FUNCTIONAL OUTCOME AND SELF-PERCEIVED OVERALL HEALTH STATUS FOLLOWING SURGERY TO REMOVE PRIMARY BRAIN TUMOR

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By
JEFFREY KRUG

Dr. N. Scott Litofsky
&
Dr. Anand Chandrasekhar,
Thesis Supervisors

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The undersigned, appointed by the Dean of the Graduate School, have examined the thesis entitled

FUNCTIONAL OUTCOME AND QUALITY OF LIFE FOLLOWING SURGERY TO REMOVE PRIMARY BRAIN TUMOR

Presented by Jeffrey Krug

A candidate for the degree of Master of Science

And hereby certify that in their opinion it is worthy of acceptance.

_______________________________________________
Dr. N. Scott Litofsky

_______________________________________________
Professor Anand Chandrasekhar

_______________________________________________
Professor Brick Johnstone
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Functional Outcome and Self-perceived Overall Health Status Following Surgery to Remove Primary Brain Tumor

Introduction

Health outcome in oncology was once believed to be limited to survival and treatment toxicity end-points. However, a great deal more than treatment and survival happens between the beginning and end of the disease process (Weitzner et al., 1995).

Treatment techniques for brain tumor vary and are continually evolving, and advances have prolonged lives (Huang, Wartella, Kreutzer, Broaddus, & Lyckholm, 2001). But what is the state of this prolonged life of brain cancer patients? What is their quality of life and self-perceived health status? What are these individuals’ mobility skills and functional abilities? What impairments are impacting these skills?

Impaired functional abilities, especially those associated with ambulation and standing balance, are common sequelae of brain tumors (Ragnarsson and Thomas, 2003). Secondary impairments affecting function include the presence of specific cognitive and motor deficits. Decreased ambulation and balance skills result in a reduction in overall functional abilities, thereby reducing independence with daily activities. Effective surgery to remove or reduce the brain tumor has the goal of improving brain function, thereby resulting in improved motor skills, functional abilities, and overall quality of life (Ragnarsson and Thomas, 2003).

This study focused on quantifying the physical issues associated with, as well as self-perceived overall health status (OHS) for, individuals following diagnosis and resulting surgery for removal of brain tumor (BT).
Determination of the effectiveness of invasive surgery may be done through measurement of both self-perceived HS and physical functioning. It is debated in the literature whether brain invaded by tumor remains functional and active (Ojemann, Miller, & Silbergeld, 1996). For this reason, some surgeons propose full resection of brain tumors while others advocate for partial resection with the goal of preserving function. Ojemann et al (1996) described their results for 14 patients who had surgery for removal of primary brain tumors of varying malignancies where tumor invaded functional areas of the brain (as determined by preoperative mapping). Their results showed that mapping of the brain to identify functional areas and then resecting only inactive tissue results in improved postoperative function (Ojemann et al., 1996). Even though four of their fourteen patients developed new neurological deficits, 3 of these four had their symptoms resolve over the 2 weeks post-surgery. However, one problem with this study is the lack of specific measurement of neurological or functional deficits; the type and severity of deficits was not noted.

Regardless, the effectiveness of surgery and other treatments for brain tumor requires further research. An important way to measure and justify treatment is through measurement with appropriate instruments. The best way to measure effectiveness of surgery or other treatment in brain tumor is by measuring physical functioning and OHS objectively and observing the change in scores over time (Steffen and Seney, 2008). The current study is a step toward this process as it supports measurement of results beyond survival time, recurrence rate, and amount of tissue resected. Instead, the aim is for measurement of OHS and specific physical functioning as meaningful methods to determine surgical effectiveness when removing primary brain tumor.
While multiple studies exist that measure effectiveness of invasive techniques to reduce the size of the brain tumor, to monitor recurrence rates, or to measure length of life following diagnosis (Stafford et al., 2001; Khan et al., 2006; Kondziolka et al., 2003; Quarshi, Geocadin, Suarez, & Ulatowski, 2000; Kowalczuk et al., 1997; Little et al., 2005) very few have specifically measured functional outcomes using reliable and valid instruments (O’Dell, Barr, Spanier, & Warwick, 1998; Huang et al., 2001). Heimans and Taphoorn (2002) call for “severity of neurological impairments (to) be recorded” and treatment effectiveness to be measured by tumor characteristics such as size but also by changes in OHS.

