other	2	1.7
No pathological report	11	9.2
Grade		
WHO I	85	70.8
WHO II	14	11.7
WHO III	4	3.3
WHO IV	6	5.0
No pathological report	11	9.2

Table 4.2 Clinical Characteristic of the Participants (n = 120) (cont.)

Characteristic	N	%
Status		
Residual	75	62.5
Recurrent	29	24.2
New case	10	8.3
Residual with new lesions	6	5.0
Laterality		
Left side	37	30.8
Right side	50	41.7
Both sides	11	9.2
Central part	22	18.3
Tumor location/origin		
Anterior part	19	15.8
Middle part	66	55.0
Posterior part	29	24.2
Multiple sites	6	5.0
Type of surgery		
Partial removes	45	37.5
Totally remove	12	10.0
Subtotal removes	8	6.7
Near totally removes	7	5.8
Tumor removes with nerve decompress	9	7.5
Not specific type	29	24.2
No surgery	10	8.3
Type of RT		
IMRT	45	37.5
Cyber-Knife	40	33.3
X-Knife	35	29.2

	Range	Mean/SD	Median	Mode
Total dose (IMRT, Cyber-Knife, X-Knife, n=120)	2000-6996	4072.51/1413.89	4500.00	4500
Total dose IMRT (n = 45)	2500-6996	5323.02/832.60	5400.00	5400
Total dose Cyber-Knife (n = 40)	2000-3375	2303.13/277.19	2312.50	2500
Total dose X-Knife (n = 35)	3000-5040	4486.86/286.23	4500.00	4500
Dose/Fraction	180-675	284.98/132.56	200.00	180

Part 2 The Results according to the Purpose of the Study

Objective 1: To describe the symptom occurrence, severity, and life interferences experienced by Thai adults with primary brain tumor receiving radiotherapy at time 1 (before receiving RT), time 2 (after receiving RT 8-10 Gy), and time 3 (at the end of receiving RT).

Symptom occurrence: The patients experienced number of symptoms when evaluated at time 1. They reported 1-20 symptoms with a mean of 8.10 symptoms, a median and a mode of 8 symptoms. The top five most common symptoms occurred in all patients were visual impairment, problem with remembering, upset, feeling drowsy, and pain. There was a very few patients who did not experience any symptom at time 2 and 3. However, at time 2 most of them experienced 1-20 symptoms with a mean of 10.10 symptoms, a median of 10, and a mode of 6 symptoms. The most common symptoms were visual impairment, fatigue, feeling drowsy, problem with remembering, and disturbed sleep. At time 3 the occurrence in term of symptoms and the ranking was similar at time 2. The majority of participants experienced 0-20 symptoms with a mean of 10.07 symptoms, a median of 10, and a mode of 8 symptoms. The most common symptoms were visual impairment, fatigue, problem with remembering, feeling drowsy, and disturbed sleep. The summary of symptom occurrence at time 1, time 2, and time 3 is demonstrated in Table 4.3

Symptom severity: The mean score of symptom severity was rather high, especially the symptoms which most occurrences. The mean score of symptom severity at time 1 was 1.56 ranged from 0.05-5.18. Five symptoms were rated as the most severity consists of visual impairment, upset, change in appearance, problem with remembering, and feeling drowsy. The least severe symptom was seizures. At time 2 the mean score of symptom severity was 1.94 ranged from 0.09-4.55. The most common symptom severity were visual impairment, feeling drowsy, fatigue, disturbed sleep, and problem with remembering. At time 3 the mean score of symptom severity was 2.07 ranged from 0-4.91. The most common severity symptoms were visual impairment, change in appearance, feeling drowsy, fatigue, and disturbed sleep. The summary of symptom severity at time 1, time 2, and time 3 is demonstrated in Table 4.3.

Symptom interference**:** The patients reported relatively high level of symptom interference. The mean score of symptom interference at time 1 was 3.14 ranging from 0-8.33. The livings styles that received most interfere from symptoms were work, walking, mood, general activity, and enjoyment of life. At time 2 the most interfere from symptoms were rated similar as time 1. The mean score of symptom interference was 3.46 ranging from 0-8.50. At time 3, the mean score of symptom interference was 3.35 ranging from 0-8.50. The most interfere from symptoms composed of work, mood, general activity, walking, and enjoyment of life. The low-level rating indicates a minor impact of symptoms at three time points was relation with other people. The detail of symptom interference at three times is presented in Table 4.3

Table 4.3 Symptom Experience in Adult with Primary Brain Tumor Receiving Radiation therapy at 3 Times (n=120)

Symptom dimensions	**Time1**	**Time2**	**Time3**
Symptom Occurrence (22 symptoms)			
Range (0-22)	1-20	1-20	0-20
Mean	8.10	10.10	10.07
SD	4.03	4.25	4.09
Symptom Severity			
Range (0-10)	.05-5.18	.09-4.55	0-4.91
Mean	1.56	1.94	2.07
SD	0.91	0.97	1.06
Symptom Interference			
Range (0-10)	0-8.33	0-8.50	0-8.50
Mean	3.14	3.46	3.35
SD	2.04	1.95	2.06

Table 4.4 Top Five Symptom Experiences in Adult with Primary Brain Tumor Receiving Radiation therapy at Time1, Time2 and Time3 (n=120)

Variable	Time1	Time2	Time3
Symptom Occurrence	1. Visual impairment 2. Problem with remembering 3. Upset 4. Feeling drowsy 5. Pain	1. Visual impairment 2. Fatigue 3. Feeling drowsy 4. Problem with remembering 5. Disturbed sleep	1. Visual impairment 2. Fatigue 3. Problem with Remembering 4. Feeling drowsy 5. Disturbed sleep
Symptom Severity	1. Visual impairment 2. Upset 3. Change in appearance 4. Problem with remembering 5. Feeling drowsy	1. Visual impairment 2. Feeling drowsy 3. Fatigue 4. Disturbed sleep 5. Problem with remembering	1. Visual impairment 2. Change in appearance 3. Feeling drowsy 4. Fatigue 5. Disturbed sleep
Symptom Interference	1. Work 2. Walking 3. Mood 4. General activity 5. Enjoyment of life 6. Relation with other people	1. Walking 2. Work 3. Mood 4. General activity 5. Enjoyment of life 6. Relation with other people	1. Work 2. Mood 3. General activity 4. Walking 5. Enjoyment of life 6. Relation with other People

This table shows the most frequent symptoms experiences. Visual impairment, problem with remembering, upset, feeling drowsy, pain, fatigue, disturbed sleep, and change in appearance were reported by the participants. Visual impairment was rated as the highest level of occurrence and severity, whereas seizures were rated as the lowest level of occurrence and severity.

Objective 2: To analyze the changes over time in symptom occurrences, severity, and life interferences experienced by Thai adults with PBT receiving radiotherapy during time 1 to time 2 and time 2 to time 3.

Responding to this objective, a repeat-measure ANOVA was conducted to analyze the pattern of the symptom experiences (occurrences, severity, and life interferences) over time. The following assumptions were tested: independently of observation, normality, and sphericity. Independent of observation and normality were met. The assumption of sphericity was violated (the epsilon is less than 1.0). Thus, the Greenhouse-Geisser is used.

Pattern of symptom occurrence: Results indicated that the participants did rate the symptom occurrences differently over time and that these differences were statistically significant, F (1.46, 173.96) = 36.46, p< .001, eta^2= .235 (Table 4.5). The eta squared in within-subject effect is .235, which indicated that 23.5% of variance in symptom occurrence is explained by the time effect. The within-subjects contrasts indicated that there was a statistically significant linear trend, F (1, 119) = 36.436, p= .000, eta^2= .234, however this finding was qualified by the statistically significant quadratic pattern, F (1, 119) = 36.58, p= .000, eta^2= .235, reflecting a little bit lower rating symptom occurrence at time 3 than those at time 2. The means and standard deviations for symptom occurrences listed from time 1 to time 3 are presented in Table 4.3. This analysis of means reflects that participants rate the most symptom occurrences appearing on time 2.

Table 4.5 Tests for Symptom Occurrence Change Over Time (n=120)

Within –subjects effects						
Source		df	Mean Square	F	P-valve	Eta^2
Time		1.462	215.311	36.463	.000	.235
Error (Time)		173.962	5.905			
Within –subjects contrasts						
Source	Time	df	Mean Square	F	P-valve	Eta^2
Time	Linear	1	232.067	36.436	.000	.234
	Quadratic	1	82.689	36.538	.000	.235
Error (Time)	Linear	119	6.369			
	Quadratic	119	2.263			

Pattern of symptom severity: The results reflected that the participants did rate the severity of symptom statistically significant diverse from time1 to time3, F (1.48, 176.01) = 31.02, p= .000, eta^2=.207 (Table 4.6). The eta squared is .207, which indicated that 20.7 % of variance in symptom severity is explained by the time effect. The within-subjects contrasts appeared a statistically significant linear trend, F (1, 119) = 36.265, p=.000, eta^2 = .234. However, this finding was qualified by statistically significant quadratic trend, F (1, 119) = 11.02, p=.001, eta^2 = .085, reflecting a linear pattern is the best way to describe the symptom severity over time. The means and standard deviations for symptom severity reflected that participants rate the most severity of symptom appearing on time 3 (Table 4.3).

Table 4.6 Tests for Symptom Severity Change over Time (n=120)

Within –subjects effects						
Source		df	Mean Square	F	P-valve	Eta^2
Time		1.479	5388.531	31.016	.000	.207
Error (Time)		176.012	173.734			
Within –subjects contrasts						
Source	Time	df	Mean Square	F	P-valve	Eta^2
Time	Linear	1	7381.504	36.265	.000	.234
	Quadratic	1	588.613	11.018	.001	.085
Error (Time)	Linear	119	203.546			
	Quadratic	119	53.422			

Pattern of symptom interference: As seen in the Table 4.7, the results indicated that participants did rate symptom interference significantly different over time, F (1.79, 213.20) = 3.88, p = .026, eta^2=.032. The eta squared is .032, which indicated that 3.2 % of variance in symptom interference is explained by the time effect. Polynomial contrasts indicated that there was a statistically significant in a quadratic function, F (1,119) = 6.561, p = .012, eta^2 = .052. The means and standard deviations as seen in Table 4.3 reflected that the participant has perceived the symptoms interfere their daily activities at time 2 more than time 1 and time 3.

Table 4.7 Tests for Symptom Interference Change over Time (n=120)

Within –subjects effects						
Source		df	Mean Square	F	P-valve	Eta^2
Time		1.792	127.581	3.880	.026	.032
Error (Time)		213.198	32.884			
Within –subjects contrasts						
Source	Time	df	Mean Square	F	P-valve	Eta^2
Time	Linear	1	92.504	2.423	.122	.020
	Quadratic	1	136.068	6.561	.012	.052
Error (Time)	Linear	119	38.176			
	Quadratic	119	20.738			

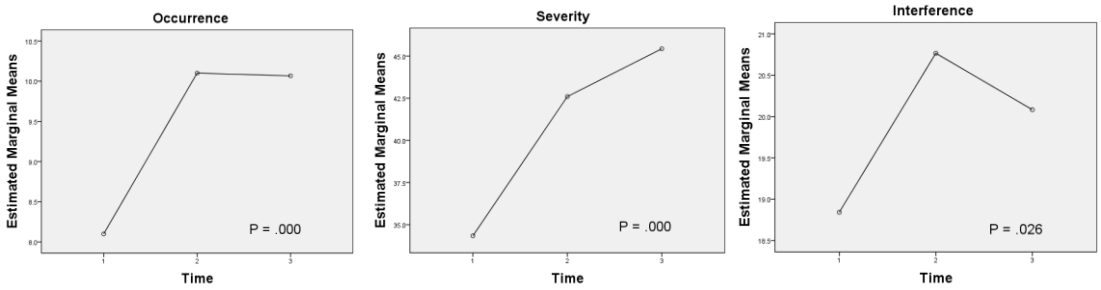


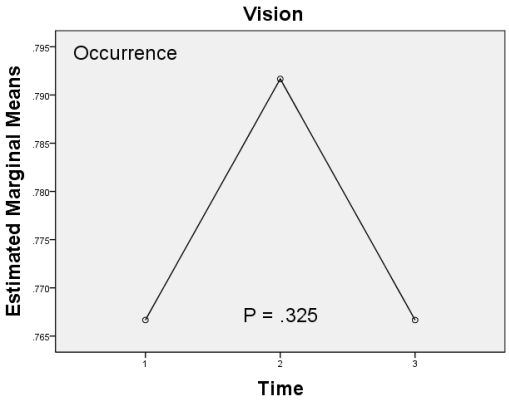
Figure 4.1 Pattern of Time on Symptom Experience Mean

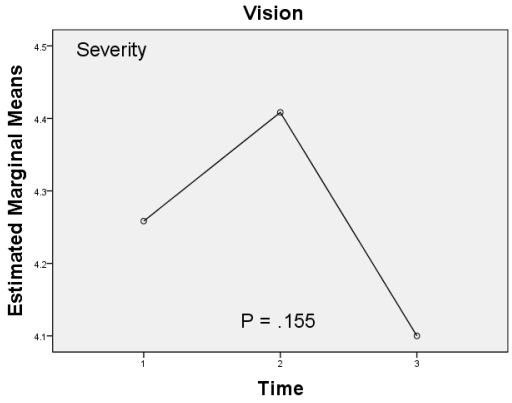
The most common symptoms on the change over time in occurrence and severity dimensions were analyzed. Therefore, in occurrence dimension added ‘change in appearance’ and combine ‘pain’ in severity dimension. Final 8 symptoms were used to analyze the pattern of change over time in occurrence and severity dimensions. For visual impairment and pain, mean scores increased from time 1 to time 2 and decreased from time 2 to time 3 in both occurrence and severity dimensions, which there were no significant changes. Similarly, fatigue and feeling drowsy in occurrence dimension mean scores increased from time 1 to time 2 and slightly decreased from time 2 to time 3, which were statistically significant differences. For problem with remembering and disturbed sleep in both occurrence and severity dimensions, the mean scores increased over time from baseline to the end of treatment, which there were statistically significant differences. Similar to fatigue and feeling drowsy in severity dimension, the mean scores increased over time, whereas the rating from time

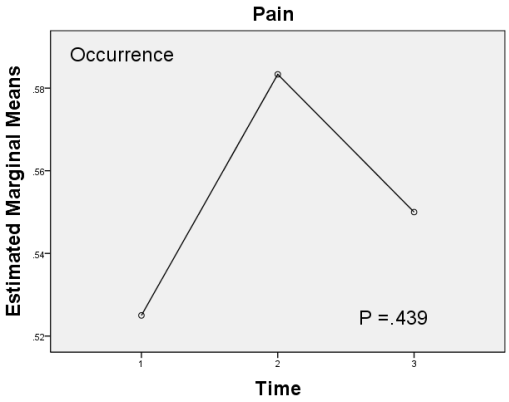
2 to time 3 was slightly increased. For the change in appearance in both occurrence and severity dimensions, the mean score slightly increased from time 1 to time 2 and rapidly increased, which statistically significant difference. However, there was a tendency decreased over time in upset, which was no statistically significant difference. For the mean scores of occurrence, a high score denotes a higher number of symptoms and the mean scores of severity, a high score denotes poorer and more severe of symptoms.

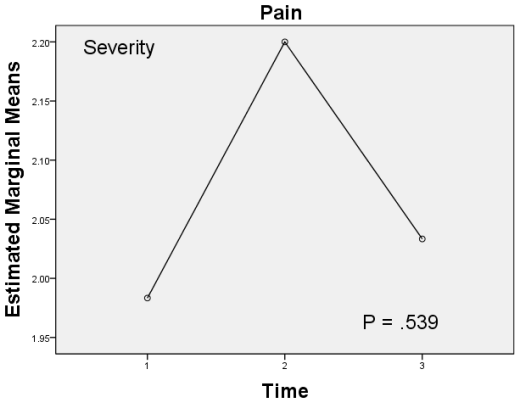
Table 4.8 Change in Most Common Symptom Experience over Time (n=120)

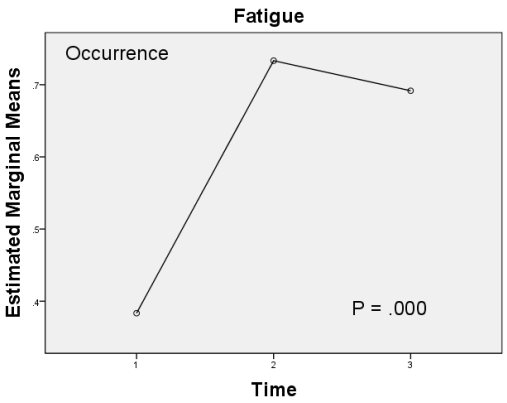
Symptom Experience	Time 1			Time 2			Time 3			P-valve
	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Symptom Occurrence										
Visual impairment	92	.77	.425	95	.79	.408	92	.77	.425	.325
Problem with remembering	69	.58	.496	74	.63	.484	81	.68	.470	.006
Upset	67	.56	.499	63	.53	.501	62	.52	.502	.575
Feeling drowsy	64	.53	.501	82	.70	.460	80	.67	.473	.000
Pain	63	.53	.501	69	.58	.495	66	.55	.500	.439
Disturbed sleep	50	.42	.495	73	.62	.488	77	.64	.482	.000
Fatigue	46	.38	.488	87	.73	.444	83	.69	.464	.000
Change in appearance	55	.46	.500	60	.50	.502	72	.60	.492	.000
Symptom Severity										
Visual impairment	92	4.26	3.050	95	4.41	2.297	92	4.10	2.994	.155
Upset	67	2.42	2.703	63	2.32	2.560	62	2.25	2.623	.703
Change in appearance	55	2.33	3.047	60	2.52	3.160	72	3.57	3.533	.000
Problem with remembering	69	2.30	2.559	76	2.62	2.491	81	2.88	2.558	.001
Feeling drowsy	64	2.27	2.510	84	3.05	2.483	80	3.27	2.845	.000
Disturbed sleep	50	1.98	2.770	74	2.80	2.585	77	3.09	2.805	.000
Fatigue	46	1.45	2.157	88	2.91	2.271	83	3.24	2.741	.000
Pain	63	1.98	2.257	69	2.20	2.214	66	2.03	2.245	.539
Symptom Interference										
Work	90	3.96	3.008	95	4.08	2.925	92	4.17	2.900	.507
Walking	83	3.87	3.122	99	4.48	2.916	86	3.79	3.037	.000
Mood	91	3.58	2.949	100	3.82	2.583	88	3.91	2.956	.390
General activity	85	3.44	2.950	93	3.79	2.625	87	3.83	2.816	.102
Enjoyment of life	57	2.03	2.683	68	2.38	2.708	57	2.21	2.801	.040
Relation with other people	50	1.97	2.747	52	2.23	2.880	51	2.18	2.789	.137

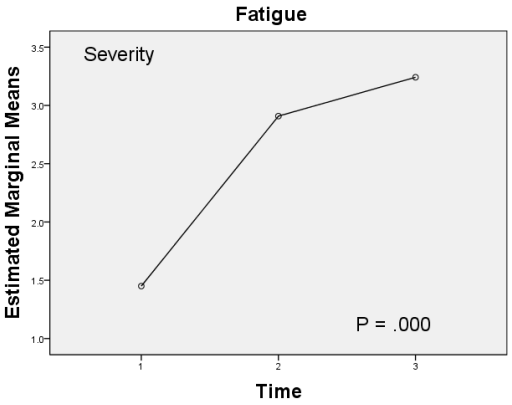

Vision
Occurrence
P = .325
Estimated Marginal Means
Time

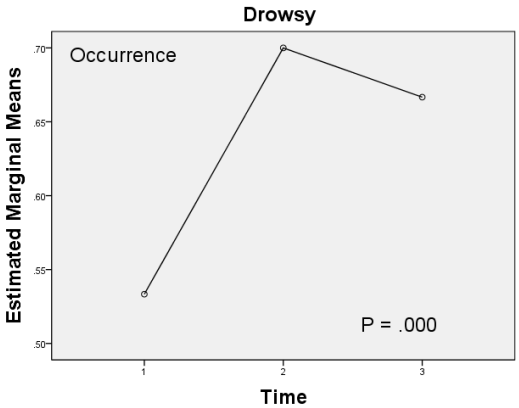

Vision
Severity
P = .155
Estimated Marginal Means
Time

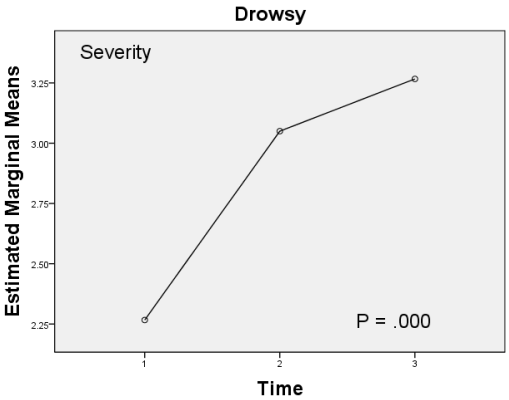

Pain
Occurrence
P =.439
Estimated Marginal Means
Time


Pain
Severity
P = .539
Estimated Marginal Means
Time


Fatigue
Occurrence
P = .000
Estimated Marginal Means
Time


Fatigue
Severity
P = .000
Estimated Marginal Means
Time


Drowsy
Occurrence
P = .000
Estimated Marginal Means
Time


Drowsy
Severity
P = .000
Estimated Marginal Means
Time

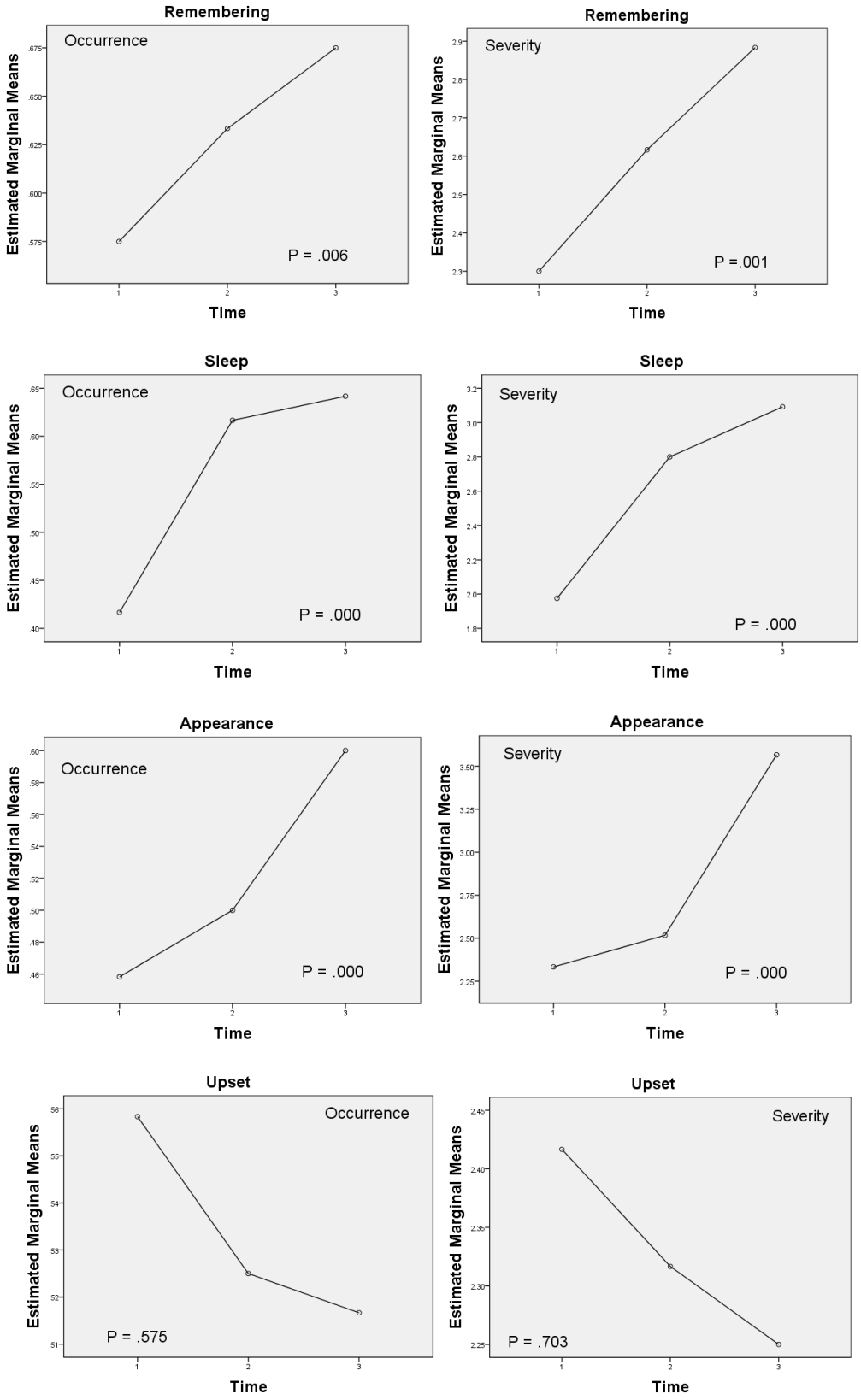


Figure 4.2 Pattern of Most Common Symptoms in Occurrence and Severity Dimensions over Time

The pattern of symptom interference on the change over time, the six items of symptom interference were analyzed (Table 4.8). For walking, the means score increased from time 1 to time 2 and decreased from time 2 to time 3, which was statistically significant over time. Similar to enjoyment of life and relation with other people, the means score increased from time 1 to time 2 and slightly decreased in time 3, which were not statistically different. For work mean scores increased over time from before treatment to the end of treatment. Similar to mood and general activity increased over time, whereas rating from time 2 to time 3was slightly increased. For the mean scores of interference, a high score denotes higher interfere life (Figure 4.3).

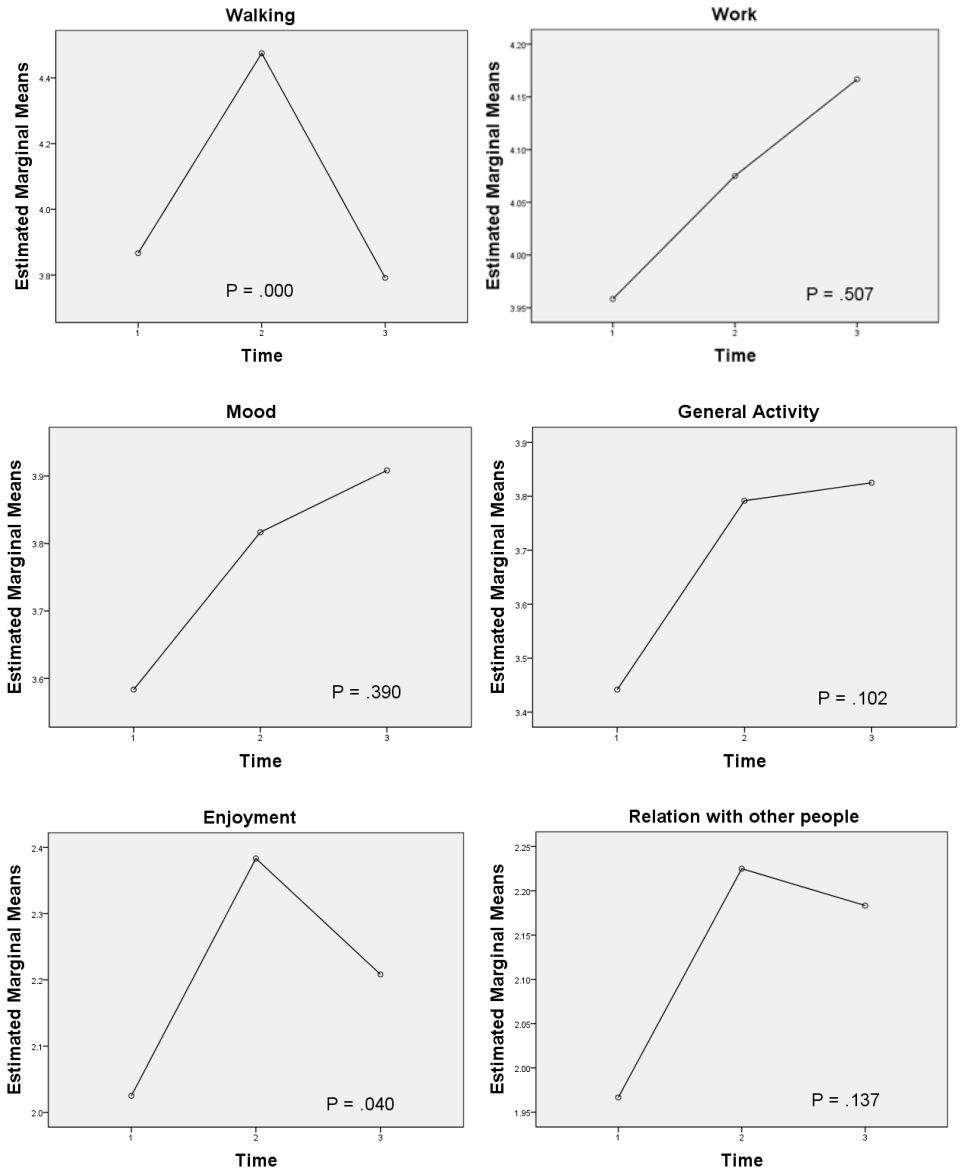


Figure 4.3 Pattern of Symptom Interference over Time

Objective 3: To determine the effect of tumor factors (type, laterality, location) and types of radiotherapy on symptom experiences (occurrence, severity, and life interferences) at each time point.

To determine whether tumor factors (type, laterality, and location) and type of radiation have different on symptom experience scores, whether there were interactions between these factors, a multivariate analysis of variance was conducted. All assumptions were initially tested. This study is time-ordered effect that may violate the assumption of independence of observations. The potential solution is analyzed the group's average instead of the scores of the separate respondents (Hair, Black, Babin, & Anderson, 2010). In this study used an average score of symptom experience dimensions instead individual symptom score. The Box' M was used to test homogeneity of covariance. The results indicated no differences between the groups (time 1, P = .148, time 2, P = .140, and time 3, P = .335).

As seen in Table 4.9, the univariate test indicated interaction and main effect on symptom experience, when significant interactions were found, only the significant findings were reported. The result indicated that the interaction between tumor laterality and tumor type was statistically significant on symptom occurrence, F (3,81) = 2.839, p = .043 and symptom severity, F (3,81) = 3.437, p = .021. The main effect for tumor type was statistically significant on symptom occurrence, F (3,81) = 2.985, p = .016, symptom severity F (5,81) = 4.662, p = .001, symptom interference F (3,81) = 2.385, p = .021. This indicated that the linear combination of symptom occurrence, symptom severity, and symptom interference test differs for tumor type. The main effect of other independent variables, including the type of radiotherapy, tumor laterality, and tumor location were not statistically significant difference.

Table 4.9 Effects of Factors on Symptom Experience at Time 1 (n=120)

Source	DV	df	Mean Square	F	P-valve	Eta^2
Type RT	Occurrence[a]	2	5.396	.413	.663	.010
	Severity[b]	2	626.362	2.214	.116	.051
	Interference[c]	2	190.329	1.279	.284	.030
Laterality	Occurrence	3	10.238	.783	.507	.028
	Severity	3	175.603	.621	.604	.022
	Interference	3	32.805	.220	.882	.008
Location	Occurrence	3	12.850	.983	.405	.035
	Severity	3	360.387	1.274	.289	.045
	Interference	3	96.854	.651	.585	.023
Type	Occurrence	5	39.011	2.985	.016	.154
	Severity	5	1319.212	4.662	.001	.221
	Interference	5	421.965	2.835	.021	.147
Lateraity * Type	Occurrence	3	37.107	2.839	.043	.094
	Severity	3	972.381	3.437	.021	.112
	Interference	3	107.371	.721	.542	.026
Error	Occurrence	82	13.070			
	Severity	82	282.944			
	Interference	82	148.836			

a. R Squared = .445 (Adjusted R Squared = .195)
b. R Squared = .508 (Adjusted R Squared = .287)
c. R Squared = .312 (Adjusted R Squared = .002)

The interaction effects between tumor laterality and tumor type, it revealed significantly predicting symptom occurrence and symptom severity (Table 4.10). For patients with left side tumor, rated occurrence (CI: 10.85 – 19.15) and severe (CI: 53.61 – 92.32) from symptoms being as HGG higher score than being meningioma (occurrence, CI: 6.43 – 9.44 severity, CI: 26.98 – 40.98). HGG at left sided is not different to schwannoma (CI: 3.60 – 12.40) and LGG (CI: .92 – 11.09) in occurrence dimension, whereas HGG is difference to schwannoma and LGG in severity dimension. However, being as schawannoma at left sided tumor is not difference to meningioma and LGG in both occurrence and severity dimensions.

For patients with right side tumor, being as schwannoma (CI: 3.51 – 8.76) rated lower score than other tumor (pineocytoma, endophatic sac tumor) (CI: 8.81 – 23.19) in predicting symptom occurrence and severity and lower than LGG (CI:

8.92 – 19.09) in occurrence dimension. However, LGG at right sided is not difference to other tumor for predicting symptom occurrence and symptom severity.

In other pairwise comparison, there is no more significant difference of mean symptom occurrence among tumor location (both sides and central part) and tumor types because of CI overlapping.

Table 4.10 Descriptive statistics of interaction between tumor laterality and tumor type on symptom occurrence and symptom severity at Time 1

DV	Laterality	Type	Mean	Std. Error	95% Confidence Interval	
					Lower	Upper
Occurrence	Left Side	Meningioma	7.930[a]	.756	6.426	9.435
		Schwannoma	8.000[a]	2.214	3.596	12.404
		HGG	15.000[a]	2.087	10.848	19.152
		LGG	6.000[a]	2.556	.915	11.085
	Right side	Meningioma	8.757[a]	.780	7.206	10.308
		Schwannoma	6.133[a]	1.320	3.507	8.759
		HGG	12.667[a]	2.087	8.514	16.819
		LGG	14.000[a]	2.556	8.915	19.085
		Other	16.000[a]	3.615	8.808	23.192
	Both sides	Meningioma	7.300[a]	1.320	4.674	9.926
		Schwannoma	6.000[a]	2.556	.915	11.085
	Central part	Meningioma	3.000[a]	3.615	-4.192	10.192
		Pituitary adenoma	7.176[a]	.824	5.536	8.816
		Other	7.000[a]	3.615	-.192	14.192
Severity	Left Side	Meningioma	33.983[a]	3.519	26.982	40.983
		Schwannoma	32.250[a]	10.301	11.759	52.741
		HGG	73.000[a]	9.712	53.681	92.319
		LGG	19.500[a]	11.894	-4.161	43.161
	Right side	Meningioma	35.749[a]	3.628	28.531	42.967
		Schwannoma	23.233[a]	6.142	11.015	35.452
		HGG	51.000[a]	9.712	31.681	70.319
		LGG	56.500[a]	11.894	32.839	80.161
		Other	80.000[a]	16.821	46.538	113.462
	Both sides	Meningioma	37.067[a]	6.142	24.848	49.285
		Schwannoma	20.000[a]	11.894	-3.661	43.661
	Central part	Meningioma	13.000[a]	16.821	-20.462	46.462
		Pituitary adenoma	27.955[a]	3.835	20.325	35.584
		Other	25.000[a]	16.821	-8.462	58.462

a. Based on modified population marginal mean.

↑ Some level is not presented because that level combination of factors is not observed, thus the corresponding population marginal mean is not estimable.

As seen in Table 4.11, the interaction between tumor location and tumor type was statistically significant on symptom severity, F (1, 82) = 7.082, p = .009. The main effect for type of radiotherapy was statistically significant on symptom occurrence, F (2, 81) = 3.160, p = .048 and symptom severity F (2, 81) = 3.193, p = .046. This indicated that the linear combination of symptom occurrence and symptom severity tests differed for various types of radiotherapy. The main effect for tumor type was also statistically significant on symptom occurrence, F (5, 81) = 2.325, p = .050, symptom severity F (5, 81) = 3.539, p = .006, and symptom interference, F (5, 81) = 2.349, p = .048. This indicates that the linear composite of symptom occurrence, symptom severity, and symptom interference tests differed for various types of tumor. The main effect of other independent variables, including tumor laterality and tumor location were not statistically significant.

Table 4.11 Effects of factors on Symptom Experience at Time 2 (n = 120)

Source	DV	df	Mean Square	F	P-valve	Eta^2
Type RT	Occurrence [a]	2	45.472	3.160	.048	.072
	Severity [b]	2	1006.070	3.193	.046	.072
	Interference [c]	2	5.535	.042	.959	.001
Laterality	Occurrence	3	16.197	1.126	.344	.040
	Severity	3	521.116	1.654	.183	.057
	Interference	3	27.767	.211	.889	.008
Location	Occurrence	3	10.325	.717	.544	.026
	Severity	3	251.020	.797	.499	.028
	Interference	3	107.598	.818	.488	.029
Type	Occurrence	5	33.461	2.325	.050	.124
	Severity	5	1114.951	3.539	.006	.177
	Interference	5	309.098	2.349	.048	.125
Location * Type	Occurrence	1	16.296	1.132	.290	.014
	Severity	1	2231.144	7.082	.009	.079
	Interference	1	502.976	3.822	.054	.045
Error	Occurrence	82	14.391			
	Severity	82	315.064			
	Interference	82	131.607			

a. R Squared = .451 (Adjusted R Squared = .204)
b. R Squared = .526 (Adjusted R Squared = .312)
a. R Squared = .337 (Adjusted R Squared = .038)

Table 4.12, the result revealed that the interaction effects between tumor location and tumor type on symptom severity. For patients with anterior part tumor rated symptom severity being as HGG (CI: 78.25 – 97.08) higher scores than being as meningiomas (CI: 26.67 – 52.66) and being as LGG (CI: 23.60 – 58.91). However, patients with meningiomas at anterior part rated symptom severity not different from patients with LGG at anterior part.

In other pairwise comparison, there is no more significant difference of mean symptom severity among tumor location (middle part, posterior part, and multiple sites) and tumor types because of CI overlapping.

Table 4.12 Descriptive statistics of interaction between tumor location and tumor type on symptom severity at Time 2 (n=120)

DV	Location	Type	Mean	Std. Error	95% Confidence Interval	
					Lower	Upper
Severity	Anterior part	meningioma	39.667[a]	6.532	26.673	52.661
		HGG	82.667[a]	7.246	68.251	97.082
		LGG	41.250[a]	8.875	23.595	58.905
	Middle part	meningioma	45.099[a]	3.604	37.930	52.268
		pituitary adenoma	31.667[a]	4.047	23.616	39.717
		HGG	43.500[a]	12.551	18.532	68.468
		Other	23.000[a]	17.750	-12.310	58.310
	Posterior part	meningioma	38.875[a]	5.124	28.682	49.068
		schwannoma	34.350[a]	5.292	23.822	44.878
		Other	100.000[a]	17.750	64.690	135.310
	Multiple sites	meningioma	42.056[a]	8.011	26.119	57.992

a. Based on modified population marginal mean.
↑ Some level is not presented because that level combination of factors is not observed, thus the corresponding population marginal mean is not estimable.

As seen in Table 4.13, the interaction effect between tumor location and tumor type was statistically significant on symptom severity F (1, 82) = 6.832, p = .011 and symptom interference, F (1, 82) = 5.529, p = .021. The main effect for type of radiotherapy was statistically significant on symptom occurrence, F (2, 81) = 4.882, p = .010 and symptom severity F (2, 81) = 6.795, p = .002. This indicated that the linear combination of symptom occurrence and symptom severity tests differed for various

types of radiotherapy. The main effect for type laterality was statistically significant on symptom occurrence, F (2, 81) = 2.976, p = .036. This indicated that the linear combination of symptom occurrence tests differed for various types laterality. The main effect for tumor type was also statistically significant on symptom severity, F (5, 81) = 3.564, p = .006, and symptom interference, F (5, 81) = 3.01, p = .014. This indicates that the linear composite of symptom severity and symptom interference tests differed for various types of tumor. Tumor location was the main effect was not statistically significant on symptom experience at time 2.

Table 4.13 Effects of factors on Symptom Experience at Time 3 (n=120)

Source	DV	df	Mean Square	F	P-valve	Eta^2
Type RT	Occurrence [a]	2	59.566	4.882	.010	.106
	Severity [b]	2	2059.941	6.795	.002	.142
	Interference [c]	2	41.524	.298	.743	.007
Laterality	Occurrence	3	36.314	2.976	.036	.098
	Severity	3	740.719	2.444	.070	.082
	Interference	3	18.009	.129	.942	.005
Location	Occurrence	3	7.378	.605	.614	.022
	Severity	3	8.161	.027	.994	.001
	Interference	3	163.192	1.172	.325	.041
Type	Occurrence	5	19.941	1.634	.160	.091
	Severity	5	1080.235	3.564	.006	.179
	Interference	5	426.025	3.061	.014	.157
Location* Type	Occurrence	1	23.001	1.885	.174	.022
	Severity	1	2071.144	6.832	.011	.077
	Interference	1	769.543	5.529	.021	.063
Error	Occurrence	82	12.202			
	Severity	82	303.136			
	Interference	82	139.189			

a. R Squared = .497 (Adjusted R Squared = .269)
b.R Squared = .614 (Adjusted R Squared = .440)
c. R Squared = .372 (Adjusted R Squared = .089)

The interaction effects between tumor location and tumor type on symptom severity (Table 4.14). For patients with anterior part tumor, rated severe from symptoms being as HGG (CI: 73.36 – 102.64) higher score than being as LGG (CI: 32.68 – 67.32) or meningiomas (CI: 27.80 – 53.29).

For patients with posterior part tumor being as lymphatic sac tumor (CI: 67.36 – 136.64) rated severe from symptom higher than those being meningiomas (CI: 34.84 – 54.83) or schawannoma (CI: 26.14 – 46.79). However, patients with meningioma rated symptom severity not different from patients with schawannoma at the posterior part.

In other pairwise comparison, there is no more significant difference of mean symptom severity among tumor location (middle part and multiple sites) and tumor types because of CI overlapping.

The interaction effects between tumor location and tumor type on symptom interference. For patients with anterior part tumor being as HGG (CI: 31.09 – 50.25) rated interference from symptoms higher score than being as meningioma (CI: 8.32 – 25.60) or LGG (CI: -1.99 – 21.49).

In other pairwise comparison, there is no more significant difference of mean symptom interference between tumor location (posterior part, the middle part and multiple sites) and tumor types because of CI overlapping.

Table 4.14 Descriptive statistics of interaction between tumor location and type on symptom severity and symptom interference at Time 3

DV	Location	Type	Mean	Std. Error	95% Confidence Interval	
					Lower	Upper
Severity	Anterior part	Meningioma	40.542[a]	6.407	27.796	53.287
		HGG	88.500[a]	7.108	74.360	102.640
		LGG	50.000[a]	8.705	32.682	67.318
	Middle part	Meningioma	46.993[a]	3.535	39.961	54.025
		Pituitary adenoma	32.333[a]	3.970	24.436	40.230
		HGG	54.000[a]	12.311	29.509	78.491
		Other	25.000[a]	17.411	-9.636	59.636
	Posterior part	Meningioma	44.833[a]	5.026	34.835	54.832
		Schwannoma	36.467[a]	5.191	26.140	46.793
		Other	102.000[a]	17.411	67.364	136.636
	Multiple sites	Meningioma	50.611[a]	7.858	34.979	66.243

Table 4.14 Descriptive statistics of interaction between tumor location and type on symptom severity and symptom interference at Time 3 (cont.)

DV	Location	Type	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
Interference	Anterior part	meningioma	16.958[a]	4.341	8.322	25.595
		HGG	40.667[a]	4.816	31.085	50.248
		LGG	9.750[a]	5.899	-1.985	21.485
	Middle part	meningioma	19.699[a]	2.395	14.934	24.464
		pituitary adenoma	17.068[a]	2.690	11.717	22.419
		HGG	16.000[a]	8.342	-.596	32.596
		Other	8.000[a]	11.798	-15.470	31.470
	Posterior part	meningioma	21.625[a]	3.406	14.850	28.400
		schwannoma	23.017[a]	3.517	16.019	30.014
		Other	48.000[a]	11.798	24.530	71.470
	Multiple sites	Meningioma	19.944[a]	5.325	9.352	30.537

Objective 4: To determine the predictability of tumor factors (type, laterality, and location) and types of radiotherapy on the changes of symptom experience (occurrence, severity, and life interferences) over time.

GEE will be used to assess this research objective. Before carrying out a GEE analysis, the models (additive model or interaction model) for analysis were selected and the within-subject correlation structures must be chosen. A possible choice for selection model and working correlation structure based on the smallest value of the scale parameter and standard errors of regression coefficients (ER), and highest value of Wald test.

Predicting on symptom occurrence over time: Time is added to the model as a continuous variable because the time during collection data between time 1 to time 2 and time 2 to time 3 is unequally spaced time intervals in each patient. The scale parameter of interaction model and the exchange correlation is the lowest value of the scale parameter is smallest. Suppose the interaction model and exchange correlation was selected to predict the factors influencing on symptom occurrence. The regression coefficient, the standard error of the coefficient, and the p-valve based on Wald statistic are given. If there were, no interaction observations between factors in

the samples the findings were omitted. The results with statistically significant are presented as follows.

Type of RT, the result indicated that the mean of symptom occurrence in patients receiving Cyber-Knife decreased .45 (2.27-1.82) times lower than those patients receiving an X - knife, holding other predictors being constant.

Tumor type, the result indicated that the mean of symptom occurrence in patients with high-grade glioma increased 5.99 times than those patients with meningioma, holding other predictors being constant.

The interaction between tumor laterality and tumor type, the finding indicated that the mean of symptom occurrence in patients with low-grade glioma at right side tumor increased 6.30 times than those patients with meningioma at right sided tumor, after controlling for other predictors.

However, the tumor location was not significant predicted symptom occurrence over time shown in the equation below.

Symptom Occurrence = 9.05 + 0.98 (time) - 1.82 (type of RT2) - 2.27 (type of RT3) - .06 (laterality2) - 1.15 (laterality3) - 5.18 (laterality4) + .32 (location2) – 1.05 (location3) – 1.59 (location4) + 3.05 (type2) + 1.04 (type3) + 5.99 (type4) + 3.68 (type5) + 3.11 (type6) – .39 (laterality2# type3) – 3.52 (laterality2# type4) + 6.23 (laterality2# type5 + 4.32 (laterality2# type6) – 1.09 (laterality3# type3)

Table 4.15 Predicting Factor for Symptom Occurrence over Time (n = 120)

Occurrence	Coef.	Std. Err.	Z	P>|z|	[95% Conf. Interval]	
Time	.983	.139	7.08	0.000	.711	1.255
Type of RT[a]						
2	-1.822	.777	-2.35	0.019	-3.345	-.300
3	-2.266	.774	-2.93	0.003	-3.782	-.749
Laterality[b]						
2	-.063	.761	-0.08	0.934	-1.555	1.429
3	-1.152	1.325	-0.87	0.384	-3.750	1.445
4	-5.177	3.022	-1.71	0.087	-11.101	.746
Location[c]						
2	.321	1.031	0.31	0.756	-1.700	2.341
3	-1.045	1.234	-0.85	0.397	-3.464	1.373
4	-1.586	1.742	-0.91	0.363	-5.001	1.829
Type[d]						
2	3.050	3.032	1.01	0.315	-2.893	8.993
3	1.040	1.926	0.54	0.589	-2.735	4.815
4	5.991	1.690	3.55	0.000	2.679	9.302
5	-3.679	2.304	-1.60	0.110	-8.195	.836
6	3.110	4.215	0.74	0.461	-5.152	11.372
Laterailty#Type						
2 3	-.3915	2.110	-0.19	0.853	-4.528	3.745
2 4	-3.521	2.210	-1.59	0.111	-7.852	.811
2 5	6.229	3.032	2.05	0.040	.288	12.171
2 6	4.319	5.269	0.82	0.412	-6.007	14.645
3 3	-1.089	2.993	-0.36	0.716	-6.955	4.778
_cons	9.046	1.039	8.71	0.000	7.009	11.082

a. Type of RT: 1=IMRT, 2=X-knife, 3=Cyber-knife
b. Laterality: 1= Left side, 2= Right side, 3=Both sides, 4=Central part
c. Location: 1= Anterior part, 2= Middle part, 3= Posterior part, 4= Multiple sites
d. Type:1= Meningiomas, 2= Pituitary Adenoma, 3= Schwannoma, 4=HGG, 5= LGG, 6= other tumor

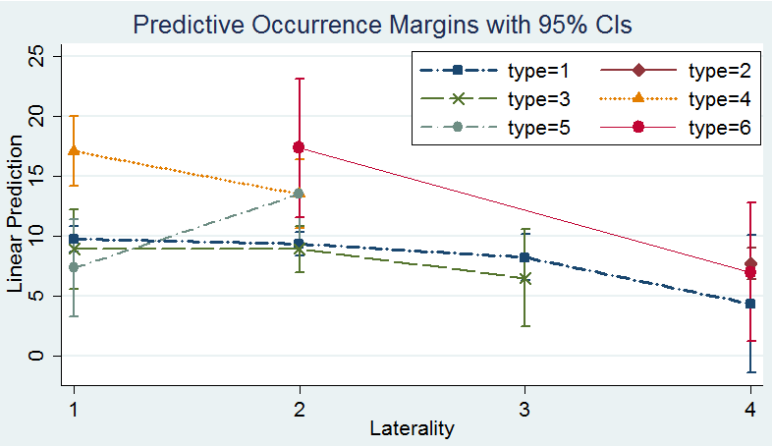


Figure 4.4 Interaction between Tumor Laterality and Tumor Type over Time

Predicting on symptom severity over time: Time is added to the model as a continuous variable. The interaction effect model the smallest scale parameter and the highest Wald test. Suppose the interaction effect model was selected to predict factors of the symptom severity over time. The autoregressive order (2) correlation and exchange correlation had scale parameter close together, whereas the coefficient error of the autoregressive order (2) correlation was smaller than those of exchange. Suppose the autoregressive order (2) correlation was chose to predict on symptom severity.

Type of RT, the result indicated that the mean of symptom severity in patient receiving Cyber-Knife decreased 12.37 times lower than those patients receiving IMRT, holding other predictors being constant.

Tumor laterality, the result showed that the mean of symptom severity in patients with central part tumor decreased 30.76 times than those patients with anterior part tumor, holding other predictors being constant.

Tumor type, the mean of symptom severity in patients with high-grade glioma increased 38.90 times than those patients with meningioma. Patients with other tumors (pineocytoma, endolymphatic sac tumor) increased severity 45.98 times than those patients with meninioma, after controlling for other predictors.

The interaction effect between tumor location and tumor type, the result indicated that the means of symptom severity in patients with high grade glioma at middle part tumor decreased 35.16 times lower than those patients with meningioma at middle part tumor tumor, holding other predictors being constant.