There have also been a severely limited number of studies assessing objective changes in physical functioning despite the existence of clinical tools to measure this domain. Most BT studies refer to neurological deficits or changes in physical function, but fail to use available tools to quantify these deficits or to measure changes over time.

Dr. Patricia Ganz points out that “the price of increased longevity has sometimes been the persistence of mild to severe functional impairment either as a result of the disease or its treatment” (Ganz, 1990). She calls for attention to the functional problems of cancer patients and points out that this is important throughout the course of treatment (Ganz 1990).

Likewise, Dr. Jay Rosenberg pointed out measures of “mortality, morbidity, time to progress, survival time, magnetic resonance imaging data, and laboratory evaluations… are a reflection of what is happening to the patient but do not provide a direct measure of total impact on the patient” (Rosenberg 1998). He called for an approach emphasizing function and quality of life and determination of how different treatments impact the
patient. Dr. Rosenberg identified that there is little documented regarding symptoms, function, and little “precise, quantitative” data collected so as to monitor change over time and meaningful outcome. He went on to say that current data lacks the in depth information required to make meaningful interpretation of outcomes for BT patients and that “unless we include such measurements (clinical, functional, and well-being)… it is impossible for our patients to make appropriate and informed clinical treatment decisions, as well as for clinicians to know what treatments to offer” (Rosenberg 1998).

Since these articles were published, there has been an increase in measurement of quality of life and OHS in the brain tumor population. There have also been a few studies assessing function through use of the Barthel Index (Brazil et al. 1997) or Functional Independence Measure (FIM) (Mukand, Blackinton, Crincoli, Lee, & Santos, 2001; O’Dell et al., 1998; Huang, Cifu, & Keyser-Marcus, 1998; Huang, Cifu, Keyser-Marcus, 2000; Huang, Wartella, & Kreutzer, 2001; Tang, Rathbone, Dorsay, Jiang, & Harvey, 2008; Marciniak, Sliwa, Spill, Heineman, Semik, 1996). More has been done in the way of studying cognitive and emotional aspects of brain tumors as compared to the physical effects. While it seems generally understood that physical impairments may occur which then impact function, little has occurred to quantify meaningful physical change or OHS changes in the brain tumor population. This study is an initial step towards that goal with the focus on using a patient-centered OHS assessment and two functional outcome tools related to mobility.

**Specific Aims**

This project will establish an effective method of evaluating self-perceived OHS, motor function and balance in the primary BT population immediately pre- and post-

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surgery and after a period of time (3 months) has passed. As Huang et al note: “no studies to date have sought to determine the relationship between functional outcome and QOL in individuals with brain tumors” (Huang et al., 2001).

The primary aim of this project is to compare self-perceived OHS and functional motor skills, specifically balance and ambulation, before and after invasive surgery to remove brain tumor; these will be examined across subjects directly before and within 1 week and at 3 months post-surgery.

_Hypothesis 1:_

Individuals will demonstrate “normal” functioning with regards to balance and ambulation as demonstrated with the Timed-up-and-Go (TUG) and Tinetti Performance-Oriented Mobility Assessment (Tinetti) and normal QOL as demonstrated with the SF-36 at 3 months following surgery.

The secondary aims of this project are to establish the appropriateness of the use of the Tinetti and Timed-Up-and-Go in measuring balance and ambulation skills for this population, to determine if both tools are necessary when evaluating these areas and to establish a correlation between OHS and physical function.