Symptom Severity = 32.98 + 5.54 (time) – 7.41 (type of RT2) – 12.36 (type of RT3) – 2.52 (laterality2) – 3.50 (laterality3) – 30.76 (laterality4) + 5.37 (location2) + 3.01 (location3) + .63 (location4) + 18.76 (type2) - 3.91 (type3) + 38.90 (type4) + 1.33 (type5) + 45.98 (type6) – 35.16 (location2 # type4) – 27.29 (location2 # type6)

Table 4.16 Predicting Factor on Symptom Severity over Time

Severity	Coef.	Std. Err.	Z	P>|z|	[95% Conf. Interval]	
Time	5.546	.912	6.08	0.000	3.759	7.332
Type of RT						
2	-7.414	3.711	-2.00	0.046	-14.687	-.1412
3	-12.365	3.658	-3.38	0.001	-19.535	-5.195
Laterality						
2	-2.525	3.106	-0.81	0.416	-8.613	3.563
3	-3.504	5.571	-0.63	0.529	-14.423	7.416
4	-30.757	14.335	-2.15	0.032	-58.853	-2.660
Location						
2	5.370	5.426	0.99	0.322	-5.2636	16.005
3	3.013	6.154	0.49	0.624	-9.049	15.074
4	.6274	8.311	0.08	0.940	-15.662	16.917
Type						
2	18.756	14.428	1.30	0.194	-9.522	47.033
3	-3.906	5.359	-0.73	0.466	-14.408	6.597
4	38.895	7.463	5.21	0.000	24.269	53.522
5	1.333	8.482	0.16	0.875	-15.290	17.957
6	45.982	14.775	3.11	0.002	17.023	74.940
Location#Type						
2 4	-35.164	12.625	-2.79	0.005	-59.908	-10.420
2 6	-27.199	25.036	-1.09	0.277	-76.268	21.871
_cons	32.978	5.303	6.22	0.000	22.585	43.372

a. Type of RT: 1=IMRT, 2=X-knife, 3=Cyber-knife

b. Laterality: 1= Left side, 2= Right side, 3=Both sides, 4=Central part

c. Location: 1= Anterior part, 2= Middle part, 3= Posterior part, 4= Multiple sites

d. Type:1= Meningiomas, 2= Pituitary Adenoma, 3= Schwannoma, 4=HGG, 5= LGG, 6= other tumor

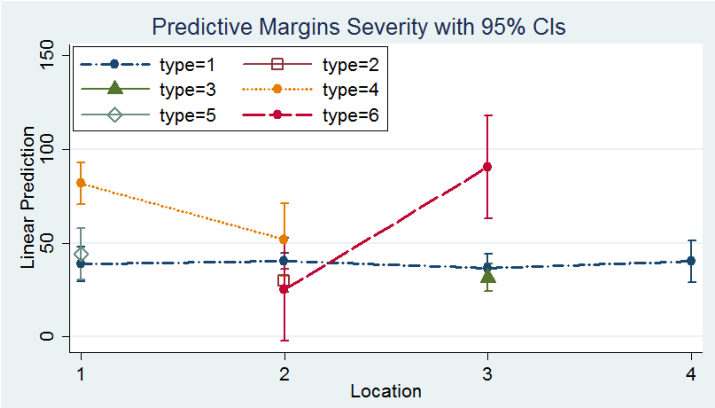


Figure 4.5 Interaction between Tumor Location and Tumor Type over Time

Predicting on symptom interference over time: Time is added to the model as a continuous variable. The scale parameter of the interaction effect model unstructured correlation matrix were the smallest value. The unstructured correlation matrix are close together, but the Wald test of the stationary (1) correlation was higher than those models. Suppose the interaction effect model and the unstructured correlation relation were selected to predict symptom interference over time.

Tumor type, the results indicated that the mean of symptom interference in patients with high-grade glioma increased 17.92 times than those patients with meningioma, after controlling for other predictors.

The interaction effect between tumor location and tumor type indicated that the means of symptom interference in patients with high-grade glioma in the middle part tumor decreased 21.34 times lower than those patients with meningioma of middle part tumor, holding other predictors being constant. However, for main effect type of RT, tumor laterality, and tumor location did not affect symptom interference showing in the equation below.

Symptom Interference = 18.65 + .82 (time) – .88 (type of RT2) – 2.78 (type of RT3) – .97 (laterality2) + 1.04 (laterality3) – 3.35 (laterality4) + .53 (location2) + 1.49 (location3) – 4.18 (location4) + .55 (type2) + 3.65 (type3) + 17.92 (type4) – 10.82 (type5) + 26.36 (type6) – 21.34 (location2 # type4) – 31.67 (location2 # type6)

Table 4.17 Predicting Factor on Symptom Interference over Time

Interference	Coef.	Std. Err.	z	P>z	[95% Conf. Interval]	
Time	.823	.372	2.22	0.027	.095	1.552
Type of RT[a]						
2	-.875	2.572	-0.34	0.734	-5.915	4.165
3	-2.780	2.535	-1.10	0.273	-7.749	2.189
Laterality[b]						
2	-.965	2.153	-0.45	0.654	-5.185	3.254
3	1.039	3.861	0.27	0.788	-6.529	8.606
4	-3.353	9.935	-0.34	0.736	-22.825	16.118
Location[c]						
2	.5273	3.760	0.14	0.888	-6.842	7.897
3	1.492	4.265	0.35	0.727	-6.868	9.851
4	-4.179	5.760	-0.73	0.468	-15.468	7.111
Type[d]						
2	.5483	9.999	0.05	0.956	-19.049	20.145
3	3.652	3.714	0.98	0.325	-3.627	10.931
4	17.924	5.172	3.47	0.001	7.787	28.061
5	-10.815	5.878	-1.84	0.066	-22.336	.705
6	26.363	10.240	2.57	0.010	6.294	46.432
Location#Type						
2 4	-21.344	8.749	-2.44	0.015	-38.492	-4.196
2 6	-31.665	17.351	-1.82	0.068	-65.671	2.342
_cons	18.651	3.537	5.27	0.000	11.718	25.585

a. Type of RT: 1=IMRT, 2=X-knife, 3=Cyber-knife
b. Laterality: 1= Left side, 2= Right side, 3=Both sides, 4=Central part
c. Location: 1= Anterior part, 2= Middle part, 3= Posterior part, 4= Multiple sites
d. Type:1= Meningiomas, 2= Pituitary Adenoma, 3= Schwannoma, 4=HGG, 5= LGG, 6= other tumor

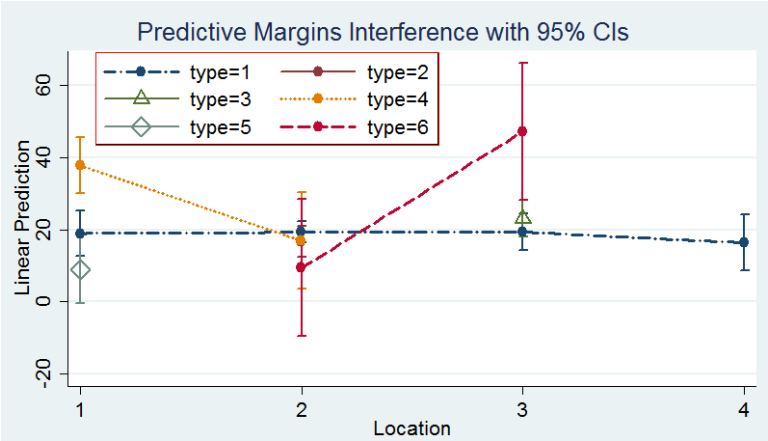


Figure 4.6 Interaction between Tumor Location and Tumor Type over Time

Objective 5: To investigate the changes over time in the HRQOL by Thai adults with PBT receiving radiotherapy during time 1 to time 2 and time 2 to time 3.

Objective 6: To describe the HRQOL and subdomains of HRQOL in Thai adults with PBT receiving radiotherapy at each time point and over time.

Responding to these two objectives, a repeated-ANOVA used to investigate the pattern of HRQOL over time and descriptive statistics were applied to describe the five domains of HRQOL at each time point and over time. The following assumptions of a repeated-ANOVA were tested: independently of observation, normality, and sphericity. Independent of observation and normality were met as mentioned before. The assumption of sphericity was violated, thus the Greenhouse-Geisser was used. Results indicated that the participants did rate HRQOL differently over time, which there were statistically significant, F (1.79, 212.77) = 13.83, p= .000, eta^2= .104 presented in Table 4.18. The eta squared is .104, which indicated that 10.4% of variance in HRQOL explained by the time effect. Polynomial contrasts indicated the linear trend and quadratic trend were significant, however the F-valve of quadratic pattern (F (1, 119) = 15.33, p = .000) is higher than F-valve of linear pattern (F (1, 119) = 13.07, p = .000). This result indicates that the best way to describe the development over time is a quadratic function. The means and standard deviations for HRQOL listed in order from time 1 to time 3 presented in Table 4.19. This analysis of means suggests that participants rate the lowest HRQOL appearing on time 2.

Table 4.18 Tests for HRQOL Change over Time (n = 120)

Within –subjects effects						
Source		df	Mean Square	F	P-valve	Eta^2
Time		1.788	1614.955	13.828	.000	.104
Error (Time)		212.770	116.789			
Within –subjects contrasts						
Source	Time	df	Mean Square	F	P-valve	Eta^2
Time	Linear	1	1809.504	13.065	.000	.099
	Quadratic	1	1078.001	15.330	.000	.114
Error (Time)	Linear	119	138.496			
	Quadratic	119	70.321			

As seen in the Table 4.19, the examination of these means suggested that patients rated overall HRQOL was decreased after start radiotherapy 8-10 Gy but rebound at the end of receiving radiotherapy the same as social/family well-being, and functional well-being domains, which were statistically significant differences over time (P = .000, P = .000, and P = .000), respectively.

Physical well-being and brain subscale, mean scores represented that patients rated these domains decreasing as time 2 and to be continued at time 3, whereas only physical well-being was a statistically significant difference over time (P = .000).

Emotional well-being, mean scores expressed that patients rated this domain increasing as time 2, and to be continued at time 3, which was statistically different (P = .000). Interpretation for overall HRQOL and subscale of HRQOL, a higher mean score denotes better functioning.

Table 4.19 Means, Standard Deviations, and Analysis of Variance of Overall HRQOL and Subdomains of HRQOL across Three Times (n = 120)

Measure	Time1	Time2	Time3	F	P-valve
HRQOL (0-200)					
Range	53-195	50-192	45-193	13.828	.000
Mean	155.09	148.68	149.60		
SD	25.924	25.272	25.895		
Physical well-being (0-28)					
Range	7-28	3-28	3-28	45.020	.000
Mean	24.24	21.24	21.02		
SD	3.872	5.097	4.76		
Social/family well-being (0-28)					
Range	4-28	3-28	2-28	17.499	.000
Mean	21.58	19.75	19.88		
SD	5.359	5.001	5.316		
Emotional well-being (0-24)					
Range	2-24	6-24	4-24	10.035	.000
Mean	18.16	19.02	19.73		
SD	5.034	4.104	4.181		

Table 4.19 Means and Standard Deviations of Overall and Subdomains of HRQOL across Three Times (n = 120) (cont.)

Measure	Time1	Time2	Time3	F	P-valve
Functional well-being (0-28)					
Range	2-28	2-28	3-28	8.953	.000
Mean	21.44	19.90	20.55		
SD	5.529	5.008	5.294		
Brain subscale (0-92)					
Range	19-91	29-92	28-92	2.411	.094
Mean	69.67	68.77	68.43		
SD	13.85	12.62	12.87		

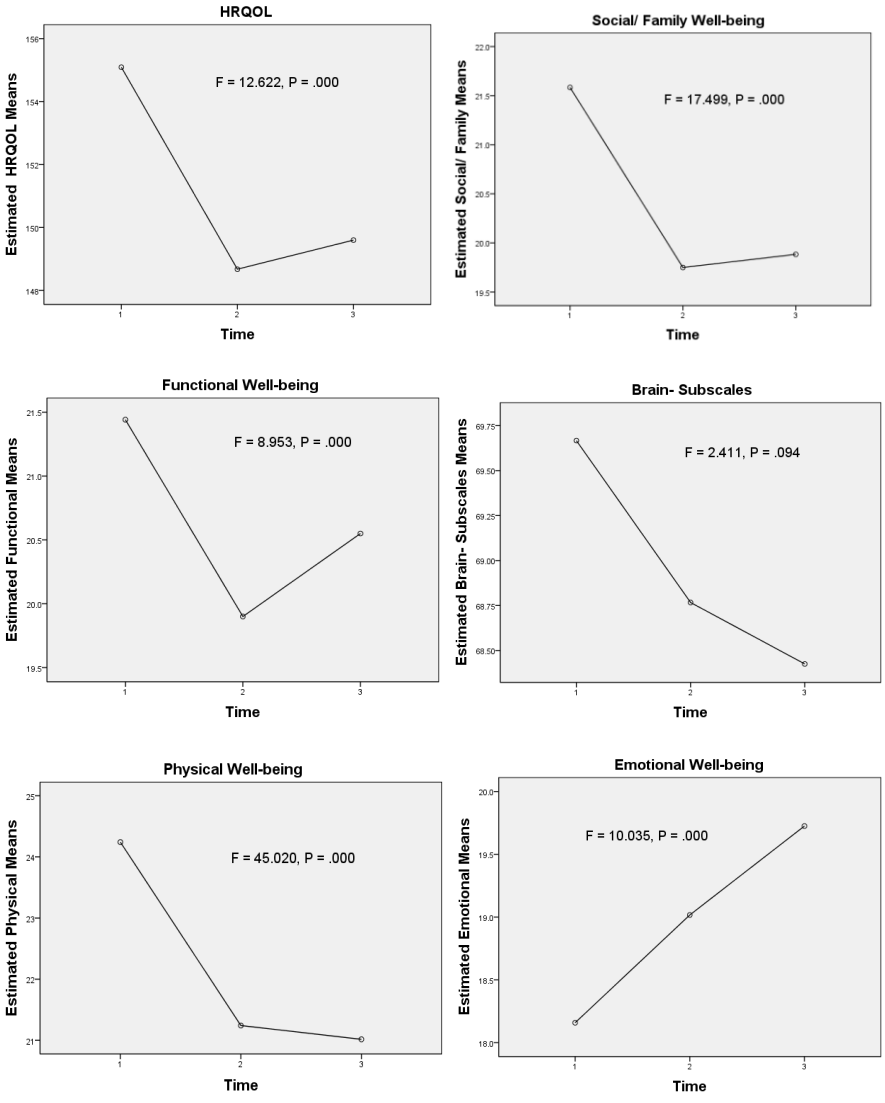


Figure 4.7 Patterns of Subdomains of HRQOL over Time

Objective 7: To determine which domains of symptom experiences (occurrence, severity, and life interferences) affected on HRQOL at each time point.

In response this research objective, the multiple regression analysis was used to identify which domains of symptom experiences predict HRQOL at each time point after all assumptions were initially tested. Normally distributed errors and independent errors were checked and met (Durbin-Watson tested, value range 1.5-2.5). Multicolinearity of independent variables was accepted by Tolerance value more than 1- R^2 and VIF not more than 2.

Bivariate correlation was used to identify the correlation among the predictor variables before computing the multiple regressions. The correlation matrix between symptom occurrence and symptom severity indicated highly correlated (above .87), there might be multicollinearity problems.

For this high correlation may affect the Tolerance values so that the regression will run without change the variables in the equation (Table 4.20). The result indicated that the tolerance values are less than 1-R^2 (In this case, adjusted R^2 is .655 so 1- R^2 is equal .345) in symptom occurrence and symptom interference. Then there was a possibility problem of multicolinearity.

Table 4.20 Test of Symptom Experience on HRQOL at Time 1 (n = 120)

Variable	B	Std. Error	Beta	Collinearity Statistics		Severity	Interference
				Tolerance	VIF		
Occurrence	-3.498	.713	-.544**	.193	5.183	.870**	.440**
Severity	-.103	.160	-.079	.640	1.562		.584**
Interference	-.681	.143	-.321**	.236	4.238		
Constant	199.804	3.350					
Adjusted R^2	.655						

a. Dependent Variable: HRQOL

**. Correlation is significant at the 0.01 level (2-tailed).

To handle multicollinearity should be removed symptom occurrence because it retrieved from symptom severity with highly correlated. Therefore, symptom severity and symptom interference remained in the equation. After eliminating symptom occurrence, the Tolerance value and VIF were checked and met (Appendix F Table 10). Criteria to select the best model in regression used the

smallest value of the Akaike information (AIC), the Mean squares (MS), and errors of regression coefficients (ER).

To predict HRQOL at time 1: The additive model of multiple regression analysis was used to determine symptom severity and symptom interference for predicting HRQOL, the mean, standard deviations, and intercorrelation were tested (Appendix F Table 11). This combination of symptom severity and interference significantly predicted HRQOL, F (2, 117) = 85.41, P = .000 (Table 4.21). The R-adjusted value was .587, which indicated that 58.7% of the variance in HRQOL was significantly explained by symptom severity and symptom interference at time 1. The patients with higher scores of symptom severity had significant lower HRQOL, after controlling for the other variables in the model. The patients with higher score of symptom interference also had significant lower HRQOL. As seen in the following equation:

HRQOL = 191.84 – .76 (Symptom Severity) – .56 (Symptom Interference)

Table 4.21 Symptom Experience Predicting HRQOL at Time 1 (n = 120)

Variable	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change (2, 117)
					.593	.587	16.669	85.408**
Constant	191.843	3.206		.000				
Severity	-.762	.094	-.585	.000				
Interference	-.562	.154	-.265	.000				

a. Dependent Variable: HRQOL, ** P < .01

Symptom severity and symptom interference predicting HRQOL at time 1: Enter method of multiple regression analysis was performed by entering all 22 symptom severity and 6 symptom interference to predict HRQOL before receiving radiotherapy. As shown in Table 4.22: the symptoms including weakness, nausea, disturbed sleep, lack of appetite, feeling sad, difficulty concentrating, change in bowel pattern and symptom interfere life including walking and enjoyment of life were statistically significant predicted HRQOL, F (9, 110) = 25.75, P = .000. The adjusted

R square value was .652, which indicated that 65.2% of the variance in HRQOL was explained by these seven symptoms and two activities that interfere from symptoms. The beta weights suggest that weakness was the strong symptom explaining the greatest proportion of the variance in HRQOL at the end of receiving radiotherapy.

Table 4.22 Symptom Severity and Interference Predicting HRQOL at Time 1 (n = 120)

HRQOL	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change
					.678	.652	15.298	25.751**
(Constant)	182.539	2.582		.000				
Weakness	-2.756	.638	-.252	.000				
Nausea	-4.674	1.330	-.212	.001				
Disturbed sleep	-1.602	.523	-.171	.003				
Lack of appetite	-2.139	.752	-.166	.005				
Change in bowel pattern	-1.751	.624	-.161	.006				
Difficulty concentrating	-1.750	.713	-.142	.016				
Feeling sad	-1.368	.661	-.125	.041				
Walking	-2.037	.492	-.245	.000				
Enjoyment of life	-1.499	.602	-.155	.014				

a. Dependent Variable: HRQOL

**. P < .01

To predict HRQOL at time 2: The additive model of multiple regression analysis was used to determine symptom severity and symptom interference for predicting HRQOL, the mean, standard deviations, and intercorrelation were tested (Appendix Table 12). This combination of two variables significantly predicted HRQOL, F (2, 117) = 68.925, P = .000 (Table 4.23). The R-adjusted value was .533, which indicated that 53.3% of the variance in HRQOL was significantly explained by symptom severity and symptom interference at time 2. The patients with higher scores of symptom severity had significant lower HRQOL, after controlling for the other variables in the model. The patients with higher score of symptom interference also had significant lower HRQOL. As seen in the following equation:

HRQOL = 188.81 – .62 (Symptom Severity) – .66 (Symptom Interference)

Table 4.23 Symptom Experience Predicting HRQOL at Time 2 (n = 120)

Variable	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change (2, 117)
					.541	.533	17.269	68.925**
Constant	188.807	3.766		.000				
Severity	-.618	.088	-.523	.000				
Interference	-.664	.160	-.308	.000				

a. Dependent Variable: HRQOL, **P < .01

Symptom severity and symptom interference predicting HRQOL at time 2: The multiple regression analysis was used to examine which symptoms predicted HRQOL and which daily activities interfere HRQOL during receiving radiotherapy 8-10 Gy. As presented in Table 4.24, weakness, irritability, vomiting, feeling drowsy, feeling sad, problem with remembering and symptom interfere life including relation with other people and walking were statistically significant predicted HRQOL, F (7, 112) = 30.887, P = .000. The adjusted R square value was .637, which indicated that 63.7% of the variance in HRQOL was explained by all these symptoms. The beta weights suggest that weakness was the strong symptom explaining the greatest proportion of the variance in HRQOL after receiving radiotherapy 8-10 Gy.

Table 4.24 Symptom Severity and Interference Predicting HRQOL at Time 2 (n = 120)

Variable	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change
					.659	.637	15.217	30.887**
(Constant)	180.093	3.123		.000				
Weakness	-3.657	.688	-.335	.000				
Irritability	-2.381	.660	-.225	.000				
Nausea	-2.024	.672	-.186	.003				
Feeling sad	-2.374	.814	-.177	.004				
Feeling drowsy	-1.633	.589	-.160	.006				
Relation with other	-2.165	.555	-.247	.000				
Walking	-1.578	.533	-.182	.004				

a. Dependent Variable: HRQOL, **P < .01,

To predict HRQOL at time 3: The additive model of multiple regression analysis was used to determine symptom severity and symptom interference for predicting HRQOL, the mean, standard deviations, and intercorrelation were tested (Appendix Table 14). This combination of variables significantly predicted HRQOL, F (2, 117) = 73.959, P = .000, with these two variables significantly contributing to the prediction. The R-adjusted value was .551, which indicated that 55.1% of the variance in HRQOL was significantly explained by symptom severity and symptom interference at time 3. The patients with higher scores of symptom severity had significant lower HRQOL, after controlling for the other variables in the model. The patients with higher score of symptom interference also had significant lower HRQOL. As seen in the following equation:

HRQOL = 189.21 – .62 (Symptom Severity) – .56 (Symptom Interference)

Table 4.25 Symptom Experience Predicting HRQOL at Time 3 (n = 120)

Variable	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change
					.558	.551	17.356	73.959**
Constant	189.211	3.622		.000				
Severity	-.622	.084	-.559	.000				
Interference	-.564	.157	-.269	.000				

a. Dependent Variable: HRQOL, ** P < .01

Symptom severity and symptom interference predicting HRQOL at time 3: The symptoms including feeling sad, weakness, irritability, feeling drowsy, difficulty concentrating, and daily activities including relation with other people and walking were statistically significant predicted HRQOL at the end of receiving radiotherapy, F (8, 111) = 24.824, P = .000 (Table 4.26). The adjusted R square value was .616, which indicated that 61.6% of the variance in HRQOL was explained by all these symptoms. The beta weights suggest that feeling sad was the strong symptom explaining the greatest proportion of the variance in HRQOL at the end of complete radiotherapy.

Table 4.26 Symptom Severity and Interference Predicting HRQOL at Time 3 (n = 120)

HRQOL	B	Std. Error	Beta	P-value	R^2	Adjust R^2	Std. Error of the estimate	F Change
					.641	.616	16.055	24.824**
(Constant)	178.052	2.912		.000				
Feeling Sad	-3.189	.743	-.275	.000				
Weakness	-2.423	.788	-.196	.003				
Irritability	-1.939	.720	-.194	.008				
Feeling drowsy	-1.599	.558	-.176	.005				
Vomiting	-1.975	.822	-.142	.018				
Difficulty concentrating	-1.693	.846	-.138	.048				
Relation with other	-1.744	.569	-.188	.003				
Walking	-1.419	.566	-.166	.014				

a. Dependent Variable: HRQOL, **. P < .01,

Table 4.27 Symptom Experience Predicting HRQOL at Three Times (n = 120)

Variables	Time1	Time2	Time3
Symptom	1. Weakness	1. Weakness	1. Feeling Sad
Severity	2. Nausea	2. Irritability	2. Weakness
	3. Disturbed sleep	3. Nausea	3. Irritability
	4. Lack of appetite	4. Feeling sad	4. Feeling drowsy
	5. Change in bowel pattern	5. Feeling drowsy	5. Vomiting
	6. Difficulty concentrating		6. Difficulty concentrating
	7. Feeling sad		
Symptom	1. Walking	1. Relation with other	1. Relation with other
Interference	2. Enjoyment of life	2. Walking	2. Walking

Symptom severity including weakness and feeling sad significantly predicted HRQOL at three time points. Vomiting, feeling drowsy, and irritability were the new symptoms that found significantly predicting HRQOL after patients receiving radiotherapy 8-10 Gy and at the end of radiotherapy. Difficulty concentrating significantly predicted HRQOL before patients receiving radiotherapy and at the end of radiotherapy. Relation with other people and walking were the daily activities that significantly predicted HRQOL.

Objective 8: To determine which domains of symptom experience (occurrence, severity, and life interferences) affected on HRQOL over time.

To analyze these research objectives, Pearson's Product-Moment Correction Coefficients was employed to test the correlations among symptom experiences (occurrence, severity, and life interferences) and HRQOL. Then the GEE was conducted to predict symptom experiences on the changes over time in HRQOL.

To predict HRQOL over time: The GEE was used to examine symptom experiences on the changes over time in HRQOL after all assumptions were initially tested. Criteria to select the best model are the smallest value of the scale parameter and errors of regression coefficients and highest on Wald test. Time is added to the model as a continuous variable. Test the interaction between symptom severity and symptom interference was not significant (Appendix F Table 17). The performances of additive model and exchange correlation were the lowest value that used to analyze the effect of symptom experiences on HRQOL, the mean, standard deviations, and intercorrelation were tested.