_Hypothesis 2:_

The Tinetti and Timed-Up-and-Go will be sensitive and appropriate measures of balance and ambulation in the brain tumor population.
Hypothesis 3:

Changes in the subjects’ scores on the MOS Medical Outcome Study (MOS) 36-Item Short Form Health Survey (SF-36) will correlate with changes on the TUG and Tinetti over time.

Background

The focus of this study will be on persons with primary brain tumors. Primary brain tumors affect roughly 130 of every 100,000 individuals (American Association of Neuroscience Nurses [AANN]) and are second only to stroke as the neurologic disorder resulting in death (Giordana and Clara, 2006). These tumors vary greatly in regards to location, where they originate, potential to grow and spread, how much the tumor will invade the brain tissue, how well the tumor responds to treatment, and rate of recurrence (AANN). Likewise, treatment for brain tumor varies greatly and may include chemotherapy, radiation, radiosurgery, gene therapy, invasive surgery, or any combination of these approaches (Giovagnoli, 1999; Weitzner et al. 1995; Lovely, 2004). Surgery may involve total or partial resection of the tumor and typically includes craniotomy (opening of the skull [AANN]) with excision of tumor tissue. For some malignant tumors, surgical treatment may be best for prolonging life and reducing symptoms. For benign tumors, surgery may provide a cure. Surgery provides increased accuracy with the diagnosis (AANN). The prevalence of brain tumors will likely increase due to improved treatment techniques resulting in greater survival rates and length of life (Mukand et al., 2001).
Brain tumor incidence: benign tumors occur in approximately 98 of every 100,000 people while malignant BT occur in approximately 30 of every 100,000. Benign tumors tend to grow slowly, have specific borders within the brain tissue, rarely spread to other areas of the nervous system, can be life-threatening depending on location and size, and typically require only a craniotomy for removal or to reduce the size. Malignant brain tumors tend to be faster growing, invade surrounding brain tissue, spread within the central nervous system, are life threatening, and require additional treatment besides the craniotomy for resection including chemotherapy, radiation or other techniques (AANN). Roughly 32% of all adults diagnosed with malignant tumors have a five-year survival rate following diagnosis. The five-year survival rate increases dramatically for those diagnosed earlier in life (0-19 years old = 63%) as compared to later in life (age 20-44 = 50%, age 45-64 = 14%, age >65 years = 5%) (AANN).

Tumors tend to be classified according to anatomical location. Supratentorial tumors, or tumors above the tentorium- “a double fold of dura matter that forms a partition between the cerebral hemispheres and the brain stem and cerebellum” (AANN)- are the most common and tend to result in signs of increased intracranial pressure, headache, mental status changes, seizures, neurologic deficits and weakness (Lovely, 2004). Infratentorial tumors are located below the tentorium and have symptoms of headache, nausea, cranial nerve deficits, gait disturbance, diplopia, vertigo, and ataxia (Mukand, 2001; Haut, Haut, & Bloomfield, 1991; Black, 1991). Surgery is also classified by anatomical location: a supratentorial approach is often used to access tumors of the “frontal, parietal, temporal, and occipital lobes” while infratentorial approach is used for cerebellar and brain stem tumors (AANN).
When viewed from a life expectancy point of view, Giordana and Clara (2006) observe that there are three groups of tumors. The first group are rapidly recurring with little to no treatment that is effective (malignant gliomas such as glioblastoma and anaplastic astrocytoma). The second group is made up of tumors with slow recurrence and years of disease free living: low grade gliomas (astrocytoma and oligodendroglioma), intracranial ependymomas, and cerebellar medulloblastoma. The final group includes nonprogressive tumors in which surgery alone is the cure (pilocytic astrocytoma, pituitary adenomas, schwannomas, and meningiomas) (Giordana and Clara, 2006).

Incidence varies slightly depending on the source. Primary brain tumors are distributed throughout the brain areas with 63% located in the brain, cranial nerves and spinal cord, 4% in the cerebellum, and 15-25% along the meninges (AANN; Stafford et al., 2001; Claus et al., 2005; Black, Morokoff, Zauberman, Claus, & Carroll, 2007).

Tumors are also classified in a variety of ways: Astrocytomas, oligodendrogliial tumors, ependymal tumors, and glioblastomas are tumors of the neuroepithelial tissue; meningiomas are tumors of the meninges; schwannomas are of the cranial nerves; lymphomas are hematopoietic; and pituitary adenomas are of the sellar region (AANN).

Brain tumors can impact a person neurologically in many aspects: cognition (memory, attention, thinking abilities, etc.), speech-language (ability to produce and understand speech), sensation (ability to feel and locate touch, pain, position of the limbs, temperature, pressure), and motor (coordination, balance, strength, muscle tone, muscle activation) (Mukand et al., 2001; Brazil et al., 1997; Lovely, 2004). Mukand et al (2001) in a study of 51 consecutive adults with a variety of brain tumors found that 78% had hemiparesis and 74.5% “had 3 or more concurrent neurological deficits.” The amount
that the tumor impacts each of these areas as well as overall function varies depending on
tumor location and size and its invasive properties (Mukand, 2001; Giordana and Clara,
2006) but symptoms are much like those seen following stroke or traumatic brain injury
(Ragnarsson & Thomas 2003; Greenberg, Treger, & Ring, 2006).

Treatment itself may cause additional neurological injury (Weitzner et al., 1996; Tang
et al., 2008; Giordana and Clara, 2006; Osaba, Brada, Prados, & Yung, 2000). Invasive
surgery to debulk a tumor is used when a tumor is located on or near the brain’s surface
or if the tumor is pressing on surrounding brain tissues and is increasing intracranial
pressure thereby interfering with the function of those areas (Bohan and Glass-Macenka,
2004) or putting the person at risk for death. Reduction in tumor size or complete tumor
removal can relieve symptoms and make use of chemotherapy or radiation safer and
more effective (Bohan and Glass-Macenka, 2004).

Surgery itself can lead to neurologic deficits due to damage to healthy tissue while
approaching the tumor, or by removal of the mass leaving a space that interferes with
neuronal communication (AANN). For example, Ojemann et al reported that four of
fourteen patients who underwent brain tumor resection had new neurological deficits
post-surgery (Ojemann et al 1996). Other neurologic complications that may arise due to
surgery include hemorrhage, increased intracranial pressure due to edema, cerebral
infarct, pneumocephalus, hyrocephalus, seizure activity, leaking of cerebrospinal fluid,
cranial nerve damage, or infection (AANN). Little et al found that 26% of their 137
meningiomas in the petroclival region developed “new postoperative cranial nerve
(23%), paresis (7%), or ataxia (4%)” (Little, Friedman, Sampson, Wanibuchi, &
Fukushima, 2005).
While not every person with a brain tumor presents with physical deficits, it is accepted that impaired strength, muscle tone, coordination, and sensation are possible. Impaired mobility and resulting fall risk are common with neurological involvement such as that seen with brain tumors. The main causes for falls and mobility deficits are muscle weakness, gait deficits, and balance deficits (Rubenstein and Josephson, 1996). Most current research measures survival rates and lifespan following surgery, amount of tumor removed, and regrowth/recurrence rates, but not patient function (Greenberg et al., 2006). A baseline neurological exam is typically completed, including a complete physical workup (Bohan and Glass-Macenka, 2004). Specific measures of physical impairments (strength, muscle tone, balance), or of functional mobility (bed mobility, transfers, ambulation) are not found in current research.

Several studies make comparison of BT and stroke. The authors point out that both stroke and BT patients can demonstrate neurological issues such as ataxia and unilateral sensorimotor deficits (Haut et al, 1991; Black, 1991) and that “disabilities from brain tumor are not unlike those found in patients who have had a stroke or traumatic brain injury (TBI) (Tang et al., 2008) or participants in rehabilitation (Giordana and Clara, 2006). Huang et al expand on this noting the presence of generalized weakness, impaired Activities of Daily Living (ADL) and problems with ambulation (Huang et al. 1998). They go on to mention that “functional outcome and recovery of (BT) patients are not well studied in the literature. Conversely, the functional outcome of stroke patients has been reviewed extensively including effects of therapy and recovery course” (Huang et al. 1998). The authors conclude that patients with stroke “may serve as a standard for
impairment of the central nervous system” which compares similarly to BT (Qureshi, Geocadin, Suarez, & Ulatowski, 2000).