The result indicated that symptom experiences (severity and interference) were statistically significant predicting on HRQOL over time. Interpreted of this result reflected that a change within one subject of 1 unit in symptom severity is negatively associated with a difference with .46 units in HRQOL. A difference with 1 unit in symptom interference is negatively associated with a difference with .58 units in HRQOL. The predicting model is presented as follow:

HRQOL = 181.74 – .46 (Symptom Severity) – .58 (Symptom Interference)

Table 4.28 Test of symptom experiences on HRQOL over Time (n = 120)

HRQOL	Coef.	Std. Err.	Z	P>|z|	[95% Conf. Interval]	
Severity	-.467	.043	-10.93	0.000	-.551	-.3832
Interfere	-.581	.090	-6.48	0.000	-.757	-.405
_cons	181.738	2.382	76.31	0.000	177.070	186.406

Symptom experience and their effects on HRQOL over time were reported in Table 4.29

In regarding to the type of RT, the coefficient of 8.85 indicated that treating with cyber-knife significantly predicted higher HRQOL 8.85 times than treating with IMRT. The coefficient of 11.77 indicated that treating with X-knife significantly predicted higher HRQOL 11.77 times than treating with IMRT.

According to the tumor laterality, the coefficient of 29.11 indicated that a patient having tumor at a central part tumor significantly predicted higher HRQOL 29.11 times than having tumor at a left side part. The coefficient of 11.02 indicated that having both sides tumor significantly predicted higher HRQOL 11.02 times than having only left sided tumor. The coefficient of 6.21 indicated that having right sided tumor significantly predicted higher HRQOL 6.21 times than having left sided tumor. However, tumor location did not significantly predicted HRQOL over time.

Type of tumor could predict HRQOL. The coefficient of -14.94 indicated HGG significantly predicted lower HRQOL 14.94 times than meningioma. The coefficient of -24.13 indicated that pituitary adenoma significantly predicted lower HRQOL 24.13 times than a patient who had meningioma.

According to symptom severity, the coefficient of -.95 indicated that increasing 1 time in pain significantly predicted lower HRQOL .95 times. The coefficient of -1.14 indicated that increasing 1 time in disturbed sleep significantly predicted lower HRQOL 1.14 times. The coefficient of -1.07 indicated that increasing 1 time in feeling drowsy significantly predicted lower HRQOL 1.07 times. The coefficient of -1.38 indicated that increasing 1 time in feeling sad significantly predicted lower HRQOL 1.38 times. The coefficient of -2.30 indicated that increasing 1 time in vomiting significantly predicted lower HRQOL 2.30 times. The coefficient of -1.78 indicated that increasing 1 time in weakness significantly predicted lower HRQOL 1.78 times. The coefficient of -1.90 indicated that increasing 1 time in difficulty concentrating significantly predicted lower HRQOL 1.90 times. Vomiting was the strongest predicted HRQOL over time.

In regarding to symptom interference, the coefficient of -1.53 indicated that increasing 1 time interfere walking significantly predicted lower HRQOL 1.53

times. The coefficient of -1.42 indicated that increasing 1 time interfere enjoyment of life significantly predicted lower HRQOL 1.42 times.

Interaction effects between vomiting, weakness, and difficulty concentration significantly predicted HRQOL over time. The predicting model can be proposed as follow:

HRQOL = 172.04 - .94 (Time) + 11.77 (Type RT2) + 8.85 (Type RT3) + 6.21 (Laterality2) + 11.02 (Laterality3) + 29.11 (Laterality4) – 4.92 (Location2) – 6.58 (Location3) – 2.08 (Location4) – 24.13 (Type2) – 2.67 (Type3) – 14.94 (Type4) + 9.6 (Type5) – 22.24 (Type6) – .95 (Pain) – 1.14 (Disturbed sleep) – 1.07 (Feeling drowsy) – 1.38 (Feeling sad) – 2.30 (Vomiting) – 1.78 (Weakness) – 1.90 (Concentrate) – 1.53 (Walking) – 1.42 (Enjoyment of life) + (Vomiting X Weakness X Difficulty concentration)

This model reveals that type of radiation therapy, tumor laterality, tumor type, severity of symptoms including pain, disturbed sleep, feeling drowsy, feeling sad, vomiting, weakness and difficulty concentrating along with the interference from difficulty walking, problems with enjoyment of life and the cluster symptoms of (or interaction among) vomiting, weakness and difficulty concentration could predict HRQOL over time in patients with PBT receiving radiation therapy. This model can be utilized to improve patients' quality of life during their early phase of transition after the first radiation treatment is initially started.

Table 4.29 Symptom experience and their effects on HRQOL over Time

Variable	Coef.	Std. Err.	Z	P>|z|	[95% Conf.	Interval]
Time	-.941	.585	-1.61	0.108	-2.087	.206
Type of RT[a]						
2	11.771	3.574	3.29	0.001	4.765	18.777
3	8.852	3.505	2.53	0.012	1.982	15.722
Laterality[b]						
2	6.209	3.011	2.06	0.039	.308	12.110
3	11.017	5.393	2.04	0.041	.447	21.588
4	29.111	11.620	2.51	0.012	6.336	51.886
Location[c]						
2	-4.919	4.782	-1.03	0.304	-14.292	4.453
3	-6.578	5.699	-1.15	0.248	-17.748	4.593
4	2.082	7.856	0.27	0.791	-13.315	17.479
Type[d]						
2	-24.131	11.615	-2.08	0.038	-46.895	-1.367
3	-2.669	5.167	-0.52	0.605	-12.795	7.457
4	-14.938	6.246	-2.39	0.017	-27.181	-2.696
5	9.632	8.109	1.19	0.235	-6.260	25.525
6	-22.236	11.606	-1.92	0.055	-44.984	.511
Severity						
Pain	-.950	.304	-3.13	0.002	-1.545	-.355
Disturbed sleep	-1.136	.277	-4.10	0.000	-1.680	-.592
Feeling drowsy	-1.071	.281	-3.81	0.000	-1.621	-.521
Feeling sad	-1.379	.357	-3.86	0.000	-2.079	-.678
Vomiting	-2.304	.395	-5.83	0.000	-3.078	-1.530
Weakness	-1.781	.452	-3.94	0.000	-2.667	-.894
Concentrate	-1.899	.441	-4.31	0.000	-2.763	-1.035
Interference						
Walking	-1.529	.296	-5.17	0.000	-2.108	-.949
Enjoyment of life	-1.418	.341	-4.16	0.000	-2.086	-.750
5#6#7[e]	.152	.046	3.29	0.001	.061	.243
_cons	172.042	4.985	34.51	0.000	162.271	181.814

a.Type of RT: 1=IMRT, 2=X-knife, 3=Cyber-knife
b.Laterality: 1= Left side, 2= Right side, 3=Both sides, 4=Central part
c.Location: 1= Anterior part, 2= Middle part, 3= Posterior part, 4= Multiple sites
d.Type:1= Meningiomas, 2= Pituitary Adenoma, 3= Schwannoma, 4=HGG, 5= LGG, 6= other tumor
e.5=vomiting, 6= weakness, 7=difficulty concentration

CHAPTER V
DISCUSSION

This study examined symptom experiences and their influence on health related quality of life (HRQOL) among adults with PBT who received radiotherapy at three times, prior to staring radiotherapy, after receiving radiotherapy 8-10 Gy, and at the completion of radiotherapy. This chapter provided discussion in association with the results of this study. The discussion focused on the interpretation of the main results and the significant clinical findings according to the study purposes.

Symptom Experience and Pattern of Change

Discussion on symptom experience consists of three interrelated components, perception (symptom occurrences), evaluation (symptom severity), and response to symptom (symptom interference). These three variables are one main component in the Symptom Management Model. They are dynamic and hypothesized affected by two core domains, including the person (tumor type, tumor laterality, and tumor location) and health/illness (type of radiotherapy). They thus confirmed that the symptom experience may change over time (Dodd et al., 2001a). Furthermore, the finding also demonstrated a positive association between each component. The correlation between each component of symptom experience will be discussed. Then the factors predicting changes of symptom experience along the illness trajectory will be discussed. Finally, the discussion will focus on the symptom experience predicted on HRQOL over time.

Perception of Symptom (Symptom Occurrence)

The result of this study revealed that prior to receiving radiotherapy, most patients experienced a wide range in the number of symptoms (mean = 8.10, range 1 to 20). Visual impairment, problem with remembering, upset, feeling drowsy, and pain were as the most occurrence symptoms at this time point. Each of these symptoms was experienced more than 52.5% of the patients. Visual impairment was the most symptom that occurred in adults with PBT before starting radiotherapy. Interpretation of this finding the majority of patients in this study presented with meningiomas, 60% (n = 72) in different lesions that affected visual pathway, including 19.4% sphenoid wing, 19.4% cavernous sinus, and 11 % of orbital apex, optic nerve sheath, or tuberculum sellae. Meningiomas can contain the anatomy of the visual pathways, which are arising from the medial sphenoid wing, cavernous sinus, orbital apex, optic nerve sheath, or tuberculum sellae. The growth of visual pathway meningiomas can affect visual dysfunction (Stiebel-Kalish et al., 2012). Likewise the study of Maclean et al. (2013), visual deficit was a common clinical problem in patients with meningiomas. They reported that 66.67% of patients with meningiomas had a visual problem at baseline. This finding is consistent with those in the study of Henzel, Fokas, Sitter, Wittig, and Engenhart-Cabillic (2013) who conducted a prospective study of 67 patients with meningiomas treat with radiotherapy. The authors reported that the most common symptoms before starting radiotherapy were visual impairment (44.78%) and ptosis and diplopia (22.39%).

After receiving radiotherapy 8-10 Gy, five major common symptoms were visual impairment, fatigue, feeling drowsy, problem with remembering, and disturbed sleep. At the end of receiving radiotherapy, five most symptom occurrences were visual impairment, fatigue, problem with remembering, feeling drowsy, and disturbed sleep. Fatigue and disturbed sleep were the new symptoms that occur during receiving radiotherapy 8-10 Gy and at the end of treatment. The results of the findings can be explained in the study of Klein (2010) who evaluated the patients with low grade gliomas treated with radiotherapy. The patients developed acute radiation encephalopathy within 2 weeks after start radiotherapy caused by vasogenic edema after disruption of the blood-brain barrier may result in somnolence (fatigue and disturbed sleep). Similar to Powell et al. (2011) addressed feeling drowsy accompany

with fatigue and disturbed sleep is the pattern of somnolence syndrome that occur during the first phase in the second week and after complete the radiotherapy. Visual impairment, problem with remembering, and feeling drowsy were reported as a high occurrence symptom at three times.

Regarding the symptom occurrence evaluated at three points in time, the symptoms appearing at these times comprised of visual impairment, problem with remembering, and feeling drowsy. Fatigue and disturbed sleep presented during receiving radiotherapy congruent with several studies conducted previously in PBT and other cancer receiving radiotherapy which revealed that fatigue and disturbed sleep or sleep disturbance or problem with sleep was the top rank of symptom occurrence (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007; Roscoe et al., 2007; Shaw & Robbins, 2006).

Evaluation of Symptom (Symptom Severity)

At the time of symptom occurrence patients evaluated how much their symptoms severe. Prior to radiotherapy the top five of symptom severity included visual impairment, upset, change in appearance, problem with remembering, and feeling drowsy. After receiving radiotherapy 8-10 Gy, top five severe of symptoms included visual impairment, feeling drowsy, fatigue, disturbed sleep, and problem with remembering. At the end of treatment, visual impairment, change in appearance, feeling drowsy, fatigue, and disturbed sleep were the most severe symptoms. At time 2 and time 3 the new symptom severity were fatigue and disturbed sleep. This finding was consistent with Armstrong et al. (2010a) study who evaluated fatigue in 201 patients with PBT at different stages in disease trajectory. Fatigue was the most severe symptom which reported by patients in this group. The therapeutic effect of radiation therapy is probably a result of damage to the blood vessels feeding the tumor. After radiotherapy, blood brain barrier (BBB) breakdown may occur acutely, which can occasionally produce symptoms worse before they are improved. The swelling increases the pressure in the head and makes the symptoms get worse (Platten & Wick, 2012). Therefore, the result in this study revealed the severity of some symptoms increasing during receiving radiotherapy until finish treatment. Focusing on ‘change in appearance’ found prior to radiotherapy because patients in this study had

facial palsy due to the tumor lesion, skull bone deformity due to craniectomy or proptosis or ptosis due to the progression of disease. In addition, the change in appearance occurred again at the end of treatment due to the side effect of radiation. Those included hair loss, skin erythema and eye irritation. Alopecia occurs 2–3 weeks after into a course of fractionated whole- or partial-brain radiation (Shaw & Robbins, 2006). Result from the change in appearance made patients feel irritable and withdraw themselves from regular social activities. Butler et al. (2006) reported the most common acute reactions with brain radiation including fatigue, hair loss, and skin erythema. Fatigue, feeling drowsiness, and disturbed sleep combine in term somnolence were the most occurrence and severe symptoms that most patients experienced during and at the end of radiotherapy may cause by vasogenic edema after disruption of the blood–brain barrier (Klein, 2010).

Response to Symptom (Symptom Interference)

Patients rated highly ranking burden from the symptoms on their daily life prior receiving radiotherapy similar to after receiving radiotherapy 8-10 Gy including walking, work, mood, general activity, enjoyment of life, relation with other people. At the end of receiving radiotherapy work, mood, and general activity were highly rated influencing on daily life. None of studies have reported the symptom interference change over time in the patients with PBT. A few studies reported the influence of symptom on daily life activities in a single time point. For example, Armstrong et al. (2010a) evaluated 201 patients with PBT supposed that the burden of symptoms on their daily activities such as mood, work, walking, and interactions with others demonstrated with more severe fatigue in a cross sectional study. Walbert et al. (2014) demonstrated 34 patients with a brain Ependymoma perceived that their disease interfered most with work, walking, enjoyment of life, general activity, relations with others, and mood respectively. Change over time in this dimension should be needed to further explore.

Change of the Symptom Experience in Adults with PBT over Time

For symptom occurrence, the result represented that means of symptom occurrence increases from time1 to time3. Combined with the result from repeated-measure ANOVA indicates that symptom occurrence had significantly developed over time in linear function (e.g. Problem with remembering increased at time 2 and continuous increased at time 3).

For symptom severity, the result revealed that the means of symptom severely also increased from time 1 to time 3. Combine with the result from repeated-measure ANOVA expressed that symptom severity developed significantly over time in linear function similar to the pattern of symptom occurrence. Change in symptom severity probably because effect symptoms usually occur after the treatment is started, increasing to its peak during the third or fourth week.

For symptom interference, the mean of symptom interference increased from time 1 to time 2 and decreased from time 2 to time 3 comparing with time 1. Combine with the result from repeated-measure ANOVA indicated that symptom interference had a significant decline over time in a quadratic pattern.

The discussion on the change over time of symptom experience dimensions will be highlighted on the top 5 leading symptom scores across occurrence and severity dimensions at each time point. Of those eight symptoms, including visual impairment, pain, fatigue, feeling drowsy, problem with remembering, change in appearance, disturbed sleep, and upset were included for discussion. Details are explained as follows.

Visual impairment and pain in both occurrence and severity dimensions increased from time 1 to time 2 and decreased from time 2 to time 3, which were not statistically significant difference. Interpretation from this result, some patients had visual improvement not only decreased the number of occurrences, but also decreased the severe level of symptom at the end of receiving radiotherapy. However the other remained more severe from visual problem (rating severity increased) during until complete radiotherapy. The result from this study supported the result from the study of Stiebel-Kalish et al. (2012). The authors conducted 16 meningiomas patients with baseline visual problem that the patients were rated improvement in 38% and 2

patients experienced worsening of visual function after treated with fractionated stereotactic radiotherapy.

Problem with remembering and change in appearance, these two symptoms were increased significantly over time in the occurrence and severity dimensions. Klein (2012) proposed that early neurocognitive dysfunction (problem with remembering) in patients with LGG is most likely a result of the tumor. This finding revealed that problem with remembering in these patients should be attributed to the tumor and/or radiotherapy that occurred in acute phase. Inconsistent with previous studies that addressed cognitive impairment (problem with remembering) occurring in late of treatment 6 months to more than 1 year (Torres et al. 2003).

Fatigue, feeling drowsy, and disturbed sleep in severity dimension increased from time 1 to time 2 and to be continued increased with time 3 but the rate of increasing from time 2 to time 3 is slightly rate than those rates from time 1 to time 2. For fatigue and feeling drowsy in the occurrence rates were slightly decreased from time 2 to time 3. This finding indicated that a number of patients improved from fatigue and feeling drowsy at the end of treatment. The severity pattern of fatigue, feeling drowsy, and disturbed sleep represented the interaction to each other and reciprocal relationship of these symptoms in term of somnolence syndrome. Consistent with the study of Powell et al. (2011) who reported 90% of patients with PBT receiving radiotherapy experience somnolence at baseline, during, and up to 10 weeks. The score increased during receiving radiotherapy with a peak at the end of treatment. In addition, pattern of fatigue represented a worsening negative change from the baseline score to peak 6 weeks at the end of receiving radiotherapy.

Upset of occurrence and severity dimensions decreased continuously in a linear pattern from time 1 to time 3, which was not a statistically significant change. Although, the patients were suffering with various unpleasant symptoms during receiving radiotherapy their feeling toward the symptom tend to improve in the positive way.

The similarities in the occurrence and severity dimensions within each symptom are slightly surprised, given the theoretical difference between the rate of occurrence and severity that are described in the literature. The occurrence and

severity dimensions were diverse but related dimension of symptom (Hofsø, Rustøen, Cooper, Bjordal, & Miaskowski, 2013; Lenz et al., 1997).

Factors Effect on Symptom Experience

The current result shows the important factors (tumor factors and type of RT) that have been identified effect on symptom experience in adults with PBT.

Tumor type significantly predicted symptom experience (occurrence, severity, and interference) at time 1 and time 2. At time 3 the tumor type significantly predicted symptom experience only severity and interference dimensions. This indicated the linear combination of symptom occurrence, symptom severity, and symptom interference test differed for various types of tumor before and during receiving radiotherapy 8-10 Gy. Interpretation of this finding the majority of patients in this study had meningiomas (tumor type) 60% with visual impairment 58/72 (80.6%) and pituitary adenoma (tumor type) 16% with visual impairment 14/20 (70%) prior receiving radiotherapy. During receiving radiotherapy 8-10 Gy mean severity of visual impairment in meningioma and pituitary (mean = 4.71, SD = 3.06) increasing compare with before receiving radiotherapy (mean = 4.53, SD = 3.04). Consistent with the study of Combs et al. (2013) who conducted 632 patients with meningiomas receiving radiotherapy in which the result appeared 51% of the patients reported visual impairment (53%) prior to radiotherapy.

Focusing on change over time, tumor type can predict symptom experience (occurrence, severity, and interference) over time. The result indicated that patients with HGG showed increases in the occurrence of symptoms by 5.99 times than those with meningiomas and showed increased symptom severity by 38.90 times than those patients with meningioma, after controlling for other predictors. Patients with other tumor (pineocytoma, endolymphatic sac tumor) showed increased in symptom interference by 8.44 (26.36 – 17.92) times than those patients with HGG, after controlling for other predictors. Considering the tumor type was the only one predicting factor that was significantly influenced on symptom interference at three time points and over time. Clinically significant change was hardly seen. None of the

studies have conducted factor affected on symptom interference over time in adults with PBT. Change of this dimension should be needed to further explore.

Type of RT significantly predicted symptom occurrence and symptom severity at time 2 and time 3. This indicated that the linear combination of symptom occurrence and symptom severity tests differed for various types of radiotherapy. Soldà et al. (2013) examined in 222 patients with benign intracranial meningiomas receiving stereotactic radiotherapy (type of radiotherapy) which the result showed treatment was associated with mild (rating of severity) transient acute toxicity such as alopecia. Worsening (rating of severity) of pre-existing cranial nerve deficit occurred in eight (3.5%) and the onset of new deficit in one (0.5%) patient.

Focusing on change over time, type of RT can predict symptom in occurrence and severity dimensions, the result indicated that patients receiving Cyber-Knife showed decreased symptom occurrence at .45 (2.27-1.82) times lower than those patients receiving an X – knife and showed decreased symptom severity by 12.37 times lower than those patients receiving IMRT, holding other predictors being constant.

Tumor laterality significantly predicted symptom occurrence in time 3, which indicated the linear composition of symptom occurrence test differed for laterality of tumor. Nwachukwu et al. (2014) assessed tumor laterality in brain tumor survivor patients with bilateral/midline tumors who reported increased fatigue compared to those with right-sided tumors (26 vs. 13, $p = 0.025$). Hahn et al. (2003) identified 68 adult patients with newly diagnosed primary brain tumors. The results indicated that patients with left hemisphere tumors had more depressive symptoms than those patients with right hemisphere tumors had. The left hemisphere patients also reported more memory problems than did the right hemisphere patients.

Focusing on change over time, tumor laterality significantly predicted symptom severity over time. Patients with central part tumor showed decreased symptom severity by 30.76 times than those patients with left sided tumor, holding other predictors being constant.

The interaction between tumor laterality and tumor type significantly predicted symptom occurrence and symptom severity before receiving radiotherapy. The interaction between HGG and left sided tumor significantly predicted symptom

occurrence and symptom severity higher than others brain tumor. Similar to Nwachukwu et al. (2014) who revealed in LGG patients the result showed that bilateral/midline tumors (tumor laterality) reported increased fatigue. Some researchers used tumor location, tumor site and tumor laterality in the same meaning, although this makes difficult to differentiate among tumor location, tumor site and tumor laterality appearance of circumscribed severity of symptom over time.

Focusing on change over time, interaction effects between laterality and type of tumor can also predict the symptom occurrence over time. The results indicated that patients having right sided tumor with LGG showed increases in the occurrence of symptoms by 6.23 times than those patients with meningioma at right sided tumor, after controlling for other predictors.

The interaction between tumor location and tumor type significantly predicted symptom severity after receiving radiotherapy 8-10 Gy and significantly predicted symptom severity and symptom interference at the end of receiving radiotherapy. After receiving radiotherapy 8-10 Gy the finding revealed that the patients had HGG at the anterior part of the brain can predict symptom severity higher than those patients with meningiomas or LGG. However, patients with meningiomas at anterior part rated symptom severity not different from patients with LGG at anterior part. At the end of receiving radiotherapy patients had HGG at anterior part of brain rated symptom severity the same as after receiving radiotherapy 8-10 Gy. For Symptom interference patients with anterior part tumor, rated interfere from symptoms being as HGG higher score than being as LGG or meningiomas.

Focusing on change over time, interaction effects between tumor location and tumor type can also predict the symptom severity and symptom interference over time. Patients had middle part tumor being as HGG rated symptom severity and symptom interference lower scores than those being as meningiomas at middle part of brain.

Interesting at each time point, the tumor laterality did not effect on symptom severity but it affected on symptom occurrence at time 3. Tumor location did not influence on symptom experience, however tumor laterality did. Interpretation this finding, the effect of tumor location may be attributed to the far-reaching effects of the

disease which can disturb functional pathway from the site of the tumor (Goffaux, Daigle, & Fortin, 2012).

Health Related Quality of Life and Pattern of Change

HRQOL is a concept in the symptom outcome domain of the Symptom Management Model selected to be an outcome of this study. The result of this study revealed that patients with PBT rated their HRQOL score at moderate to high level (above 150) 65% at time 1, 52.5% at time 2, and 54.2% at time 3.

HRQOL including social/family well-being and functional well-being, the result displayed that the average of these scores, after receiving radiotherapy 8-10 Gy to be worse than those before receiving radiotherapy but rebound improved at the end of receiving radiotherapy. However, the level of improving at the end of treatment lowers than those levels before radiotherapy. Physical well-being and brain subscales were worse at time 2 and to be continued to worse at time 3. On the other hand, emotional well-being was improved from time 1 to time 2 and to be continued to improve at time 3.

The change in average HRQOL illustrate as a quadratic pattern with lower peak during receiving 8-10 Gy. Examination of the changes in HRQOL scores from baseline showed that HRQOL did not worsen over time in patients with PBT. Some domains improved such as emotional well-being and some domains worsened such as physical well-being and brain subscales. This result consistent with Minniti et al. (2013) who analyzed change over time in elderly patients with malignant PBT that the changes in HRQOL scores from baseline did not deteriorate, and some domain improved over time such as emotional function and cognitive function, whereas some domains worsened over time such as motor function. Similar to Henzel et al. (2013) evaluated QOL pattern in patients with meningiomas during radiotherapy that the result showed general health and mental health subdomains of QOL improving at the end of treatment, whereas the other domain further decline.

The previous studies revealed that the total and subscale of HRQOL over time were various pattern depending on the grading of the tumor. For instance, Kangas, Tate, Williams, and Smee (2012) conducted a study to determine QOL and

subdomains of patients with benign and malignant brain tumor before and at the end of receiving radiotherapy. Of malignant group the patients reported total score and subdomains scores of QOL at end of radiotherapy lower than those scores before treatment, whereas benign group lower only social/family well-being domain at the end of treatment and greater improve in emotional well-being over time. In contrast to this study Powell et al. (2011) who evaluated 70 patients with benign, low and high grade brain tumor underwent radiotherapy before and at the end of treatment. The authors found that the total and subdomains scores of QOL including emotional well-being were continuously declined.

The total and subscale of HRQOL of patients with PBT in this study consistent and inconsistent with other studies may be result from various HRQOL measurements, grading of brain tumor patients, and different type of radiotherapy.

Symptom Experience Predicting on Health Related Quality of Life

Patients experience symptoms caused from both tumor and its treatment that may influence HRQOL however, it is difficult to display the accurate impact of each factor. In general, the tumor negatively affects HRQOL, whereas anti- tumor treatment may have both a negative or positive effect on HRQOL (Dirven, Reijneveld, & Taphoorn, 2014). Patients with PBT confront serious symptoms to their HRQOL. They have difficulties with not only general symptoms such as headache, anorexia, nausea, seizures, and insomnia, but also focal neurologic worsening, including motor deficits, personality changes, cognitive deficits, aphasia, or visual field defects (Liu et al., 2009). Importantly, this study focuses on symptom experiences (symptom occurrence, severity, and interference) as the predicting factors on HRQOL prior to, during, and at the end of receiving radiotherapy. The symptoms that used to predict HRQOL resulted from overall 22 symptoms reported by patients before, during, and at the end of receiving radiotherapy not result from the highest score of both occurrence and severity dimensions. It is essential to note this association used severity score to predicting higher or lower HRQOL.