The effects of rehabilitation are well documented in individuals with stroke and TBI. BT has been compared to TBI in regard to the type of neurological impairments, functional abilities and response to rehabilitation. O’Dell et al matched TBI and brain tumor patients by initial Functional Independence Measure (FIM) scores and age. They identified similar FIM efficiencies for the groups with no significant difference in FIM scores at admission and discharge from rehabilitation (O’Dell et al., 1998). Huang et al had similar findings with respect to FIM efficiency when comparing TBI and BT patients participating in rehabilitation (Huang, Cifu, & Keyser-Marcus, 2000).

Huang et al also compared rehabilitation functional outcome between stroke and BT by analyzing FIM admission and discharge scores for 63 patients of each diagnosis. They found no significant difference between groups for admission, total discharge, or total change in FIM. The mobility aspect of the FIM also was very comparable; the authors conclude that despite a difference in the cause of the deficits, the impairments and functional changes over time are similar. There was, however, significantly decreased length of hospital stay for the BT group; subjects from the BT group made similar changes but did so in far less time than the stroke group subjects (Huang et al., 1998).

Greenberg et al reinforced these findings through comparison between individuals with BT and stroke survivors. The authors found like function between the populations at admission to and discharge from rehabilitation as well as similar motor deficits. They also used the FIM as a measure of function. They concluded that BT neurologic changes
may be more readily reversible than stroke due to their less invasive nature (Greenberg et al., 2006).

With regard to rehabilitation of BT patients, Marciniak et al found that significant gains were made in overall FIM score; this was in a study of 159 patients admitted to inpatient rehabilitation due to functional impairments resulting from various cancers including a subgroup of BT patients (Marciniak et al., 1996). Mukland et al compared patients with various brain tumors and found that regardless of the type of BT, subjects had similar admission and discharge FIM scores (Mukand et al., 2001). Tang et al also found that patients with primary BT made functional improvements following rehabilitation and the greater improvement predicted longer survival (Tang et al., 2008). Huang et al compared admission and discharge scores for function and quality of life for 10 people with BT and found significant improvement in the functional scores (Huang et al., 2001). Similar patient responses to rehabilitation indicate a link between these different neurological diagnosis.

It may be concluded that people with brain tumor are similar to TBI and stroke survivors for types of neurological impairments, functional impairment (including mobility skills such as walking and moving sit to stand), and improvement in response to rehabilitation.(Huang et al., 2001)

In only one study did researchers objectively measure the physical impairments that were similar between neurological diagnoses and note function (based on FIM) improved (Tang et al, 2008). Specific measurement of deficits of strength, muscle tone, or balance (through assignment of a grade or score) or objective measurement of ambulation skills did not occur in any of the other studies reviewed. Huang et al note that “an analysis of
functional outcome of all patients with brain tumor, as opposed to just those admitted to rehabilitation, gives a better picture of the overall population (including) into the prognostic indicators of good functional outcome” (Huang et al., 2001).

Balance and mobility/ambulation ability are commonly altered by impairments to lower extremity strength and presence of abnormal muscle tone whether it be low tone or elevated tone to the presence of a syndrome of abnormal tone affecting the entire limb known as spasticity (O’Sullivan and Schmitz, 2007). All of these deficits are possible sequelae of neurological injury such as that occurs with BT or surgery for tumor removal.