The findings of this study indicated that the symptom severity and symptom interference were the predicting factors significant on HRQOL at three time

points. The result presented that the higher levels of symptom severity and symptom interference are related to the poorer HRQOL subscales and HRQOL total score at each time point. This finding is similar to Tsay et al. (2012) who reported symptom distress which composed of symptom severity and symptom interference was a factor influencing the quality of life in patients with benign primary brain tumors over time (prior to and following surgery). The symptom severity and symptom interference are common and serious clinical issues for brain tumor patients being the significant factors of HRQOL. Similar to the study of Lai et al. (2014) who showed symptom experience reported by patients can reflect their HRQOL.

Symptom Severity Predicting on Health Related Quality of Life

Before receiving radiotherapy, the most severe symptoms reported statistically significantly influencing HRQOL among brain tumor patients, including weakness, nausea, disturbed sleep, lack of appetite, change in bowel pattern, difficulty concentrating, and feeling sad these symptoms explained 65.2% of the variation in HRQOL. After receiving radiotherapy 8 to 10 Gy the main symptom severity statistically significant predicted HRQOL similar to prior receiving radiotherapy were weak and feeling sad, but the new symptom presenting included irritability, feeling drowsy, vomiting. At completed treatment, the most symptoms presented at this time similar to time 1 and time 2 including feeling sad, weakness, irritability, feeling drowsy, vomiting, and difficulty concentrating. The symptom severity influencing on HRQOL over time were described the pattern of change as follows.

Weakness represented as a significant predicting factor on HRQOL at three time points. Pattern of weakness is slightly decreased over time (mean Time1 = 1.25, mean Time 2 = 1.14, mean Time 3 = 1.02), while the pattern of HRQOL decreased from time 1 to time 2 and increased from time 2 to time 3. However, the mean score of HRQOL at baseline was higher than those at the end of receiving radiotherapy (lower HRQOL), which was clinically significant difference. Interpretation this finding, weakness slightly improved over time, while HRQOL was poor contrast with a study of Powell et al. (2011) who conducted a prospective study in patients with PBT receiving radiotherapy. The authors reported that the pattern of weakness increased gradually from baseline to at the end of receiving radiotherapy (6

weeks) associated with the pattern of HRQOL decreasing over time, which was a statistically significant difference. Nwachukwu et al. (2014) conducted 314 long-term survivors low grade gliomas, the result showed that motor weakness was a significantly predicting factor in role function (subscale of HRQOL). Interestingly, weakness is not rated highest score in severity dimension, but it is statistically significant predicting HRQOL at three time points. This finding may result from a high number of patients described their weakness from their own meaning as walking instability not muscle power. Motor weakness may result from cerebral edema as an acute reaction of brain tumor during receiving radiotherapy. Cerebral edema caused increased intracranial pressure associated with focal neurologic deficit most especially motor weakness (Diaz & Choi, 2014). Previous studies reported that fatigue appears to be the most common symptoms and was a statistical significant with HRQOL whereas it was addressed in a single point in time (Gustafsson et al., 2006; Pelletier et al., 2002).

Feeling sad was a statistical change with HRQOL at three time points. Pattern of feeling sad decreased from time 1 to time 2 and increased from time 2 to time 3 (mean Time1 = 1.37, mean Time 2 = 1.07, mean Time 3 = 1.22) without statistical significance. Interpretation this finding the patient can handle with feeling sad better than before receiving radiotherapy and had more feeling sad at the end of treatment, but the level of feeling sad was lower than those before treatment. Feeling sad is an emotional reaction and stress situation when patients are diagnosed PBT. Similar to Henzel et al. (2013) reported patients with meningiomas were characterized by a high psychological strain before application of radiotherapy, possibly due to the primary diagnosis. In addition, information from hospital staff or from another person experience caused a negative feeling (feeling sad) on patients. Negative life perspectives as the common clinical experience affects patients with brain tumor after the completion of treatment and before beginning the therapeutic program (Giovagnoli et al., 2014).

The nausea was statistically associated with poor levels of HRQOL at before and after receiving radiotherapy 8-10 Gy. Pattern of nausea, increased from time 1 to time 2 and slightly decreased from time 2 to time 3. This means nausea gets worse after patients receiving radiotherapy 8-10 Gy and slightly improved at the end

of treatment in which clinical significance is presented. These findings are similar to those of other studies that patients with PBT experience symptoms during receiving radiotherapy including nausea and impact QOL. It is important to note the score on assessing nausea did not increase over time indicating radiotherapy did not seem significant induce nausea. The reason may result from patient with malignant gliomas receiving steroid during radiotherapy improved from acute effect including nausea (Marantidou et al., 2010).

Feeling drowsy appeared clinical significant influencing on poorer HRQOL during receiving radiotherapy 8-10 Gy and at the end of receiving treatment. The pattern of feeling drowsy continually increased over time, which statistically significant difference. The acute side effects of radiotherapy are unstable and occurrence during the first few weeks of radiation. They are commonly characterized by drowsiness, headache, nausea, and vomiting worsening of pre-existing focal neurologic symptoms. Increased vasogenic edema after disruption of the blood-brain barrier is believed to be the cause of these symptoms (Diaz & Choi, 2014). Lovely (2004) addressed that drowsiness and fatigue combination with prolonged periods of sleep after cranial radiation was a cyclical pattern of somnolence symptom.

Irritability: During receiving radiotherapy, most patients reported feeling irritable from skin erythema and eye irritation at time 2 and alopecia at time 3 Combs et al. (2013) assessed on skull base meningiomas patients who reported cause of symptoms during receiving radiotherapy over time, including alopecia, skin erythema, conjunctivitis, headache or fatigue associated with QOL. Therefore, this time the patients had more emotion change such as irritability and feeling sad. The finding may result from the symptoms that patients experience not only the physical symptoms but also emotional symptoms. Arnold et al. (2008) addressed depressive symptoms often accompany increased irritability or anxiety. Anxiety may result from situational fear related to diagnosis and prognosis or may be directly related to the effects of the tumor. Symptoms of depression and/or anxiety may not be revealed in the clinical setting through simple communication between physician and patient. Implementation of easily assessment tools may allow medical caretakers to address neuropsychiatric illnesses that can significantly affect therapy, compliance, and overall quality of life.

Difficulty concentrating: The result indicated difficulty concentrating was significantly predicted lower HRQOL before and at the end of receiving radiotherapy. The pattern of difficulty concentrating, increased over time, which was not statistically significant difference. Costello, Shallice, Gullan, and Beaney (2004) evaluated early effects of radiotherapy on intellectual and cognitive functioning in patients with PBT. The authors reported that the neuropsychological tests in patients between high-grade and low-grade brain tumors appeared a differential pattern following radiotherapy. Patients with high-grade tumors presented cognitive decline at the end of treatment comparing those of before treatment, whereas patients with low-grade tumors appeared to improve with cognitive at the end of treatment.

In this study, patients who reported higher symptom severity also poorer HRQOL. The result consists in the study of Quinten et al. (2011) who reported the high prevalence of symptoms also an effect on lower patients' HRQOL. A few study reported symptoms in severity dimension as predicting factor on HRQOL in adults with PBT over time (Minniti et al., 2013; Tsay et al., 2012).

Symptom Interference on Prediction of Health Related Quality of Life

In this study, the patients with PBT perceived their symptoms interfere with their daily activities including walking, enjoyment of life, and relation with other people which clinically significantly predict HRQOL. Walking significantly predicted HRQOL at three time points, whereas relation with other people appeared to influence HRQOL after receiving radiotherapy 8-10 Gy and at the end of receiving treatment. However, enjoyment of life was a prediction of HRQOL before treatment. Limited studies explored symptom interference as predicting factor of HRQOL in patients with PBT over time. Armstrong et al. (2011b) evaluated the impact of symptom interference on recurrence of 294 patients with PBT in the cross section study. The other one study used symptom interference to combine with symptom severity as symptom distress to predict QOL before and after surgery (Tsay et al., 2012).

However, the majority of previous studies assesses symptoms from subdomains of HRQOL and interprets as symptoms associated with HRQOL. Therefore, most of all focused on treatment, predicting HRQOL and some studies

focused on the single symptom such as visual impairment, fatigue, and depression influencing on HRQOL.

Symptom Experience and Their Effects on HRQOL over Time

Type of radiotherapy significantly predicted HRQOL over time. Changes in HRQOL during receiving RT, the mean score of HRQOL (mean = 148.68, SD = 25.27) decreasing compared with before (mean = 155.09, SD = 25.92) and at the end of receiving RT (mean = 149.60, SD = 25.90). Similarity to Henzel et al. (2013) evaluated QoL in 52 patients with meningioma before and at the end of receiving stereotactic radiotherapy (SRT). After completion of SRT, the mean score of QOL and subscale decreasing compared with before treatment, whereas same subscale increasing at the end of treatment including mental health and general health. Most studies conducted radiotherapy focus on compare dose of RT predicted HRQOL. Limited study comparing type of RT associated with HRQOL.

Tumor laterality significantly predicted HRQOL over time. Similarity with the Kangas et al. (2012) conducted on benign brain tumor receiving radiotherapy over time that the authors revealed tumor laterality was a predicting factor improving on emotional well-being scores over time.

Tumor location did not significantly predicted HRQOL over time. In this study method used to group, tumor location cannot identify specific locations and difficult to differentiate from tumor laterality. The issue of patients with left or right hemisphere predicted poorer HRQOL is generally debatable in several studies. This ambiguous association between tumor location and HRQOL may result from a tumor laterality which it is not an appropriately sensitive variable for investigation of HRQOL (Cheng, Zhang, & Liu, 2009; Goffaux et al., 2012).

In regard to tumor type, only pituitary adenoma and HGG significantly predicted HRQOL. Consistent with the study of Salo, Niemela, Joukamaa, and Koivukangas (2002) who reported patients with HGG experience poorer HRQOL than patients with LGG.

The symptoms including pain, disturbed sleep, feeling drowsy, feeling sad, vomiting, weakness, and difficulty concentrating were significantly predicted lower

HRQOL over time. Focus on the daily activities that interfered from symptoms including walking and enjoyment of life were statistically significant predicted poorer HRQOL.

It is significant to note that symptom interference predicting HRQOL over time is difficulty in walking, having problem with enjoyment of life and the cluster of symptoms of vomiting, weakness, and difficulty concentrating. The explanation is that the majority of patients (60%) suffered with meningiomas and 62.5% received radiotherapy for their residual tumors. The type of tumor itself had a direct effect on patient's vitality so that the difficulty in walking and unpleasant feeling in life would eventually occur. The cluster of significant symptoms, vomiting, weakness and difficulty concentration is the remarkable interaction among each symptom. While patients suffer with vomiting, they always develop problem with electrolyte imbalance, which lead them to weakness symptom. If vomiting still persists, patients might have a problem with severe hyponatremia, which has an effect on cognitive function.

In conclusion, the inclusive predicting model as shown on page 102 demonstrates that patients with PBT receiving radiation therapy would experience altered quality of life over the period since the first radiation. The alteration of patients' quality of life depends on the type of radiation treatment, the type of tumor, tumor laterality, tumor location, severity of symptoms, interference of symptom and the cluster of three impotence symptoms including vomiting, weakness and difficulty in concentration. This finding leads to the definitive scope of nursing practice in that in order to facilitate a smooth transition during radiation therapy, nurses should be aware of these variables.

Strengths and Limitations of the Study

Strengths of the Study

This is a longitudinal study. Although all patients had to be interviewed for 3 consecutive times from prior the beginning of the radiation treatment to the end of the treatment, there is no attrition. Accordingly, the patterns of "change over time" of the symptom occurrence, severity, and interference were revealed. Instruments used to collect data on symptoms and HRQOL were validated and specific for brain tumors. Self-report was the gold standard that patients complete the tools themselves.

Limitations of the Study

The type of radiation therapy in this study might have a different effect on patients' symptom. Patients who received IMRT and X-Knife would experience gradually change while patients who received Cyber-Knife which offer the radiation in higher dose within a short duration would experience dramatic change in their symptoms.

CHAPTER VI
CONCLUSION

This chapter provides a summary of the study, conclusion, implications for the nursing practice, contributions to nursing science and recommendation for further study.

Summary of the Study

This study aimed to 1) describe the symptom experience in all dimensions, 2) analyze the change over time of symptom experience, 3) determine the factors effect on symptom experience, 4) determine the factors on the change of symptom experience, 5) investigate the HRQOL total score and subscale of HRQOL, 6) investigate change over time in the HRQOL, 7) determine the relationships between symptom experience and HRQOL, and 8) determine the relationships between symptom experience on the change of HRQOL. Prospective study (prior, during, and complete radiotherapy) was used to determine the change over time of symptom experience and HRQOL. The Symptom Management Model developed by the UCSF was used as the conceptual framework to guide this study.

Institutional Review Board (IRB) of Ramathibodi Hospital, Siriraj Hospital, and the National Cancer Institute approved this study. One hundred and thirty adults with PBT were approached in this study. Ten of these were excluded; one refused to participate, three participants have other cancers, and five used to have radiotherapy. Finally, one hundred and twenty patients with PBT were consented in this study.

The participants' age ranges from 22-78 years, with a mean of 48.6 (SD = 10.08). Three-fourths were female (80.8%). The most participants lived with the couple (75.8%), were Buddhist (98.3%), and attained a primary school grade (40.8%).

For the health care costs covered by universal health care coverage (47.5%) and government welfare (26.7%). The majority of patients was diagnosed with the histology and MRI, 60% diagnosed with meningiomas and 16.7% had pituitary adenoma. Before receiving radiotherapy 110 patients had received tumor resection for the first modality treatment, 70.8% of these patients were diagnosed as WHO grade I. Most of tumor located at anterior and middle part of brain including sellar region, cavernous sinus, sphenoid wing. Seventy five (62.5%) patients received radiotherapy for residual tumor and 29 (24.2%) patients received it for tumor recurrence. Of these, 37.5% received IMRT, 33.3% received treatment with Cyber-knife RT, and 29.2% obtained X-knife RT. All of the participants were tested cognitive function using the Mini-Mental State Examination (MMSE) and completed two questionnaires, which were the MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT) and the Functional Assessment of Cancer Therapy-Brain (FACT-Br).

The findings obtained from this study are as follows:

1. Symptom experience and patterns of change: Finding from this study provides a more complete picture of the symptom experience of adults with PBT who received radiotherapy. These finding suggest that the symptoms, including visual impairment, problem with remembering, upset, feeling drowsy, fatigue, and disturbed sleep also present at high occurring rates and most common severity rates, which these symptoms interfere with daily living, including walking, work, mood, general activity, enjoyment of life, and relation with other people. However, the change in appearance is the only symptom that patients with PBT reported highly at severity rates before receiving radiotherapy and at complete treatment, pain revealed highly in occurrence rates. The occurrence and severity paths for these eight symptoms could be grouped into three separate patterns. Problem with remembering, change in appearance, and disturbed sleep significantly increases from baseline to at the end of receiving radiotherapy in both occurrence and severity dimensions. Similar to fatigue and feeling drowsy in severity dimension were shaped in this pattern, whereas the rate of increasing from time 2 to time 3 was slightly increased. In contrast, occurrence also severity dimensions for upset decreases over the treatment period. Visual impairment and pain in both occurrence and severity dimensions displayed increasing from time 1

to time 2 and decreasing from time 2 to time 3. Similar to fatigue and feeling drowsy in occurrence dimension were shaped in this pattern, whereas the rate of decreases from time 2 to time 3 was slightly declined.

2. Factors effect on symptom experience: The tumor type reveals to be predictive over all three dimensions of symptom experience (occurrence, severity, and interference) in adults with PBT at each time point and over time. Tumor laterality influenced only on symptom occurrence at the end of receiving radiotherapy and predicted symptom severity over time. Type of radiotherapy influences on symptom occurrence and symptom severity not only each time point (during receiving and at the end of radiotherapy) but also on the change over time. Interaction between tumor laterality and tumor type affected on symptom occurrence and symptom severity prior receiving radiotherapy. Interaction between tumor location and tumor type affected on symptom severity and symptom interference during and at the end of receiving radiotherapy and predicted on symptom severity and symptom interference over time. Tumor location is not effected on symptom experience at each time point and over time.

3. HRQOL and pattern of change: The finding of this study illustrates total HRQOL and subscale of HRQOL (social/family well-being and functional well-being) in adults with PBT as a quadratic pattern, with lower peak during receiving radiotherapy 8-10 Gy but rebound increasing at the end of treatment. Contrast with Physical well-being and brain subscale is worse at time 2 and continues to be worse at time 3. Emotional well-being is worse at time 1 but it continued to be improving at time 2 to time 3.

4. Symptom experiences predict on HRQOL: Symptom severity and symptom interference are significant predicting on HRQOL at each time point and over time. Adults with PBT experience not only physical symptoms, but also cognitive symptoms, which impact on their quality of life. The patients report cognitive symptoms that significantly effect on HRQOL at three time points, including weakness and feeling sad. During receiving and at the completion of radiotherapy patients report irritability and feeling drowsy is statistically significant predicting on HRQOL. Difficulty concentration is rated significantly influencing on HRQOL before and at the end of treatment.

Implication for Nursing Practice

The research results demonstrate the patterns, relationship, and factor predicting changes in symptom experience and adverse effect on HRQOL that can imply for nursing practice as follows:

1. Implication brain tumor symptom assessment to the clinical setting: The result from this study revealed that patients with PBT experience symptoms across the treatment trajectory. Therefore, should use specific measurement to assess patients' symptoms across treatment time such as MDASI-BT.

2. Evaluation symptom experiences in multidimensional approaches: This study proposes that health care providers should not evaluate only high occurrence or severity rate of symptoms but also their interference on HRQOL and pattern of symptoms over time. Although some symptoms were more higher occurred or severed but they may not effected HRQOL at each time point, they affect HRQOL over time. Therefore, health care providers require to better understand the pattern of symptom experience and its effect on HRQOL over time.

3. Assessment HRQOL to balance between the advantages of treatment and HRQOL: For finding the impeccable radiotherapy treatment planning can be challenging as both optimize cure rate and minimize symptoms that can have significant negative effects on HRQOL. In addition, the need to clarify factor influencing symptoms when a symptom converting to destructive HRQOL.

4. Develop clinical practice guideline: This information has implications for clinical practice and research to reduce symptoms and improve the impact of symptoms on HRQOL. Health care providers need to generally comprehensive for symptoms prior to treatment, during treatment, and at the end of treatment. The symptom increased linear pattern continuously in severity during and until at the end of receiving radiotherapy including fatigue, feeling drowsy, disturbed sleep, problem with remembering, and change in appearance. In contrast, upset was declined linearly continues in occurrence and severity over time. The symptoms displayed increasing after receiving radiotherapy and decreasing at the end of receiving radiotherapy in occurrence dimension including visual impairment, pain, fatigue, and feeling drowsy. Clinical practice guideline should address the most common symptoms and prepare for management strategy to relieve or eliminate symptoms over time.

Contributions to Nursing Science

The results of this study clearly confirm the reciprocal relationship of two main concepts between symptom experience (perception occurrence; evaluation, severity; response, interfere of symptom) and symptom outcome (when a person perceives a symptom, he or she will respond to that symptom and it would reflect his or her health outcome) as proposed by the Symptom Management Model (Dodd et al., 2001a).

Patients with primary brain tumor receiving radiation therapy experienced various clinical problems or symptoms by their occurrence, severity, and the effects on their daily living such as work life, walking, general activity, mood, enjoyment of life, and interaction with others. These phenomena occurred when the patients perceived and response to those symptoms. Consequently, these created a great impact on their quality of life, which refer the symptom outcome. Moreover, the pattern of these experiences is dynamic and changes over time due to the interaction between two core domains including the person (tumor type, tumor laterality, and tumor location) and health/illness (type of radiotherapy). This result confirmed to fit the Symptom Management Model, which stated that symptom experience are multidimensional and change over time.

Recommendation for Future Research

Future research studies are recommended to fill the gap of findings and limitations of this study.

1. In current study symptom experiences were displayed in a prospective study with assessing three points in times before, during, and at the end of receiving radiotherapy, they still inaccurate for cognitive symptoms and theirs change over time. Therefore, long-term follow up study should encompass for long periods, such three months to one year with three-month assessment.

2. Qualitative study or content analysis should be studied to differentiate and to understand some emotional symptoms such as upset, irritability, or feeling sad

in the context of their patients. In addition, the causes leading to these symptoms should be further studied.

3. Some symptom from this study exhibited together, for example, fatigue comes up with disturbed sleep and feeling drowsy. Then further research should be examining these symptoms in the same period as symptom clusters which influencing HRQOL over time.

4. This study presented the symptoms in a group of new patients with PBT receiving radiotherapy. Further study should be conducted in patients with recurrent tumor because the latter group is increasing in the incidence.

5. Measurement in assessing symptom experience will be included hearing problem and dizziness as a specific symptom. It will be important in further studies using the MDASI-BT to capture data.

6. Furthermore, attention to nursing science in environment domain, such as a health care resource and family caregiver that influencing three key domains in the Symptom Management Model from now on the lack of evidence supporting should be extended in further study.

7. Effectiveness of symptom management strategies is needed. Patients symptom management strategies should be studied to evaluate the effectiveness of patient self management.

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APPENDICES

APPENDIX A
PERMISSION LETTER

ถึง: symptomresearch [symptomresearch@mdanderson.org]

Cc: Natthacha Chiannilkulchai

7 ธันวาคม 2012 14:27

Dear Nazim Ali:

Thank you for your kind sending me the Thai translated version. Regarding the permission of using the assessment tool of MDASI Brain Tumor Module (MDASI-BT) and the email authorization letter sent (Order Form for Pain Research Group Symptom Assessment Tools), there was a dialogue box filled for “Linguistically validated language(s): Chinese - Simplified, Chinese – Traditional” due to unavailable dialogue box selecting for Thai version. This authorization letter, I will use is needed to be included to my dissertation in the future. Could you please help correct this authorization letter and change the part of “Linguistically validated language (s): Chinese-Simplified, Chinese-Traditional” to “Linguistically validated language (s): Thai version” and re-submit me this letter so that I will have the correct evidence of the authorization letter when included to my dissertation.

Please give me an apology for this inconvenience and time bothered. I am looking forward to hearing from you. Thank you in advance for your help.

Sincerely,
Natthacha

จาก: symptomresearch [symptomresearch@mdanderson.org]

ส่ง : 6 ธันวาคม 2012 2:30

ถึง : Natthacha Chiannilkulchai

Cc: Orapan Thosingha; symptomresearch

เรื่อง :RE: Order Form for Pain Research Group Assessment Tools

Attached is the MDASI-BT Thai.

Regards,
Nazim

-----Original Message-----
From: Natthacha Chiannilkulchai [mailto:natthacha.chi@mahidol.ac.th]
Sent: Wednesday, December 05, 2012 7:06 AM
To: symptomresearch
Cc: Orapan Thosingha
Subject: ตอบกลับ :Order Form for Pain Research Group Assessment Tools

Dear Nazim Ali

Thank for sending me the tools. However, while searching for the tool on MD Anderson website (order form), I could not find the Thai version tool. Would you provide me with the direction to retrieve the Thai version tool from the website? It was my mistake that I previously selected the chinese version tool. Infact, I have to use the Thai version for my study but could not find any icon to select.

Sincerely yours
Natthacha

_____

จาก: symptomresearch [symptomresearch@mdanderson.org]

ส่ง :4 ธันวาคม 2012 23:47

ถึง :Natthacha Chiannilkulchai

Cc: symptomresearch

เรื่อง :RE: Order Form for Pain Research Group Assessment Tools

I have attached the MDASI-BT as you requested. Please let me know if you have any questions. Thank you for your interest in the MDASI.
The email that is sent with the tool is the authorization letter for all the non-funded academic research or educational purpose.

Best regards,
Nazim Ali

-----Original Message-----
From: Natthacha Chiannilkulchai [mailto:natthacha.chi@mahidol.ac.th]
Sent: Tuesday, December 04, 2012 6:29 AM
To: symptomresearch
Subject: Order Form for Pain Research Group Assessment Tools

Order Form for Pain Research Group Symptom Assessment Tools

Assessment Tool: MDASI Brain Tumor Module (MDASI-BT)

Psychometrically validated language(s): English

Linguistically validated language(s): Chinese - Simplified,Chinese - Traditional

Purpose: Non-funded academic research

Study Type: Descriptive study or survey

Detailed description:
Cross-sectional study

Study ID: NRNS/D 5336106

Disease Type: Primary brain tumor
Mailing Address:

First Name: Natthacha
Last Name: Chiannilkulchai
Title: Symptom Clusters influencing Quality of Life in Adults with Primary Brain Tumor
Company:
Department:
Address: 71-73 Sukhumvit 64 Bangchak Prakanong District
City: Bangkok
State:
Country: Thailand
ZIP Code:
Telephone: 081-710-8175
Fax:
E-mail: natthacha.chi@mahidol.ac.th

Billing Address: Same as Mailing Address
Natthacha Chiannilkulchai

การดำเนินการในการตอบข้อความจาก Ali,Nazim N, 3/12/2012

ถึง: Ali,Nazim N [NNAli@mdanderson.org]

Sent Items

4 ธันวาคม 2012 19:44

Dear Nazim Ali

Thank you so much for your helping and I already filled the form to submit a request, please let me know if any process will need to do.

Sincerely yours,

Natthacha

Natthacha Chiannilkulchai

การดำเนินการ

ถึง :Orapan Thosingha

Sent Items

4 ธันวาคม 2012 9:49

Ali,Nazim N [NNAli@mdanderson.org]

การดำเนินการ

ถึง: Natthacha Chiannilkulchai

3 ธันวาคม 2012 22:36

คุณตอบกลับเมื่อ 4/12/2012 19:44

Please fill our online form (links below) to submit a request, and on the form, please provide the details of the studies and any other relevant information. As soon as we receive the request, it will be processed by our personnel. If needed, the request will be forwarded to faculty for review and approval.

==========

http://www.mdanderson.org/symptom-research

http://www.mdanderson.org/BPI

http://www.mdanderson.org/BFI

http://www.mdanderson.org/MDASI

==========

Please do not hesitate to contact us if you have further questions.

Kind regards,

Nazim Ali

Nazim N. Ali, MBA
Senior Research Data Coordinator
Department of Symptom Research
1400 Pressler Street, Unit 1450
Houston, TX 77030

Cleeland,Charles [ccleeland@mdanderson.org]

การดำเนินการ

ถึง: Natthacha Chiannilkulchai

Cc: Armstrong,Terri S [tsarmstr@mdanderson.org]

4 ธันวาคม 2012 0:57

This is to introduce you to Dr. Terri Armstrong, who developed the MDASI BT. She is in the neuro-onc unit here at MDACC and also a professor of nursing. She might be useful to talk to about future studies.

Charles S. Cleeland, PhD
McCullough Professor of Cancer Research
Chair, Department of Symptom Research
Division of Internal Medicine
U.T. M.D. Anderson Cancer Center, Unit 1450
1400 Pressler
Houston, Texas 77030
713:745-3470

Natthacha Chiannilkulchai

การดำเนินการ

ถึง: Orapan Thosingha

สิ่งที่แนบมา: MDASI-BT_Thai_CURRENT.pdf (467 กิโลไบต์([เปิดในเบราว์เซอร์]

Sent Items 4 ธันวาคม 2012 9:42

Ali,Nazim N [NNAli@mdanderson.org]

การดำเนินการ ในการตอบข้อความจาก Natthacha Chiannilkulchai, 1/12/2012

ถึง: Natthacha Chiannilkulchai

Cc: Armstrong,Terri S [tsarmstr@mdanderson.org]; Mendoza,Tito R [tmendoza@mdanderson.org]; Cleeland,Charles [ccleeland@mdanderson.org]

สิ่งที่แนบมา: MDASI-BT_Thai_CURRENT.pdf (467 กิโลไบต์([เปิดในเบราว์เซอร์]

3 ธันวาคม 2012 23:21

คุณส่งต่อข้อความนี้เมื่อ 4/12/2012 9:42

Dear Mrs. Chiannikulchai,

Attached is the MDASI-BT Thai that was requested.

Regards,

Nazim Ali

From: Cleeland,Charles
Sent: Monday, December 03, 2012 10:19 AM
To: Ali,Nazim N
Cc: Armstrong,Terri S; Mendoza,Tito R
Subject: RE: ask for a permission to translate MDASI-BT

Great – Please send her that. Terri, would you be interested in working with her on a Thai psychometric evaluation? See her request, below. Thanks, Charlie

---

From: Ali,Nazim N
Sent: Monday, December 03, 2012 10:13 AM
To: Cleeland,Charles
Cc: Armstrong,Terri S; Mendoza,Tito R
Subject: RE: ask for a permission to translate MDASI-BT

Dear Dr. Cleeland,

We already have MDASI-BT Thai in our database. Attached is the copy.

Nazim

From: Cleeland,Charles
Sent: Monday, December 03, 2012 10:06 AM
To: Ali,Nazim N
Cc: Armstrong,Terri S; Mendoza,Tito R
Subject: RE: ask for a permission to translate MDASI-BT

Would you forward a draft copy of the core to this person in Thailand? She would then only have to translate the BT items. Terri, do you know anyone working on a Thai translation of the BT?

From: Ali,Nazim N
Sent: Monday, December 03, 2012 9:38 AM
To: Cleeland,Charles
Subject: RE: ask for a permission to translate MDASI-BT

Good Morning Dr. Cleeland,

Yes, we do have MDASI-core Thai in our database.

Nazim

From: Cleeland,Charles
Sent: Saturday, December 01, 2012 2:41 PM
To: Ali,Nazim N
Subject: FW: ask for a permission to translate MDASI-BT

Do we have a Thai version of the mdasi core?

Natthacha Chiannilkulchai

การดำเนินการ

ถึง: ccleeland@mdanderson.org

Cc: Orapan Thosingha
Sent Items

2 ธันวาคม 2012 21:09

Dear Prof. Cleeland,
I really appreciate on your early reply and will wait for the answer.
Sincerely yours
Natthacha

Cleeland,Charles [ccleeland@mdanderson.org]

การดำเนินการ

ถึง: Natthacha Chiannilkulchai

2 ธันวาคม 2012 3:42

คุณส่งต่อข้อความนี้เมื่อ 2/12/2012 18:15

Let me check to see if a Thai translation of the MDAI core items has been done.

Natthacha Chiannilkulchai

การดำเนินการ

ถึง: ccleeland@mdanderson.org

Cc: Orapan Thosingha

Sent Items

1 ธันวาคม 2012 7:01

Natthacha Chiannilkulchai
71-73 Sukhumvit 64 Bangchak
Prakanong District, Bangkok 10260, Thailand
E-mail: natthacha.chi@mahidol.ac.th natthacha@gmail.com
December 1, 2012

Professor Dr. Charles S. Cleeland
McCullough Professor of Cancer Research and Chair
Department of Symptom Research
The University of Texas MD Anderson Cancer Center
Dear Professor Dr. Charles S. Cleeland
May I introduce myself as Mrs. Natthacha Chiannikulchai. I am now a doctoral student of Nursing Program, Mahidol University, Thailand. In this semester, I have developed the dissertation proposal (without funding support) under the supervision of Asst. Prof. Dr. Orapan Thosingha who serves as my dissertation advisor. The purpose of my dissertation is to study the symptom experience and quality of life in patients with primary brain tumor. While searching the literature, I have found that MDASI-BT will be well employed to measure the symptom experience of the patients in my study. Accordingly, I would like to ask for a permission to translate MDASI-BT into the Thai language and use this instrument in my study. This research study is a partial fulfillment of the requirements for my doctoral degree.

Please let me know whether you would allow me to translate and use MDASI-BT in my study and please provide me with the guidance to apply to MD Anderson Center for an official permission to use this instrument (if necessary).

Thank you for your time and I am look forward to hearing from you as soon as your convenience.

Sincerely,
Natthacha Chiannilkulchai
Doctoral student, Faculty of Nusing and School of Nursing, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Thailand

Asst. Prof. Orapan Thosingha, PhD
Dissertation advisor

FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT) LICENSING AGREEMENT

October 3, 2013

The Functional Assessment of Chronic Illness Therapy system of Quality of Life questionnaires and all related subscales, translations, and adaptations ("FACIT System") are owned and copyrighted by David Cella, Ph.D. The ownership and copyright of the FACIT System - resides strictly with Dr. Cella. Dr. Cella has granted FACIT.org (Licensor) the right to license usage of the FACIT System to other parties. Licensor represents and warrants that it has the right to grant the License contemplated by this agreement. Licensor provides to ***Natthacha Chiannilkulchai*** *the licensing agreement outlined below.*

This letter serves notice that **Natthacha Chiannilkulchai** ("INDIVIDUAL") is granted license to use the **Thai** version of the **FACT-Br** in one study.

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8) There are no fees associated with this license.

_____

APPENDIX B

DOCUMENTARY PROOF OF ETHICAL CLEARANCE ON HUMAN RIGHTS

คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
๒๗๐ ถนนพระราม ๖ แขวงทุ่งพญาไท เขตราชเทวี กทม. ๑๐๔๐๐
โทร. ๐-๒๓๕๔-๗๒๗๕, ๐-๒๒๐๑-๑๒๙๖ โทรสาร ๐-๒๓๕๔-๗๒๓๓
Faculty of Medicine Ramathibodi Hospital, Mahidol University
270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand
Tel. (+66) 2354-7275, (+66) 2201-1296 Fax (+66) 2354-7233

Documentary Proof of Ethical Clearance
Committee on Human Rights Related to Research Involving Human Subjects
Faculty of Medicine Ramathibodi Hospital, Mahidol University

No. MURA2013/578

Title of Project	Symptom Experience and Their Effects on Health-related Quality of Life Over Time in Adults with Primary Brain Tumor Receiving Radiotherapy
Protocol Number	ID 10 – 56 – 21
Principal Investigator	Mrs. Natthacha Chiannilkulchai
Official Address	Ramathibodi School of Nursing Faculty of Medicine Ramathibodi Hospital Mahidol University

The aforementioned project has been reviewed and approved by the Committee on Human Rights Related to Research Involving Human Subjects, based on the Declaration of Helsinki.

Signature of Chairman Committee on Human Rights Related to Research Involving Human Subjects	..... Prof. Duangrurdee Wattanasirichaigoon, M.D.
Signature of Chairman Committee on Human Rights Related to Research Involving Human Subjects	..... Prof. Boonsong Ongphiphadhanakul, M.D.
Date of Approval	October 29, 2013
Duration of Study	14 Months

2 PRANNOK Rd. BANGKOKNOI
BANGKOK 10700

Tel. +66 2419 2667-72
Fax. +66 2411 0162

Siriraj Institutional Review Board

Certificate of Approval

COA no. Si 730/2013

Protocol Title : Symptom experience and their effects on health-related quality of life over time in adults with primary brain tumor receiving radiotherapy

Protocol number : 709/2556(EC3)

Principal Investigator/Affiliation : Mrs. Natthacha Chiannilkulchai / Faculty of Nursing, Mahidol University

Research site : Faculty of Medicine Siriraj Hospital

Approval includes :

1. SIRB submission form
2. Proposal
3. Participant Information Sheet
4. Informed Consent Form
5. The mini–mental state examination, Thai version (MMSE-Thai 2002)
6. The M. D. Anderson Symptom Inventory-Brain Tumor Module (MDASI-BT)
7. The Functional Assessment of Cancer Therapy-Brain (FACT-Br) Version 4 dated 19 April 2012
8. Personal data, Disease and Treatment Record Form
9. Principle Investigator's curriculum vitae

Approval date : December 16, 2013

Expired date : December 15, 2014

This is to certify that Siriraj Institutional Review Board is in full Compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Jarupim Soongswang — 25 DEC 2013

(Prof. Jarupim Soongswang, M.D.) — date

Chairperson

Udom K — 26 DEC 2013

(Clin. Prof. Udom Kachintorn, M.D.) — date

Dean of Faculty of Medicine Siriraj Hospital

พิมพ์ที่หน่วยพิมพ์โรงพยาบาลศิริราช 2341 / 3,000 แผ่น / มิ.ย.55 / M / Mat.10023252

Certificate of Approval

Research Committee of National Cancer Institute

Title of Project	Symptom experience and their effects on Health-related quality of life over time in adults with primary brain tumor receiving radiotherapy
Project Number	1_2014T_OUT331
Principle Investigator	Mrs.Natthacha Chiannilkulchai
Affiliation	Faculty of Medicine Ramathibodi Hospital Faculty of Nursing Mahidol University
Date of Approval	December 11,2013

We confirm that the prior mentioned project has been approved by the Research Committee of National Cancer Institute.

Signature of Chairman .....

(Arkom Chaiwerawattana ,M.D.)

Signature of Director .....

(Weerawut Imsamran, M.D.)

APPENDIX C
INFORMATION SHEET AND CONSENT FORM (THAI)

เอกสารชี้แจงข้อมูล/คำแนะนำแก่ผู้เข้าร่วมการวิจัย

(Patient/Participant Information Sheet)

ชื่อโครงการ ประสบการณ์การเกิดอาการ และอิทธิพลของการเกิดอาการต่อคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพ ตามระยะเวลาที่เปลี่ยนแปลงไปในผู้ป่วยเนื้องอกสมองปฐมภูมิที่ได้รับการรักษาด้วยรังสีรักษา(Symptom experience and their effects on health-related quality of life over time in adults with primary brain tumor receiving radiotherapy)

ชื่อผู้วิจัย นางณัฏฐชา เจียรนิลกุลชัย

สถานที่วิจัย 1. โรงพยาบาลรามาธิบดี
2. โรงพยาบาลศิริราช
3. สถาบันมะเร็งแห่งชาติ

บุคคลและวิธีการติดต่อเมื่อมีเหตุฉุกเฉินหรือความผิดปกติที่เกี่ยวข้องกับการวิจัย

1. นางณัฏฐชา เจียรนิลกุลชัย
   สาขาการพยาบาลผู้ใหญ่ โรงเรียนพยาบาลรามาธิบดี
   คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
   โทรศัพท์ 081-710-8175
2. ผู้ช่วยศาสตราจารย์ ดร. อรพรรณ โตสิงห์
   ภาควิชาพยาบาลศัลยศาสตร์ คณะพยาบาลศาสตร์ มหาวิทยาลัยมหิดล
   โทรศัพท์ 087-592-0375

ผู้สนับสนุนการวิจัย -

ความเป็นมาของโครงการ

เนื้องอกสมองปฐมภูมิเป็นสาเหตุใหญ่ของการเสียชีวิตและทุพพลภาพ ทั้งในระดับสากลและในประเทศ อุบัติการณ์เพิ่มขึ้นเป็น 19.87 ต่อประชากรแสนคนต่อปี (2555) สำหรับประเทศไทยมีรายงานจากสถาบันมะเร็งแห่งชาติ สถาบันประสาทวิทยา พบว่าเนื้องอกปฐมภูมิมี

อุบัติการณ์เพิ่มขึ้น (2553-2555) ถึงแม้ว่าอุบัติการณ์การเกิดเนื้องอกสมองจะไม่มากเมื่อเทียบกับการเกิดมะเร็งจากอวัยวะอื่น แต่การรักษาเนื้องอกสมองปฐมภูมิแตกต่างจากการรักษามะเร็งชนิดอื่นคือปัญหาเรื่องโครงสร้างของผนังหลอดเลือดฝอยในสมองทำหน้าที่ป้องกันสารเคมีที่เป็นอันตรายในเลือดมิให้ผ่านเข้าไปในเซลล์สมอง ทำให้วิธีการรักษายากมากขึ้น มีการพัฒนาวิธีการรักษามากขึ้นเพื่อยืดระยะเวลาการมีชีวิตผู้ป่วยให้ยืนยาวขึ้น ผลข้างเคียงของการรักษาทำให้เกิดการเปลี่ยนแปลงของร่างกาย ส่งผลกระทบต่อการดำเนินชีวิตประจำวันและอัตราการมีชีวิตรอด รายงานการศึกษาที่ผ่านมาพบว่าผู้ป่วยเนื้องอกสมองปฐมภูมิต้องเผชิญกับความทุกข์ทรมานทั้งที่เกิดจากตัวเนื้องอกเองและที่เกิดจากผลของการรักษา ผู้ป่วยจะมีการเปลี่ยนแปลงการทำงานของสมอง การรับรู้และกระบวนการคิด ประสบการณ์การเกิดอาการ เป็นเหตุผลสำคัญทำให้ผู้ป่วยเข้ารับการรักษา อาการที่พบส่วนใหญ่ประกอบอาการด้วย ปวดศีรษะ ชัก คลื่นไส้ อาเจียน อาการเกี่ยวกับการรับรู้และกระบวนการคิด และบุคคลิกเปลี่ยนแปลง ประสบการณ์การเกิดอาการในผู้ป่วยแต่ละรายมีความแตกต่างกันขึ้นกับปัจจัยต่างๆได้แก่ ปัจจัยด้านตัวผู้ป่วย (เพศ อายุ ภาวะสุขภาพก่อนการวินิจฉัย) ปัจจัยที่เกี่ยวกับก้อนเนื้องอกสมอง (ตำแหน่งเนื้องอก ขนาดของเนื้องอก อัตราการเจิญเติบโตของเนื้องอก) รูปแบบของการรักษา (การผ่าตัด รังสีรักษา เคมีบำบัด)

ผู้ป่วยส่วนใหญ่เริ่มต้นการรักษาด้วยวิธีการผ่าตัดเพื่อลดอาการปวดศีรษะเกิดที่ขึ้นเนื่องจากขนาดก้อนเนื้องอกที่เพิ่มขึ้นทำให้ความดันในสมองสูงตามเพิ่มขึ้น การรักษาด้วยรังสีรักษาเป็นการรักษาร่วมที่ทำให้ผลลัพธ์ทางคลินิคของผู้ป่วยดีขึ้น ดังนั้นผู้ป่วยเกือบทุกรายจึงได้รับรังสีรักษาหลังการผ่าตัด หรือบางรายที่ไม่สามารถรักษาด้วยการผ่าตัดได้ ก็จะได้รับการรักษาด้วยรังสีเพียงอย่างเดียว สำหรับการรักษาด้วยเคมีบำบัด ตัวยาเคมีที่ใช้ยังอยู่ในวงจำกัด มีเพียงไม่กี่ชนิดเท่านั้นที่สามารถผ่าน blood brain barrier ไปได้ จึงถือว่าเคมีบำบัดยังอยู่ในขั้นพัฒนาสำหรับการรักษาเนื้องอกสมองแบบปฐมภูมิ ดังนั้นการรักษาส่วนใหญ่จึงขึ้นอยู่กับการผ่าตัดและการให้รังสีรักษา

ดอร์ดและคณะ (2001) นิยามประสบการณ์การเกิดอาการว่า เป็นประสบการณ์ของบุคคลต่อการเปลี่ยนแปลงทีเกิดขึ้นในร่างกาย และส่งผลกระทบให้เกิดความไม่สุขสบายทางกาย จิตใจ อารมณ์ สังคม การรับรู้และกระบวนการคิด ประสบการณ์การเกิดอาการตามแนวทางของดอร์ดและคณะ (2001) ประกอบด้วยการรับรู้ต่ออาการ การแปลความหมายของอาการ และการตอบสนองต่อการเปลี่ยนแปลงที่เกิดขึ้น ประสบการณ์การเกิดอาการเป็นข้อมูลที่จะนำไปสู่การจัดการเกี่ยวกับอาการ ที่เกิดขึ้นได้อย่างมีประสิทธิภาพ ดังนั้นการศึกษาเกี่ยวกับการเกิดอาการที่เปลี่ยนแปลงไปตามเวลา จะทำให้เห็นภาพรวมของการเกิดอาการอย่างต่อเนื่อง นำไปสู่การจัดการเกี่ยวกับอาการอย่างมีประสิทธิภาพในลำดับต่อไป

จากการทบทวนวรรณกรรมทั้งในและต่างประเทศ ตั้งแต่ ปีค.ศ. 2000 ถึง ปีค.ศ. 2013 พบว่าผู้ป่วยเนื้องอกสมองปฐมภูมิ มักจะเกิดขึ้นอาการมากกว่าหนึ่งอาการ ส่งผลต่อการดำเนินชีวิตประจำวัน ความสามารถในการทำหน้าที่ของร่างกาย การรับรู้และกระบวนการคิด และกระทบต่อคุณภาพชีวิตในด้านที่เกี่ยวข้องกับสุขภาพ การศึกษาอาการที่เกิดขึ้นในผู้ป่วยเนื้องอกสมองที่ผ่านมาสวนใหญ่เน้นที่การรายงานอาการแสดง (sign) ที่วัดโดยการสังเกตจากบุคคลากรสุขภาพ สำหรับการวัดอาการจากมุมมองหรือการรับรู้ของผู้ป่วยยังมีจำนวนจำกัด ทั้งๆที่การวัดจากการรับรู้ของผู้ป่วยเป็นการวัดที่สามารถสะท้อนผลลัพธ์การรักษา และเชื่อมโยงกับคุณภาพชีวิตของผู้ป่วยได้อย่างดี นอกจากนั้นการรักษาด้วยวิธีการที่แตกต่างกัน ย่อมส่งผลต่อการเกิดอาการที่ต่างกันด้วย ผู้ป่วยที่ได้รับการรักษาด้วยการผ่าตัดร่วมกับรังสีรักษาในภายหลัง หรือรับการรักษาด้วยรังสีรักษาเพียงอย่างเดียว หรือการรักษาด้วยรังสีรักษาร่วมกับเคมีบำบัด จะเกิดอาการในแต่ละช่วงเวลาของการรักษาแตกต่างกัน อาทิเกิดอาการทางกาย เช่น ปวดศีรษะ ชัก คลื่นไส้ อาเจียน เกิดอาการด้านการรักรู้และกระบวนการคิด เช่น สูญเสียความจำ มีความล่าช้าในการสื่อสาร หรือบุคคลิกภาพเปลี่ยนแปลง อาการต่างๆดังกล่าวอาจเกิดเพียงอาการเดียว หรือเกิดร่วมกันเฉพาะอาการทางกาย หรือเกิดร่วมกันทั้งอาการทางกาย จิตใจ อารมณ์ และการรู้คิด ซึ่งการเกิดอาการดังกล่าว ย่อมส่งผลต่อคุณภาพชีวิตในด้านที่เกี่ยวข้องกับสุขภาพในแต่ละช่วงเวลาของการเจ็บป่วยและการรับการรักษาเช่นกัน

เมื่อทบทวนการศึกษาที่ผ่านมาทั้งในระดับประเทศและระดับนานาชาติ พบว่ายังไม่มีการศึกษาที่วิเคราะห์การเปลี่ยนแปลงของประสบการณ์การเกิดอาการของผู้ป่วยเนื้องอกปฐมภูมิ ในแต่ละช่วงเวลาของการเจ็บป่วยและการรักษา หรือคุณภาพชีวิตในด้านที่เกี่ยวข้องกับสุขภาพที่เปลี่ยนแปลงไปในแต่ละช่วงของการเจ็บป่วยและการรักษา ผู้วิจัยจึงสนใจที่จะศึกษาเพื่อวิเคราะห์ปรากฏการณ์ที่เกิดขึ้น โดยคาดว่าผลของการศึกษาครั้งนี้จะเป็นข้อมูลพื้นฐานสำคัญสำหรับบุคคลากรสุขภาพ ในการวางแผนให้การรักษาพยาบาลเพื่อควบคุมและจัดการอาการที่เกิดขึ้นกับผู้ป่วยในแต่ละระยะ เพื่อช่วยส่งเสริมให้ผู้ป่วยเนื้องอกสมองปฐมภูมิเกิดคุณภาพชีวิตที่ดี ในการอธิบายปรากฏการณ์การเกิดอาการที่เกิดขึ้น ผู้วิจัยได้นำรูปแบบการจัดการเกี่ยวกับอาการ (symptom management model; SMM) มาเป็นกรอบแนวคิดในการศึกษานี้

วัตถุประสงค์

1. เพื่ออธิบายประสบการณ์การเกิดอาการ ความรุนแรงและระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันในผู้ป่วยเนื้องอกสมองปฐมภูมิ ตั้งแต่ระยะก่อนการรักษา ช่วงระหว่างการรักษา และระยะเสร็จสิ้นการรักษาด้วยรังสีรักษา

2. เพื่ออธิบายการเปลี่ยนแปลงตามเวลาของอุบัติการณ์การเกิดอาการ ความรุนแรง และระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันของผู้ป่วย ตั้งแต่ก่อนการรักษา จนถึงเสร็จสิ้นการรักษา

3. เพื่อศึกษาความสัมพันธ์ระหว่าง ขนาดเนื้องอกสมอง ตำแหน่ง อัตราการเติบโตของเนื้องอก ชนิดของรังสีรักษากับอุบัติการณ์การเกิดอาการ ความรุนแรง และระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันของผู้ป่วยเนื้องอกสมองปฐมภูมิ ตั้งแต่ระยะก่อนการรักษา ช่วงระหว่างการรักษา และระยะเสร็จสิ้นการรักษาด้วยรังสีรักษา

4. เพื่อศึกษาความสัมพันธ์ที่มีการเปลี่ยนแลงตามระยะเวลาระหว่าง ขนาดเนื้องอกสมอง ตำแหน่ง อัตราการเติบโตของเนื้องอก ชนิดของรังสีรักษา กับอุบัติการณ์การเกิดอาการ ความรุนแรง และระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันของผู้ป่วยเนื้องอกสมองปฐมภูมิ ตั้งแต่ระยะก่อนการรักษา ช่วงระหว่างการรักษา และระยะเสร็จสิ้นการรักษาด้วยรังสีรักษา

5. เพื่ออธิบายคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพในผู้ป่วยเนื้องอกสมองปฐมภูมิ ตั้งแต่ระยะก่อนการรักษา ช่วงระหว่างการรักษา และระยะเสร็จสิ้นการรักษาด้วยรังสีรักษา

6. เพื่ออธิบายการเปลี่ยนแปลงตามเวลาของคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพในผู้ป่วยเนื้องอกสมองปฐมภูมิตั้งแต่ก่อนการรักษา จนถึงเสร็จสิ้นการรักษา

7. เพื่อศึกษาความสัมพันธ์ระหว่างประสบการณ์การเกิดอาการ ความรุนแรงและระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันในผู้ป่วยเนื้องอกสมองปฐมภูมิ กับคุณภาพชีวิตที่เกี่ยวกับสุขภาพ ตั้งแต่ก่อนการรักษา จนถึงเสร็จสิ้นการรักษา

8. เพื่อศึกษาความสัมพันธ์ที่มีการเปลี่ยนแลงตามระยะเวลาระหว่างประสบการณ์การเกิดอาการ ความรุนแรงและระดับการรบกวนของอาการต่อการดำเนินชีวิตประจำวันในผู้ป่วยเนื้องอกสมองปฐมภูมิ กับคุณภาพชีวิตที่เกี่ยวกับสุขภาพ ตั้งแต่ก่อนการรักษา จนถึงเสร็จสิ้นการรักษา