The focus of this study will be to determine changes in physical function and OHS after surgery to remove primary brain tumor. While tumor removal or reduction may increase lifespan, the resulting OHS and affect on function is not specifically known. Likewise, measurement instruments specific to BT are not known. Therefore the focus of this study was comparison of subjects’ physical abilities prior to and following surgery for any primary brain tumor regardless of tumor type, size, or location using measures found reliable and valid for similar neurological diagnoses such as stroke and TBI.

It is anticipated that improvement on the primary measures will occur thereby indicating improved balance and ambulation skills. OHS is also likely to improve as a consequence.

Summary of Research Literature Related to Brain Tumor Surgery

Safford et al (2001) performed an extensive study specific to treatment of meningiomas with radiosurgery in which measurements of the tumor size and identified location were taken. Outcome was based on 5 and 7 year survival rates and size of tumor
at 5 years post-surgery. The authors identified the existence of neurological deficits after surgery. They did not specifically identify what these deficits were other than to indicate that they were related to cranial nerve injury or ischemic events. There was no discussion of the patients’ functional abilities or OHS in this study.

Khan, Gutin, Rai, Zhang, Krol, and DeAngelis (2006) performed pre- and postoperative neurological exams to determine functional and performance status for 82 patients who had craniotomy for resection of their tumors. The authors used MRI to predict postoperative outcome of neurological deficits following the surgery. The functional tools used were the Karnofsky Performance Scale (KPS) and the National Institutes of Health Stroke Scale (NIHSS). 24 of the patients experienced worsening (21) of or onset of new (3) neurological deficits. 13 of these had recovered by day 7 post-surgery. Several neurological deficits were identified including dysphasia, partial facial weakness, quadriparesis, and ataxia. The study identified “that presence of pre-existing neurological deficit was significant in predicting new or increased deficits after craniotomy” (Khan et al., 2006). However, specific measurement of the level of the neurological deficits or of functional abilities were not performed as part of this study.

Polin et al (2005) studied 280 patients with unilateral gliomas so as to determine “functional outcomes and survival in patients with high-grade gliomas in dominant and nondominant hemispheres”; they had 140 subjects in each group. The researchers collected sound data regarding survival, the percentage of subjects in each group that presented with various deficits (language, motor), and tumor location and size. The problem is, they failed to define what the motor deficits were. Also, they used the KPS
total as their measure of functional outcome but failed to describe what this score meant or what specifically the functional limitations were.

Claus et al (2005) discussed meningiomas and identified associated clinical symptoms such as loss of vision, seizures, and neurological deficits (difficulty with speech and cognition and “weakness with an arm or leg causing problems with writing, gait, or walking”). The authors concluded that up to 30% of patients have significantly altered skills of daily living including inability to write, drive, or read (Claus et al., 2005). Specifics of physical impairments or functional abilities were not objectively measured. Kondziolka et al (2003) determined long term results after radiosurgery for benign intracranial tumors. The study included 285 patients with a variety of benign tumor types. The researchers focused on tumor growth control and morbidity rates and also outlined need for follow-up treatment, radiosurgery or resection when needed. The authors state that there is little information regarding clinical and imaging results for either radiosurgery or surgical resection (Kondziolka et al., 2003). Other than identifying the number of patients with cranial nerve impairments, there was no clinical information detailing associated physical impairments.

Qureshi et al (2000) looked at long term outcome after reversal of transtentorial herniation in patients with supratentorial mass lesions. The authors did incorporate two functional outcome scales: the Rankin score and the Barthel Index (BI). The BI scores a person’s ability to perform feeding, bathing, toileting, dressing, transfers on/off toilet, chair, and bed, ambulation, and stair walking. The Rankin score determines the amount of disability for the patient. These measures were administered by telephone; 11 of the 23 patients went from a “decreased level of consciousness” to being functionally
independent (Qureshi et al., 2000). While the lesions in this study were not confined to those resulting from brain tumors, it is encouraging to see that reliable and valid functional measures were used to study outcome. However, these measures were conducted by phone interview with the patient’s caregivers and were not done by direct examination and measurement with the patient.

Kowalczuk et al (1997) used imaging to measure amount of surgical resection of malignant astrocytomas; they then utilized various information including age, gender, tumor grade, radiation dose, chemotherapy, seizure activity, tumor location, KPS level at presentation, and degree of resection as well as a few other factors to predict survival. KPS status was one of the factors significant as a predictor of survival. As this was a retrospective study, no information regarding functional performance or OHS was available. Again it is notable that survival was the main outcome measure but physical ability and functional status were not measured. The authors even call for this to be rectified in future research stating “further studies in this area (measures of outcome other than survival) are urgently needed” (Kowalczuk et al., 1997).

In the study mentioned earlier by Little et al (2005), new or worsened neurological deficits were a common occurrence following surgery. The types of neurological deficits were identified but functional performance was not measured.

Benesch et al (2006) did a retrospective analysis of 69 long-term survivors of individuals with childhood gliomas. The authors identified the incidence of various deficits, including neurological impairment, by location of tumor and by treatment option. However, no specific measures of physical function or functional mobility were utilized.
This review of the literature regarding treatment of brain tumor through use of surgery emphasizes the need for objective function and OHS data in order to specify functional outcomes following the treatment.

Methods

It is believed that the greatest significance of impairment and loss of function associated with BT occurs “immediately after surgery” (Ragnarsson and Thomas, 2003) and it is after some time has passed and the patient stabilizes that the most improvement is seen in these areas. There is a need, then, to measure physical performance and quality of life not just within the week after surgery, but after a period of time (in this study, at 3 month follow-up with the surgeon) during which the person can heal from the effects of surgery. The following measures were utilized in this study of primary brain tumor patients before and after surgery: Medical Outcome Study (MOS) 36-Item Short Form Health Survey (SF-36), Timed-Up-and-Go (TUG) and the Tinetti Performance Oriented Assessment of Balance and Ambulation (Tinetti). Details on these tools can be found in the Methods section.

Participants:

10 adults with diagnosis of brain tumor were chosen as part of a convenience sample over a six-month period. One was unable to complete the final assessment and was excluded leaving a total of 9 participants.

Inclusion Criteria: Individuals with primary brain tumor undergoing surgical resection. These individuals will had an intact lower body structure.
Exclusion Criteria: Individuals were not < 18 years old, and did not have a history of dementia, preexisting balance conditions, or abnormal lower body structure. The participants did not have a preexisting neurological disorder. They were not cognitively unable to follow directions for standardized measures.

Outcome Measures:

Wood-Dauphinee (2005) stated that “an evaluative measure assesses…a group at baseline and again at one or two points, usually to determine if change has occurred. It needs to be responsive to reflect change in patient status when it occurs.” The following measures will be utilized both prior to and within 1 week and 3 months post-surgery:

*Self-perceived Overall Health Status (OHS): Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)*

*Procedure:* The SF-36 contains 36 questions that cover 8 functional domains: Physical Functioning (PF) (10 items), role limitations due to physical health problems (RP) (4 items), bodily pain (BP) (2 items), role limitations due to emotional problems (RE) (3 items), vitality (VT) (4 items), social functioning (SF) (2 items), mental health (MH) (5 items), general health perceptions (GP) (5 items). There are 5 levels of response for each item. Scores for each domain range from 0 to 100 once they are scaled according to the manual; higher scores indicate better health status for that domain. There are also 2 component summary scores: physical health component (PHC) and mental health component (MHC). The mean scores for each domain and the PHC and MHC will be calculated using the SF-36 manual. The SF-36 can be completed by the individual or with
help from a caregiver or the tester who will read the question and indicate on the test the answer given by the subject.

Persons unable to complete the SF-36 due to not understanding the questions or responses thereby limiting accuracy of QOL of score will be exempt from the study.