รายละเอียดที่จะปฏิบัติต่อผู้เข้าร่วมการวิจัย

เมื่อผู้วิจัยได้รับการอนุมัติจากคณะกรรมการจริยธรรมการวิจัยในคนของ โรงพยาบาลรามาธิบดีแล้ว ผู้วิจัยจะอธิบายวัตถุประสงค์ของการวิจัย กระบวนการเก็บข้อมูล โดยที่กลุ่มตัวอย่างจะไม่ถูกบังคับหรือกดดันในการเข้าร่วมการวิจัย รวมทั้งเปิดโอกาสให้ผู้เข้าร่วมโครงการได้ซักถามข้อสงสัยหรือข้อข้องใจ ถ้าผู้เข้าร่วมโครงการยินดีที่จะเข้าร่วมโครงการวิจัยแล้ว ผู้วิจัยจะขอให้ผู้เข้าร่วมโครงการลงชื่อในหนังสือยินยอมโดยได้รับการบอกกล่าวและเต็มใจ ผู้เข้าร่วมโครงการจะได้รับแบบสอบถามจำนวน 4 ฉบับ คือ แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา (ผู้เข้าร่วมโครงการจะได้รับแบบบันทึกเฉพาะในการตอบครั้งแรก) แบบทดสอบสภาพสมองเบื้องต้น แบบวัดอาการเนื้องอกสมองของนายแพทย์แอนเดอร์สัน และแบบวัดคุณภาพชีวิตผู้ป่วยเนื้องอกสมอง

ผู้ป่วยจะใช้เวลาในการตอบแบบสอบถามทั้ง 4 ฉบับ (เอกสารแนบแบบสอบถามชุดที่ 1, 2, 3, และ 4) ประมาณ 45-60 นาที การตอบแบบสอบถามจัดทำในสถานที่เป็นส่วนตัว ปราศจากการรบกวน ผู้ป่วยสามารถตอบแบบสอบถามด้วยตนเอง หรือให้ผู้วิจัยอ่านข้อคำถามให้ผู้ป่วยตอบตรงตามแบบสอบถาม หากผู้ป่วยมีความประสงค์จะกรอกข้อมูลที่บ้านหรือทางโทรศัพท์ ผู้วิจัยยินดีที่จะดำเนินการตามความประสงค์ของผู้ป่วยโดยอธิบายวิธีการตอบแบบสอบถาม พร้อมแนบแบบสอบถาม ซองจดหมาย ที่อยู่และติดแสตมป์พร้อมส่งกลับมายังที่อยู่ของผู้วิจัย ผู้เข้าร่วมโครงการจะได้รับการตอบแบบสอบถาม 3 ครั้ง ครั้งที่ 1 ก่อนการรักษาด้วยรังสี ครั้งที่ 2 หลังการรักษาด้วยรังสีรักษา 1 สัปดาห์ ครั้งที่ 3 เมื่อเสร็จสิ้นการรักษาด้วยรังสีรักษา โดยที่ข้อมูลส่วนตัวของผู้เข้าร่วมโครงการจะถูกเก็บรักษาไว้โดยไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลส่วนรวมโดยไม่สามารถระบุข้อมูลรายบุคคลได้ ข้อมูลของผู้เข้าร่วมโครงการเป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น ผู้ให้ทุนวิจัย สถาบัน หรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ รวมถึงคณะกรรมการจริยธรรมการวิจัยในคน เป็นต้น เพื่อการพิทักษ์สิทธิของผู้เข้าร่วมโครงการ แบบสอบถามทุกฉบับจะบันทึกเป็นรหัส โดยไม่มีชื่อของผู้เข้าร่วมโครงการในแบบสอบถาม ข้อมูลของผู้เข้าร่วมโครงการจะจัดเก็บในตู้เอกสารที่มีเพียงผู้วิจัยกับอาจารย์ที่ปรึกษาของงานวิจัยเท่านั้นที่สามารถเข้าถึงข้อมูลได้ รวมทั้งผู้วิจัยจะทำการทำลายแบบสอบถามเหล่านั้นด้วยตนเองภายหลังเสร็จสิ้นการวิจัย รวมทั้งผู้เข้าร่วมโครงการมีสิทธิ์ถอนตัวออกจากโครงการวิจัยเมื่อใดก็ได้ โดยไม่ต้องแจ้งให้ทราบล่วงหน้า และการไม่เข้าร่วมการวิจัยหรือถอนตัวออกจากโครงการวิจัยนี้ จะไม่มีผลกระทบต่อการบริการและการรักษาที่ผู้เข้าร่วมโครงการสมควรจะได้รับตามมาตรฐานแต่ประการใด

ประโยชน์และผลข้างเคียงที่จะเกิดแก่ผู้เข้าร่วมการวิจัย

การศึกษาครั้งนี้อาจไม่เกิดกับผู้ป่วยโดยตรงในขณะที่ศึกษา แต่ผู้เข้าร่วมโครงการสามารถประเมินการเกิดอาการที่เกิดขึ้นกับตนเองได้อย่างครอบคลุม เข้าใจรูปแบบการเปลี่ยนแปลงของอาการที่เกิดขึ้น สามารถที่จะป้องกันและจัดการกับอาการที่เกิดขึ้นระหว่างได้รับรังสีรักษา รวมทั้งการดูแลตนเองได้อย่างเหมาะสม ซึ่งจะนำไปสู่การพัฒนาคุณภาพชีวิตของผู้ป่วยเนื้องอกสมองปฐมภูมิต่อไป และผลจากการศึกษาจะช่วยทำให้บุคคลากรทางการแพทย์มีความรู้ความเข้าใจเกี่ยวกับ การเกิดอาการและอิทธิพลของการเกิดอาการที่มีต่อคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพของผู้ป่วยเนื้องอกสมองปฐมภูมิระหว่างได้รับรังสีรักษาเพิ่มมากขึ้น และสามารถนำข้อมูลเบื้องต้นที่ได้ไปใช้ในการวางแผนการจัดการอาการและดูแล เป็นแนวทางในการพัฒนาวิธีการรักษาที่มีประสิทธิภาพ นอกจากนั้นการเข้าใจเกี่ยวกับการเกิดอาการที่เปลี่ยนแปลงไประหว่างได้รับรังสีรักษา จะเป็นแนวทางนำไปสู่การพัฒนาวิธีการให้รังสีรักษา เพื่อลดการเกิดอาการข้างเคียงและ

ผลกระทบของการเกิดอาการที่มีต่อคุณภาพชีวิตของผู้ป่วยได้ รวมทั้งสามารถนำความรู้ที่ได้ไปช่วยเหลือให้ผู้ป่วยมะเร็งเนื้องอกสมองปฐมภูมิและครอบครัว พัฒนาทักษะหรือวิธีการในการชลอหรือยับยั้งลดความทุกข์ทรมานจากผลกระทบของการเกิดอาการที่เกิดขึ้นได้อย่างมีประสิทธิภาพ

การวิจัยครั้งนี้ไม่มีความเสี่ยงที่อาจจะเกิดขึ้นเมื่อเข้าร่วมการวิจัย เนื่องจากเป็นการตอบแบบสอบถาม ซึ่งเป็นข้อมูลที่ผู้เข้าร่วมโครงการมีประสบการณ์โดยตรงอยู่แล้ว และใช้ระยะเวลาสั้น ไม่มีการทดลองในบุคคล จึงไม่มีผลข้างคียงที่กระทบต่อด้านร่างกาย แต่อาจมีบางคำถามที่ผู้เข้าร่วมโครงการไม่สะดวกใจที่จะตอบ ผู้เข้าร่วมโครงการสามารถยกเว้นการตอบคำถามในข้อดังกล่าวได้ โดยไม่มีผลกระทบใดๆกับผู้เข้าร่วมโครงการ และหากพบว่าผู้เข้าร่วมโครงการกำลังมีอาการรุนแรงและทุกข์ทรมานในหลายอาการ และมิได้รายงานให้แพทย์ผู้เกี่ยวข้องทราบ ผู้วิจัยจะให้คำแนะนำในการปรึกษาแพทย์ที่ทำการรักษาหรือประสานงานกับพยาบาลผู้เกี่ยวข้องในสถานที่เก็บข้อมูลต่อไป เพื่อให้มีการช่วยเหลือผู้เข้าร่วมโครงการอย่างเหมาะสมต่อไป รวมทั้งที่ผ่านมาพบว่างานวิจัยทำนองเดียวกับโครงการวิจัยนี้ ที่ทำทั้งในต่างประเทศและในประเทศไทย ไม่มีเหตุการณ์ไม่พึงประสงค์ใดๆ เกิดขึ้นกับผู้เข้าร่วมโครงการ แต่อาจจะทำให้ผู้เข้าร่วมโครงการเสียเวลาบ้าง ในการให้สัมภาษณ์หรือการตอบแบบสอบถาม

การเก็บข้อมูลเป็นความลับ

ชื่อและรายละเอียดข้อมูลส่วนตัวของผู้เข้าร่วมโครงการจะถูกเก็บรักษาเป็นความลับ การรายงานผลการศึกษาจะเป็นเพียงข้อมูลวิเคราะห์โดยรวมเท่านั้น และจะไม่มีการระบุชื่อ รวมทั้งไม่เปิดเผยต่อสาธารณะ การเปิดเผยข้อมูลเกี่ยวกับผู้เข้าร่วมวิจัยต่อหน่วยงานต่างๆที่เกี่ยวข้อง กระทำได้เฉพาะกรณีที่จำเป็นด้วยเหตุผลทางวิชาการเท่านั้น ข้อมูลในการสัมภาษณ์ผู้เข้าร่วมวิจัยจะเก็บไว้เป็นความลับ และจะถูกทำลายโดยผู้วิจัยเมื่อเสร็จสิ้นการศึกษา

ถ้าท่านมีปัญหาข้องใจหรือรู้สึกกังวลใจกับการเข้าร่วมในโครงการวิจัยนี้ ท่านสามารถติดต่อกับประธานกรรมการจริยธรรมการวิจัยในคน สำนักงานวิจัยคณะฯ อาคารวิจัยและสวัสดิการ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี

หนังสือยินยอมโดยได้รับการบอกกล่าวและเต็มใจ

(Informed Consent Form)

ชื่อโครงการ ประสบการณ์การเกิดอาการ และอิทธิพลของการเกิดอาการต่อคุณภาพชีวิตในด้านที่เกี่ยวกับสุขภาพ ตามระยะเวลาที่เปลี่ยนแปลงไปในผู้ป่วยเนื้องอกสมองปฐมภูมิที่ได้รับการรักษาด้วยรังสีรักษา

ชื่อผู้วิจัย นางณัฏฐชา เจียรนิลกุลชัย

*ชื่อผู้เข้าร่วมการวิจัย……

อายุ ……. เลขที่เวชระเบียน ……

คำยินยอมของผู้เข้าร่วมการวิจัย

ข้าพเจ้า นาย/นาง/นางสาว ……...ได้ทราบรายละเอียดของโครงการวิจัยตลอดจนประโยชน์ และข้อเสี่ยงที่จะเกิดขึ้นต่อข้าพเจ้าจากผู้วิจัยแล้วอย่างชัดเจน ไม่มีสิ่งใดปิดบังซ่อนเร้นและยินยอมให้ทำการวิจัยในโครงการที่มีชื่อข้างต้น และข้าพเจ้ารู้ว่าถ้ามีปัญหาหรือข้อสงสัยเกิดขึ้นข้าพเจ้าสามารถสอบถามผู้วิจัยได้ และข้าพเจ้าสามารถไม่เข้าร่วมโครงการวิจัยนี้เมื่อใดก็ได้ โดยไม่มีผลกระทบต่อการรักษาที่ข้าพเจ้าพึงได้รับ นอกจากนี้ผู้วิจัยจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับและจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆที่เกี่ยวข้อง กระทำได้เฉพาะกรณีจำเป็นด้วยเหตุผลทางวิชาการเท่านั้น

ลงชื่อ……(ผู้เข้าร่วมการวิจัย)

……..(พยาน)

……..(พยาน)

วันที่ ……

คำอธิบายของผู้วิจัย

ข้าพเจ้าได้อธิบายรายละเอียดของโครงการ ตลอดจนประโยชน์ของการวิจัย รวมทั้งข้อเสี่ยงที่อาจจะเกิดขึ้นแก่ผู้เข้าร่วมการวิจัยทราบแล้วอย่างชัดเจนโดยไม่มีสิ่งใดปิดบังซ่อนเร้น

ลงชื่อ…… (ผู้วิจัย)

วันที่……

<u>หมายเหตุ</u> : <u>กรณีผู้เข้าร่วมการวิจัยไม่สามารถอ่านหนังสือได้ ให้ผู้วิจัยอ่านข้อความในหนังสือยินยอมฯ นี้ให้แก่ผู้เข้าร่วมการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้เข้าร่วมการวิจัยลงนามหรือพิมพ์ลายนิ้วหัวแม่มือรับทราบในการให้ความยินยอมดังกล่าวข้างต้นไว้ด้วย</u>

* ผู้เข้าร่วมการวิจัย หมายถึง ผู้ยินยอมตนให้ทำวิจัย

APPENDIX D
THAI VERSION OF ALL INSTRUMENTS

1. แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา
2. แบบทดสอบสภาพสมองเบื้องต้นฉบับภาษาไทย (MMSE – Thai 2002)
3. แบบวัดอาการเนื้องอกในสมองของนายแพทย์แอนเดอร์สัน (MDASI - BT)
4. แบบวัดคุณภาพชีวิตในผู้ป่วยเนื้องอกสมอง

แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา

เลขที่แบบสอบถาม……ครั้งที่……วันที่……..โรงพยาบาล…….

ส่วนที่ 1: แบบสัมภาษณ์ข้อมูลส่วนบุคคล

คำชี้แจง กรุณาตอบแบบสอบถามเกี่ยวกับตัวท่าน โดยทำเครื่องหมายกากบาท **(X)** หรือเติมคำลงในช่องว่างหน้าข้อความที่ตรงกับตัวท่าน

1. อายุ……..
2. สภาพสมรส
   ( ) โสด ( ) คู่ ( ) หม้าย / หย่า / แยก
3. ศาสนา
   ( ) พุทธ ( ) คริสต์ ( ) อิสลาม
   ( ) อื่นๆ (โปรดระบุ) ……..
4. อาชีพ
   ( ) รับราชการ/ รัฐวิสาหกิจ ( ) ค้าขาย
   ( ) พนักงานบริษัท/ รับจ้าง ( ) แม่บ้าน
   ( ) เกษตรกร ( ) อื่นๆ (โปรดระบุ) ……
5. การศึกษา
   ( ) ไม่ได้เรียน ( ) ประถมศึกษา
   ( ) มัธยมศึกษาตอนต้น ( ) มัธยมศึกษาตอนปลาย / ปวช.
   ( ) ประกาศนียบัตร / ปวส ( ) ปริญญาตรี
   ( ) สูงกว่าปริญญาตรี
6. ……
7. ……
8. ……
9. ……
10. ……
11. …….
12. สมาชิกในครอบครัวที่ให้การดูแลและช่วยเหลือระหว่างการรักษา
    ( ) มี ( ) ไม่มี

ส่วนที่ 2: ข้อมูลบันทึกทางการแพทย์ (สำหรับผู้วิจัย)

1. วันที่ได้รับการวินิจฉัย……
2. ชนิดของเนื้องอกสมองปฐมภูมิที่พบ……
3. ระยะของโรค……
4. การรักษาที่ได้รับก่อนหน้าการรักษาครั้งนี้……
   วันที่……...
5. ชนิดของรังสีที่ได้รับครั้งนี้……

   ( ) X-Knife ( ) SRS
   ( ) HSRT
   ( ) CSRT
   ( ) CyberKnife ( ) SRS
   ( ) HSRT
   ( ) Other (please specify)……

6. ……..
7. ……..
8. ……..
9. ……..
10. ……..
11. ……..
12. ยาที่ได้รับระหว่างได้รับรังสี

    ( ) มี (โปรดระบุ)……
    ( ) ไม่มี

แบบทดสอบสภาพสมองเบื้องต้นฉบับภาษาไทย (MMSE – Thai 2002)

เลขที่แบบสอบถาม……ครั้งที่……วันที่……..โรงพยาบาล…….

ในกรณีที่ผู้ถูกทดสอบอ่านไม่ออกเขียนไม่ได้ ไม่ต้องทำข้อ 4,9 และ 10

	บันทึกคำตอบไว้ทุกครั้ง (ทั้งคำตอบที่ถูกและผิด)	**คะแนน**

1. **Orientation for time** (5 คะแนน)

(ตอบถูกข้อละ 1 คะแนน)

1.1 วันนี้วันที่เท่าไร …….. ☐

1.2 วันนี้วันอะไร ……. ☐

1.3 เดือนนี้เดือนอะไร ……..…… ☐

1.4 ปีนี้ปีอะไร ……..…… ☐

1.5 ฤดูนี้ฤดูอะไร ……..…… ☐

2. Orientation for place (5 คะแนน) **(ให้เลือกข้อใดข้อหนึ่ง)**

(ตอบถูกข้อละ 1 คะแนน)

2.1 <u>กรณีอยู่ที่สถานพยาบาล</u>

2.1.1 สถานที่ตรงนี้เรียกว่า อะไร และชื่อว่าอะไร ……. ☐

2.1.2 ขณะนี้ท่านอยู่ที่ชั้นที่เท่าไรของตัวอาคาร ……..... ☐

2.1.3 ที่อยู่ในอำเภอ - เขตอะไร ……..... ☐

2.1.4 ที่นี่จังหวัดอะไร …….. ☐

2.1.5 ที่นี่ภาคอะไร …….. ☐

2.2 <u>กรณีที่อยู่ที่บ้านของผู้ถูกทดสอบ</u>

2.2.1 สถานที่ตรงนี้เรียกว่าอะไร และบ้านเลขที่อะไร ……..…….. ☐

2.2.2 ที่นี่หมู่บ้าน หรือละแวก/คุ้ม/ย่าน/ถนนอะไร ……..... ☐

2.2.3 ที่นี่อำเภอเขต / อะไร ……..…… ☐

2.2.4 ที่นี่จังหวัดอะไร ……..…… ☐

2.2.5 ที่นี่ภาคอะไร ……..…… ☐

3. Registration (3 คะแนน)

ต่อไปนี้เป็นการทดสอบความจำผม (ดิฉัน) จะบอกชื่อของ 3 อย่าง คุณ (…….) ตั้งใจฟังให้ดีนะ เพราะจะบอกเพียงครั้งเดียว ไม่มีการบอกซ้ำอีก เมื่อ ผม (ดิฉัน) พูดจบ ให้ คุณ (……)

พูดทบทวนตามที่ได้ยิน ให้ครบทั้ง 3 ชื่อ แล้วพยามจำไว้ให้ดีเดี๋ยวดิฉันจะถามซ้ำ

*การบอกชื่อแต่ละคำให้ห่างกันประมาณหนึ่งวินาที ต้องไม่ช้าหรือเร็วเกินไป

(ตอบถูก 1 คำได้ 1 คะแนน)

○ ดอกไม้ ○ แม่น้ำ ○ รถไฟ

ในกรณีที่ทำแบบทดสอบซ้ำภายใน 2 เดือน ให้ใช้คำว่า

○ ต้นไม้ ○ ทะเล ○ รถยนต์ ……. □

4. Attention/Calculation (5 คะแนน) (ให้เลือกข้อใดข้อหนึ่ง)

ข้อนี้เป็นการคิดเลขในใจเพื่อทดสอบสมาธิ คุณ (…….....) คิดเลขในใจเป็นไหม ?

ถ้าตอบคิดเป็นทำข้อ 4.1 ถ้าตอบคิดไม่เป็นหรือไม่ตอบให้ทำข้อ 4.2

4.1 “ข้อนี้คิดในใจเอา 100 ตั้ง ลบออกทีละ 7 ไปเรื่อยๆ ได้ผลเท่าไรบอกมา”

…… …… …… …… …… □

บันทึกคำตอบตัวเลขไว้ทุกครั้ง (ทั้งคำตอบที่ถูกและผิด) ทำทั้งหมด 5ครั้ง

ถ้าลบได้ 1,2,หรือ 3 แล้วตอบไม่ได้ ก็คิดคะแนนเท่าที่ทำได้ ไม่ต้องย้ายไปทำข้อ 4.2

4.2 “ผม (ดิฉัน) จะสะกดคำว่า มะนาว ให้คุณ (…….....) ฟังแล้วให้คุณ (……)

สะกดถอยหลังจากพยัญชนะตัวหลังไปตัวแรก คำว่ามะนาวสะกดว่า

มอม้า-สระอะ-นอหนู-สระอา-วอแหวน ไหนคุณ (ตา,ยาย....) สะกดถอยหลัง ให้ฟังซิ

…… …… …… …… …… □

ว า น ะ ม

5. **Recall** (3 คะแนน)

เมื่อสักครู่ที่ให้จำของ 3 อย่างจำได้ไหมมีอะไรบ้าง” (ตอบถูก 1 คำได้ 1 คะแนน)

○ ดอกไม้ ○ แม่น้ำ ○ รถไฟ …… □

ในกรณีที่ทำแบบทดสอบซ้ำภายใน 2 เดือน ให้ใช้คำว่า

○ ต้นไม้ ○ ทะเล ○ รถยนต์ …… □

6. **Naming** (2 คะแนน)

6.1 ยื่นดินสอให้ผู้ถูกทดสอบดูแล้วถามว่า

“ของสิ่งนี้เรียกว่าอะไร” ……. □

6.2 ชี้นาฬิกาข้อมือให้ผู้ถูกทดสอบดูแล้วถามว่า

"ของสิ่งนี้เรียกว่าอะไร" …… □

7. **Repetition** (1 คะแนน)

(พูดตามได้ถูกต้องได้ 1 คะแนน)

ตั้งใจฟังผม (ดิฉัน) เมื่อผม (ดิฉัน) พูดข้อความนี้

แล้วให้คุณ (……) พูดตาม ผม (ดิฉัน) จะบอกเพียงครั้งเดียว

"ใครใคร่ขายไก่ไข่" …… □

8. **Verbal command** (3 คะแนน)

ข้อนี้"ฟังดีๆ นะเดี๋ยวผม (ดิฉัน) จะส่งกระดาษให้คุณ แล้วให้คุณ (……..)

รับด้วยมือขวา พับครึ่งกระดาษ แล้ววางไว้ที่....." (พื้น, โต๊ะ,เตียง)

ผู้ทดสอบแสดงกระดาษเปล่าขนาดประมาณ เอ-4 ไม่มีรอยพับ ให้ผู้ถูกทดสอบ

○ รับด้วยมือขวา ○ พับครึ่ง ○ วางไว้ที่ (พื้น, โต๊ะ, เตียง) …….. □

9. **Written command** (1 คะแนน)

ต่อไปเป็นคำสั่งที่เขียนเป็นตัวหนังสือ ต้องการให้คุณ (…….....) อ่าน

แล้วทำตาม (…….....) จะอ่านออกเสียงหรืออ่านในใจก็ได้

ผู้ทดสอบแสดงกระดาษที่เขียนว่า "หลับตา"

○ หลับตาได้……..…….. □

10. Writing (1 คะแนน)

ข้อนี้จะเป็นคำสั่ง "ให้คุณ (…….....) เขียนข้อความอะไรก็ได้ที่อ่านแล้วรู้เรื่อง

หรือมีความหมายมา 1 ประโยค"

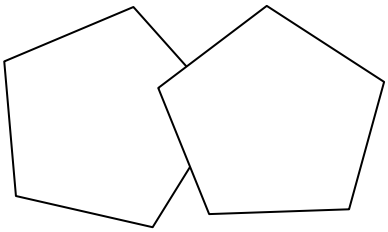
.....

○ ประโยคมีความหมาย …….. □

11. **Visuoconstruction** (1 คะแนน)

ข้อนี้เป็นคำสั่ง "จงวาดภาพให้เหมือนภาพตัวอย่าง" ……..……. □

(ในช่องว่างด้านขวาของภาพตัวอย่าง)



คะแนนรวม.....

แบบวัดอาการเนื้องอกในสมองของนายแพทย์แอนเดอร์สัน (MDASI - BT)

เลขที่แบบสอบถาม……ครั้งที่……..วันที่…….โรงพยาบาล…….

ส่วนที่ 1. อาการของคุณรุนแรงเพียงใด?

ผู้ป่วยที่เป็นมะเร็งมีอาการที่บ่อยครั้งมีสาเหตุมาจากโรคเองหรือจากการรักษา เราขอให้คุณประเมินว่าอาการต่อไปนี้รุนแรงเพียงใด ***ใน 24 ชั่วโมงที่ผ่านมา*** สำหรับแต่ละข้อ กรุณาระบายในวงกลมข้างล่าง จาก 0 (ไม่มีอาการ) ถึง 10 (อาการเลวร้ายมากเท่าที่คุณสามารถจะจินตนาการว่ามันจะเป็นไปได้)

	ไม่มี										เลวร้ายมากเท่าที่คุณสามารถจินตนาการได้
	0	1	2	3	4	5	6	7	8	9	10
1. อาการ**ปวด**ของคุณเลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O
2. อาการ**อ่อนเพลีย (เหนื่อย)** ของคุณตอนที่เลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O
3. อาการ**คลื่นไส้**ของคุณตอนที่เลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O
4. **การนอนที่ถูกรบกวน**ของคุณตอนที่เลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O
5. ความรู้สึก**เป็นทุกข์ (ไม่สบอารมณ์)**ของคุณที่เลวร้ายที่สุด	O	O	O	O	O	O	O	O	O	O	O
6.	O	O	O	O	O	O	O	O	O	O	O
7.	O	O	O	O	O	O	O	O	O	O	O
8.	O	O	O	O	O	O	O	O	O	O	O
9.	O	O	O	O	O	O	O	O	O	O	O
10.	O	O	O	O	O	O	O	O	O	O	O
11.	O	O	O	O	O	O	O	O	O	O	O
12.	O	O	O	O	O	O	O	O	O	O	O
13.	O	O	O	O	O	O	O	O	O	O	O
14.	O	O	O	O	O	O	O	O	O	O	O
15. ความลำบากในด้านความคิดความเข้าใจ ของคุณตอนที่เลวร้ายที่สุด	O	O	O	O	O	O	O	O	O	O	O

หน้า 1 จาก 2 หน้า

	ไม่มี							เลวร้ายมากเท่าที่คุณสามารถจินตนาการได้			
	0	1	2	3	4	5	6	7	8	9	10
16. ความลำบาก**ในการพูด** (การหาคำ) ของคุณตอนที่เลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O
17.	O	O	O	O	O	O	O	O	O	O	O
18.	O	O	O	O	O	O	O	O	O	O	O
19.	O	O	O	O	O	O	O	O	O	O	O
20.	O	O	O	O	O	O	O	O	O	O	O
21.	O	O	O	O	O	O	O	O	O	O	O
22. อาการ **หงุดหงิด** ของคุณตอนที่เลวร้ายที่สุด?	O	O	O	O	O	O	O	O	O	O	O

ส่วนที่2 อาการของคุณ**รบกวน**ชีวิตของคุณมากน้อยเพียงใด?

บ่อยครั้งที่อาการรบกวนความรู้สึกและการทำหน้าที่ของเรา อาการของคุณรบกวนสิ่งต่อไปนี้เพียงใด **ใน 24 ชั่วโมงที่ผ่านมา**:

	ไม่รบกวน							รบกวนทั้งหมด			
	0	1	2	3	4	5	6	7	8	9	10
23. **กิจกรรม**ทั่วๆ ไป?	O	O	O	O	O	O	O	O	O	O	O
24.	O	O	O	O	O	O	O	O	O	O	O
25.	O	O	O	O	O	O	O	O	O	O	O
26.	O	O	O	O	O	O	O	O	O	O	O
27.	O	O	O	O	O	O	O	O	O	O	O
28. **ความรื่นรมย์**ในชีวิต?	O	O	O	O	O	O	O	O	O	O	O

หน้า 2 จาก 2 หน้า

MDASI-BT – Thai 2006

แบบวัดคุณภาพชีวิตในผู้ป่วยเนื้องอกสมอง

เลขที่แบบสอบถาม……ครั้งที่……..วันที่…….โรงพยาบาล……

ข้อความต่างๆ ด้านล่างนี้คือสิ่งที่ผู้ป่วยโรคเดียวกับท่านกล่าวว่ามีความสำคัญ

ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านใน<u>ช่วง 7 วันที่ผ่านมา</u>หรือไม่ อย่างไร จากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน

	<u>ความผาสุกด้านร่างกาย</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GP 1	ข้าพเจ้ารู้สึกหมดเรี่ยวแรง……..	0	1	2	3	4
GP 2	ข้าพเจ้ามีอาการคลื่นไส้……..	0	1	2	3	4
GP 3	……	0	1	2	3	4
GP 4	……	0	1	2	3	4
GP 5	……	0	1	2	3	4
GP 6	……	0	1	2	3	4
GP 7	ข้าพเจ้าจำต้องใช้เวลาส่วนใหญ่นอนอยู่บนเตียง	0	1	2	3	4

	<u>ความผาสุกด้านสังคม/ ครอบครัว</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GS 1	ข้าพเจ้ารู้สึกใกล้ชิดสนิทสนมกับเพื่อนๆ	0	1	2	3	4
GS 2	ข้าพเจ้าได้รับกำลังใจจากครอบครัว	0	1	2	3	4
GS 3	**……**	0	1	2	3	4
GS 4	**……**	0	1	2	3	4
GS 5	**……**	0	1	2	3	4
GS 6	**……**	0	1	2	3	4
Q1	*ไม่ว่าในปัจจุบันท่านจะมีเพศสัมพันธ์มากน้อยเพียงใด ก็ตามกรุณาตอบคำถามต่อไปนี้หากท่านไม่ต้องการตอบคำถามในส่วนนี้กรุณากาเครื่องหมาย X ลงในช่องนี้ □ แล้วข้ามไปทำข้อต่อไป*					
GS 7	ข้าพเจ้าพึงพอใจกับชีวิตทางเพศของตนเอง (ไม่ว่าขณะนี้จะมีเพศสัมพันธ์หรือไม่ก็ตาม)	0	1	2	3	4

ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านใน<u>ช่วง 7 วันที่ผ่านมา</u>หรือไม่อย่างไร จากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน

	<u>ความผาสุกด้านอารมณ์ จิตใจ</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GE 1	ข้าพเจ้ารู้สึกเศร้าใจ……	0	1	2	3	4
GE 2	…….	0	1	2	3	4
GE 3	…….	0	1	2	3	4
GE 4	…….	0	1	2	3	4
GE 5	…….	0	1	2	3	4
GE 6	ข้าพเจ้ากังวลว่าอาการจะแย่ลง……..	0	1	2	3	4

	<u>ความผาสุกด้านการปฏิบัติกิจกรรม</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GF 1	ข้าพเจ้าสามารถทำงานทั่วไปได้ (รวมถึงงานบ้าน)……..	0	1	2	3	4
GF 2	…….	0	1	2	3	4
GF 3	……..……	0	1	2	3	4
GF 4	……..	0	1	2	3	4
GF 5	……..	0	1	2	3	4
GF 6	……..	0	1	2	3	4
GF 7	ข้าพเจ้าพึงพอใจกับคุณภาพชีวิตของตนเองในขณะนี้……	0	1	2	3	4

ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านใน<u>ช่วง 7 วันที่ผ่านมา</u>หรือไม่ อย่างไร จากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน

	<u>ด้านอื่นๆ เพิ่มเติม</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
Br1	ข้าพเจ้าสามารถที่จะมีสมาธิ....	0	1	2	3	4
Br2	ข้าพเจ้าเคยมีอาการชัก (เกร็งกระตุก)	0	1	2	3	4
Br3	……..	0	1	2	3	4
Br4	……..	0	1	2	3	4
Br5	……...	0	1	2	3	4
Br6	……...	0	1	2	3	4
Br7	ข้าพเจ้ารู้สึกว่าพึ่งตนเองได้……..	0	1	2	3	4
NTX6	……	0	1	2	3	4
Br8	……	0	1	2	3	4
Br9	……	0	1	2	3	4
Br10	……	0	1	2	3	4
Br11	ข้าพเจ้าสามารถตัดสินใจและรับผิดชอบได้..	0	1	2	3	4
Br12	……	0	1	2	3	4
Br13	……	0	1	2	3	4
Br14	……	0	1	2	3	4
Br15	……...	0	1	2	3	4
Br16	ข้าพเจ้าสามารถอ่านได้เหมือนเดิม	0	1	2	3	4
Br17	……	0	1	2	3	4
Br18	……	0	1	2	3	4
Br19	……	0	1	2	3	4
Br20	……	0	1	2	3	4
Br21	ข้าพเจ้ามีปัญหาในการเคลื่อนไหวอวัยวะต่างๆตามประสาทสั่งการ	0	1	2	3	4
An10	ข้าพเจ้าปวดศีรษะ.....	0	1	2	3	4

APPENDIX E

ENGLISH VERSION OF ALL INSTRUMENTS

1. Demographic and medical record form (DMRF)
2. Mini-Mental State Examination (MMSE)
3. M.D. Anderson Symptom Intervention-Brain Tumor (MDASI - BT)
4. FACT-BR (Version 4)

DEMOGRAPHIC AND MEDICAL RECORD FORM (DMRF)

Participation code……Time……Date……..Hospital ……

Part 1: Demographic data

1. Date of birth……..
2. Marital status

   ( ) Single ( ) Married ( ) Widowed / Divorced / Separated
3. Religion

   ( ) Buddhist ( ) Christian ( ) Islam

   ( ) Other (please specify) ……..
4. Occupation

   ( ) Government employee ( ) Business person

   ( ) Company employee ( ) Housewife

   ( ) Famer ( ) Other (please specify)……
5. Level of Education

   ( ) No formal education ( ) Primary school

   ( ) Secondary School ( ) Diploma / Certificate

   ( ) Bachelor degree ( ) Postgraduate degree
6. ……..
7. ……..
8. ……..
9. ……..
10. ……

Part 2 Data from medical record (For researcher)

1. Date of diagnosis……..
2. Type of primary brain tumor……
3. Stage of disease……
4. Other Treatment receives before radiotherapy……...

   Date of other treatment……..
5. Type of current radiotherapy……

   ( ) X-Knife ( ) SRS

   ( ) HSRT

   ( ) CSRT

   ( ) CyberKnife ( ) SRS

   ( ) HSRT

   ( ) Other (please specify)……
6. ……..
7. ……..
8. ……..
9. ……..
10. ……
11. ……
12. Medicine received during radiotherapy?

    ( ) Yes (please specify)……

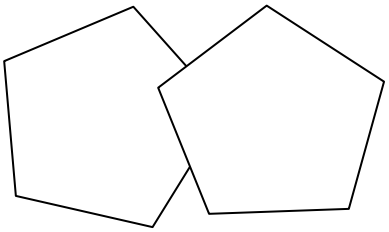
    ( ) No

Mini-Mental State Examination (MMSE)

Participation code……Time……Date……..Hospital ……

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	**Patient's Score**	**Questions**
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient

		a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

M.D. Anderson Symptom Intervention-Brain Tumor (MDASI - BT)

Participation code……Time……Date……..Hospital ……

Part I. How severe are your symptoms?

People with cancer frequently have symptoms that are caused by their disease or by their treatment. We ask you to rate how severe the following symptoms have been in the last 24 hours. Please fill in the circle below from 0 (symptom has not been present) to 10 (the symptom was as bad as you can imagine it could be) for each item.

	Not Present									As Bad As You Can Imagine
	1	2	3	4	5	6	7	8	9	10
1. Your **pain** at its WORST?	o	o	o	o	o	o	o	o	o	o
2. Your **fatigue (tiredness)** at its WORST?	o	o	o	o	o	o	o	o	o	o
3. Your **nausea** at its WORST?	o	o	o	o	o	o	o	o	o	o
4. Your **disturbed sleep** at its WORST?	o	o	o	o	o	o	o	o	o	o
5. Your feeling of being distressed **(upset)** at its WORST?	o	o	o	o	o	o	o	o	o	o
6.	o	o	o	o	o	o	o	o	o	o
7.	o	o	o	o	o	o	o	o	o	o
8.	o	o	o	o	o	o	o	o	o	o
9.	o	o	o	o	o	o	o	o	o	o
10.	o	o	o	o	o	o	o	o	o	o
11.	o	o	o	o	o	o	o	o	o	o
12.	o	o	o	o	o	o	o	o	o	o
13.	o	o	o	o	o	o	o	o	o	o
14.	o	o	o	o	o	o	o	o	o	o
15. Your difficulty understanding at its WORST?	o	o	o	o	o	o	o	o	o	o

	Not Present										As Bad As You Can Imagine
	0	1	2	3	4	5	6	7	8	9	10
16. Your difficulty speaking (finding the words) at its WORST?	o	o	o	o	o	o	o	o	o	o	o
17.	o	o	o	o	o	o	o	o	o	o	o
18.	o	o	o	o	o	o	o	o	o	o	o
19.	o	o	o	o	o	o	o	o	o	o	o
20.	o	o	o	o	o	o	o	o	o	o	o
21.	o	o	o	o	o	o	o	o	o	o	o
22. Your irritability at its WORST?	o	o	o	o	o	o	o	o	o	o	o

Part II How have your symptoms interfered with your life?

Symptoms frequently interfere with how we feel and function. How much have your symptoms interfered with the following items in the last 24 hours

	Not Present										As Bad As You Can Imagine
	0	1	2	3	4	5	6	7	8	9	1
23. General activity?	o	o	o	o	o	o	o	o	o	o	o
24.	o	o	o	o	o	o	o	o	o	o	o
25.	o	o	o	o	o	o	o	o	o	o	o
26.	o	o	o	o	o	o	o	o	o	o	o
27.	o	o	o	o	o	o	o	o	o	o	o
28. Enjoyment of life?	o	o	o	o	o	o	o	o	o	o	o

FACT-BR (Version 4)

Participation code……Time……Date……..Hospital ……

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the <u>the past 7 days.</u>**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some what**	**Quite a bit**	**Very much**
GP1	I have lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	…….	0	1	2	3	4
GP4	…….	0	1	2	3	4
GP5	…….	0	1	2	3	4
GP6	…….	0	1	2	3	4
GP7	I forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	…….	0	1	2	3	4
GS4	…….	0	1	2	3	4
GS5	……..	0	1	2	3	4
GS6	……..	0	1	2	3	4
Q1	*Regardless of your current level of sexual activities, please answer the following question. If you prefer not to answer it, please check this box* ☐ *and go to the next section*					
GS7	I am satisfied with my sex life	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to <u>the past 7 days.</u>

	EMOTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some what**	**Quite a bit**	**Very much**
GE1	I feel sad	0	1	2	3	4
GE2	……..	0	1	2	3	4
GE3	……..	0	1	2	3	4
GE4	……..	0	1	2	3	4
GE5	……..	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some what**	**Quite a bit**	**Very much**
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	…….	0	1	2	3	4
GF3	…….	0	1	2	3	4
GF4	…….	0	1	2	3	4
GF5	…….	0	1	2	3	4
GF6	…….	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to <u>the past 7 days.</u>

	ADDITIONAL CONCERNS	**Not at all**	**A little bit**	**Some what**	**Quite a bit**	**Very much**
Br1	I am able to concentrate	0	1	2	3	4
Br2	I have had seizure (convulsions)	0	1	2	3	4
Br3	……	0	1	2	3	4
Br4	……	0	1	2	3	4
Br5	……	0	1	2	3	4
Br6	……	0	1	2	3	4
Br7	I feel independent	0	1	2	3	4
NTX6	……	0	1	2	3	4
Br8	.....	0	1	2	3	4
Br9	……	0	1	2	3	4
Br10	.....	0	1	2	3	4
Br11	……	0	1	2	3	4
Br12	……	0	1	2	3	4
Br13	……	0	1	2	3	4
Br14	……	0	1	2	3	4
Br15	……	0	1	2	3	4
Br16	I am able to read like I used to	0	1	2	3	4
Br17	…….	0	1	2	3	4
Br18	…….	0	1	2	3	4
Br19	…….	0	1	2	3	4
Br20	I have weakness in my arms or legs	0	1	2	3	4
Br21	I have trouble with coordination	0	1	2	3	4
An10	I get headaches	0	1	2	3	4

APPENDIX F
CHARTS FOR ASSUMPTION TESTING OF ALL VARIABLES

Table 1 Symptom Occurrence in Adult with Primary Brain Tumor Receiving Radiation therapy at 3 Times (n = 120)

Symptom	Time1			Time2			Time3		
	N	%	Rank	N	%	Rank	N	%	Rank
1. Pain	63	52.5	5	70	58.3	7	66	55.0	10
2. Fatigue	46	38.3	12	88	73.3	2	83	69.2	2
3. Nausea	13	10.8	20	55	45.8	13	46	38.3	16
4. Disturbed sleep	50	41.7	11	74	61.7	5	77	64.2	5
5. Feeling distress	67	55.8	3	63	52.5	10	62	51.7	11
6. Shortness of breath	14	11.7	19	10	8.3	21	8	6.7	21
7. Problem with remembering	69	57.5	2	76	63.3	4	81	67.5	3
8. Lack of appetite	29	24.2	17	53	44.2	14	53	44.2	13
9. Feeling drowsy	64	53.3	4	84	70.0	3	80	66.7	4
10. Dry mouth	34	28.3	15	71	58.2	6	75	62.5	6
11. Feeling sad	39	32.5	14	38	31.7	17	36	30.0	17
12. Vomiting	7	5.8	21	21	17.5	20	20	16.7	20
13. Numbness	53	44.2	10	56	46.7	12	50	41.7	15
14. Weakness	32	26.7	16	30	25.0	19	29	24.2	18
15. Difficulty understanding	60	50.0	6	65	54.2	9	74	61.7	7
16. Difficulty speaking	55	45.8	9	66	55.0	8	72	60.0	9
17. Seizures	4	3.3	22	2	1.7	22	0	0	22
18. Difficulty concentrating	43	35.8	13	50	41.7	16	54	45.0	12
19. Visual impairment	92	76.7	1	95	79.2	1	92	76.7	1
20. Change in appearance	55	45.8	8	60	50.0	11	72	60.0	8
21. Change in bowel pattern	26	21.7	18	33	27.5	18	28	23.3	19
22. Irritability	57	47.5	7	52	43.3	15	50	41.7	14

Table 2 Symptom Severity in Adult with Primary Brain Tumor Receiving Radiation therapy at 3 Times (n=120)

Symptom	Time1			Time2			Time3		
	N	Mean (SD)	Rank	N	Mean (SD)	Rank	N	Mean (SD)	Rank
1. Pain	63	1.98 (2.26)	6	70	2.20 (2.21)	8	66	2.03 (2.25)	12
2. Fatigue	46	1.45 (2.16)	12	88	2.91 (2.27)	3	83	3.24 (2.74)	4
3. Nausea	13	0.38 (1.18)	20	55	1.85 (2.33)	14	46	1.64 (2.42)	15
4. Disturbed sleep	50	1.98 (2.77)	7	74	2.80 (2.59)	4	77	3.09 (2.81)	5
5. Upset	67	2.42 (2.70)	2	63	2.32 (2.56)	7	62	2.25 (2.62)	10
6. Shortness of breath	14	0.40 (1.18)	19	10	.29 (1.09)	21	8	.31 (1.19)	21
7. Problem with remembering	69	2.30 (2.56)	4	76	2.62 (2.49)	5	81	2.88 (2.56)	6
8. Lack of appetite	29	0.97 (2.02)	18	53	1.98 (2.59)	11	53	2.43 (3.12)	8
9. Feeling drowsy	64	2.27 (2.51)	5	84	3.05 (2.48)	2	80	3.27 (2.85)	3
10. Dry mouth	34	1.08 (2.06)	16	71	2.18 (2.39)	9	75	2.83 (2.78)	7
11. Feeling sad	39	1.37 (2.37)	13	38	1.08 (1.88)	19	36	1.22 (2.24)	17
12. Vomiting	7	0.21 (0.88)	21	21	.73 (1.81)	20	20	0.76 (1.87)	20
13. Numbness	53	1.83 (2.46)	9	56	1.96 (2.45)	12	50	1.71 (2.37)	14
14. Weakness	32	1.23 (2.37)	15	30	1.14 (2.32)	18	29	1.02 (2.10)	19
15. Difficulty understanding	60	1.69 (2.17)	11	65	1.87 (2.17)	13	74	2.28 (2.32)	9
16. Difficulty speaking	55	1.82 (2.39)	10	66	1.99 (2.26)	10	72	2.19 (2.23)	11
17. Seizures	4	0.08 (0.43)	22	2	.08 (0.69)	22	0	.00 (.00)	22
18. Difficulty concentrating	43	1.35 (2.11)	14	50	1.52 (2.15)	16	54	1.58 (2.11)	16
19. Visual impairment	92	4.26 (3.05)	1	95	4.41 (3.00)	1	92	4.10 (2.99)	1
20. Change in appearance	55	2.33 (3.05)	3	60	2.52 (3.16)	6	72	3.57 (3.53)	2
21. Change in bowel pattern	26	1.08 (2.38)	17	33	1.40 (2.71)	17	28	1.21 (2.46)	18
22. Irritability	57	1.88 (2.53)	8	52	1.71 (2.39)	15	50	1.82 (2.59)	13

Table 3 Symptoms Interference in Adult with Primary Brain Tumor Receiving Radiation therapy at 3 Times (n=120)

Symptom	Time1			Time2			Time3		
	N	Mean	Rank	N	Mean	Rank	N	Mean	Rank
Work	90	3.96 (3.01)	1	95	4.08 (2.93)	2	92	4.17 (2.90)	1
Walking	83	3.87 (3.12)	2	99	4.48 (2.92)	1	86	3.79 (3.04)	4
Mood	91	3.58 (2.95)	3	100	3.82 (2.58)	3	88	3.91 (2.96)	2
General activity	85	3.44 (2.95)	4	93	3.79 (2.63)	4	87	3.83 (2.82)	3
Enjoyment of life	57	2.03 (2.68)	5	68	2.38 (2.71)	5	57	2.21 (2.80)	5
Relation with other people	50	1.97 (2.75)	6	52	2.23 (2.88)	6	51	2.18 (2.79)	6

Table 4 Criteria for Select Models to Predict Symptom Occurrence

Model		Scale parameter	Wald test
Additive:	Occurr ∝ Time, Type of RT, Laterality, Location, Type	12.282	112.95
Interaction:	Occurr ∝ Time, Type of RT, Laterality, Location, Type Laterality # Type	11.694	125.43

Table 5 Criteria for Select Correlation Structure to Predict Symptom Occurrence

Correlation structure	Scale parameter	Wald Test
Exchange	11.694	125.43
AR1	11.760	109.95
AR2	11.857	105.82
Stationary1	11.874	121.46
Stationary2	11.857	105.82
Unstructured	12.072	81.05

Table 6 Criteria for Select Models to Predict Symptom Severity

Model		Scale parameter	Wald test
Additive:	Severe ∝ Time, Type of RT, Laterality, Location, Type	310.236	138.81
Interaction:	Severe ∝ Time, Type of RT, Laterality, Location, Type Location # Type	291.871	156.87

Table 7 Criteria for Select Correlation Structure to Predict Symptom Severity

Correlation structure	Scale Parameter	Wald Test
Exchange	291.871	156.87
AR1	292.619	142.40
AR2	294.871	140.16
Stationary1	294.126	162.02
Stationary2	294.871	140.16
Unstructured	295.265	133.40

Table 8 Criteria for Select Models to Predict Symptom Interference

Model		Scale parameter	Wald test
Additive:	Interfere ∝ Time, Type of RT, Laterality, Location, Type	120.838	32.28
Interaction:	Interfere ∝ Time, Type of RT, Laterality, Location, Type Location#Type	113.758	43.52

Table 9 Criteria for Select Correlation Structure to Predict Symptom Interference

Correlation structure	Scale Parameter	Wald Test
Exchange	113.758	43.52
AR1	114.058	45.54
AR2	113.785	43.49
Stationary1	114.400	70.73
Stationary2	113.785	43.49
Unstructured	113.814	46.22

Table 10 Test Multicolinearity of Symptom Experience at three time points

	Severity			Interference			Durbin-Watson		
	Time1	**Time2**	**Time3**	**Time1**	**Time2**	**Time3**	**Time1**	**Time2**	**Time3**
							2.171	1.952	1.897
Tolerance	.659	.713	.669	.659	.713	.669			
VIF	1.517	1.402	1.494	1.517	1.402	1.494			

Table 11 Means, Standard Deviation, and Intercorrelation for HRQOL and Predictors Variables (N= 120) at Time 1

Variable	**Mean**	**SD**	**Severity**	**Interference**
HRQOL	155.09	25.92	-.740**	-.606**
Predictor Variable				
Severity	34.34	19.92		.584**
Interference	18.84	12.21		

**. Correlation is significant at the 0.01 level (2-tailed).

Table 12 Comparison of Models for predicting HRQOL at Time 2

Model	**AIC**	**MSE**	**SE of Severity**	**SE of Interfere**
Additive model: HRQOL ∝ Severity, Interference	1027.25	298.23	.087	.160
Interaction model: HRQOL ∝ Severity,Interference, (Severity X Interference)	1027.18	295.63	.153	.280

Table 13 Mean, Standard Deviation, and Intercorrelation for HRQOL and Predicting Variables (N = 120) at Time 2

Variable	**Mean**	**SD**	**Severity**	**Interference**
HRQOL	148.68	25.27	-.686**	-.588**
Predictor Variable				
Severity	42.60	21.40		.535**
Interference	20.77	11.70		

**. P < .01

Table 14 Comparison of Models for predicting HRQOL at Time3

Model	AIC	MSE	SE of Severity	SE of Interfere
Additive model: HRQOL ∝ Severity, Interference	1028.45	301.21	.083	.157
Interaction model: HRQOL ∝ Severity,Interference, (Severity X Interference)	1030.06	302.83	.139	.261

Table 15 Mean, Standard Deviation, and Intercorrelation for HRQOL and Predicting Variables (N = 120) at Time 3

Variable	Mean	SD	Severity	Interference
HRQOL	149.60	25.90	-.714**	-.591**
Predictor Variable				
Severity	45.43	23.27		.575**
Interference	20.08	12.36		

**. P < .01

To select model for predicting HRQOL over time: As seen in Table 16 performances of additive model are all the smallest value. Suppose the additive model is selected to predict HRQOL over time.

Table 16 Comparison of Models for predicting HRQOL over time

Model	Scale parameter	Wald	SE Severity	SE Interfere
Additive model: HRQOL ∝ Severity, Interference	305.573	272.00	.043	.089
Interaction model: HRQOL ∝ Severity,Interference, (Severity X Interference)	306.199	271.38	.071	.148

Table 4.17 Test of symptom experiences on HRQOL over Time (n = 120)

HRQOL	Coef.	Std. Err.	Z	P>|z|	[95% Conf. Interval]	
Severity	-.478	.071	-6.74	0.000	-.617	-.339
Interfere	-.605	.148	-4.08	0.000	-.896	-.315
Severity#Interference	.001	.003	0.20	0.839	-.004	.005
_cons	182.181	3.279	55.57	0.000	175.755	188.607

Table 18 Mean, Standard Deviation, and Intercorrelation for HRQOL and Predicting Variables (N = 120) over time

Variable	Mean	SD	Severity	Interference
HRQOL	151.12	25.78	-.713**	-.597**
Predictor Variable				
Severity	40.79	22.02		.561**
Interference	19.90	12.09		

**. P < .01

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