Background: QOL measurement in BT research has only occurred in the past 10 years as “most studies have focused on performance status and length of survival (Weitzner et al., 1996; Weitzner and Meyers, 1997; [Efficace and Bottomly, 2002]; Efficace and Bottomly state that “aspects of treatment-related Quality-of-Life (QOL) should be of primary importance when comparing new or different medical therapies”. Slevin et al’s (1988) statement that “no gold standard exists against which QOL assessment methodology in cancer trials can be measured” is important to note. Huang et al (2001) note that while QOL did not improve for BT patients during rehabilitation, it did improve by 3 months after discharge.

The Karnofsky Performance Scale (KPS) has been used commonly as a QOL measure, especially by surgeons, in a variety of disease populations; there are multiple studies on gliomas which utilize the KPS as a QOL measure (Weitzner and Meyers, 1997). The problem is that QOL “is a multidimensional construct composed of multiple areas of a person’s functioning that may be affected by the illness or its treatment” (Weitzner et al, 1996). The KPS seems to lack the properties needed to fully measure QOL; it addresses function, but really measures only one area of QOL: what the patient can do (Cusimano, 1999) while it leaves out other aspects that impact QOL, namely disease symptoms and treatment side effects, psychological status, social functioning, and
cognitive function (Cusimano, 1999; Velikova, Stark, & Selby, 1999; Huang et al., 2001; Weitzner and Meyers, 1997; Osaba et al., 1997; Osaba, Brada, Prados, & Yung, 2000; Aiken, 1994). Other authors cite a lack of insight into patients’ cognition and the impact of pain on QOL (Grieco and Long, 1984; Osaba et al, 2000). Likewise, Taphoorn et al note that the KPS fails to recognize factors such as fatigue, anger or mood, depression, and stress and these can influence the psychological and physical components of QOL. These would all be important factors in determining QOL for BT patients, with Giovagnoli finding that depression and performance status are uniquely affected QOL in the BT population when compared to other neurological conditions (Giovagnoli, Tamburini, & Boiardi, 1996). The studies mentioned support for use of a QOL measure that incorporates aspects beyond just physical functioning.

As part of determining QOL, the patient should at least have input if not decide entirely by themselves how they are doing (Cusimano, 1999). The KPS is scored by a health-care provider instead of directly by the patient (Cusimano, 1999; Knippenberg and de Haes, 1988). A significant point by Efficace and Bottomly (2002) in their study of outcomes of primary brain tumor patients is that self-reported measures are important as physician or other health care-assessed QOL measures aren’t as accurate. The authors cite articles which demonstrated large variance in physician-assessed (ex: KPS) compared to patient self-assessed QOL measures, thereby indicating poor accuracy in determining QOL when its done by someone other than the patient themselves (Slevin et al, 1988; Titzer, Fisch & Kristeller, 2001; Sprangers and Aaronson, 1992). The important picture of the patient’s self-perceived QOL is then lost. Caregivers and surgeons also cannot possibly rate pain, fatigue, or emotional issues, as they may also impart bias due to
wanting the best possible outcome as a result of their intervention (Cusimano, 1999). Stephens, Hopwood, and Girling (1997) had clinicians and 700 patients complete the Rotterdam Symptom Checklist and found that “clinicians frequently under-assessed the level of functioning of the patient and under-reported symptoms that the patient reported”. Titzer et al (2001) studied 163 cancer patients and found that only 54% of physician assessments correlated with patient self-assessments. Patient-reported questionnaires have become more common as well as more appropriate for assessing QOL due to these concerns (Bottomly, 2007). The KPS has use when the client rates themselves, but other researchers question its sensitivity citing a lot of room for interpretation between the scores (Giovagnoli et al., 1996; Chang and Hawes, 1983).

Gill and Feinstein (1994) identified the existence of 159 QOL measures just for cancer patients. To assess overall quality-of-life (QOL) a generic quality-of-life measure that has become increasingly more common in both clinical and research work was used for this study: the SF-36. This is a quick (10-15 minutes to complete) survey that can be administered by interview or by having the subject complete the form themselves. Its been used with a variety of diagnoses including over 50 publications each pertaining to arthritis, COPD, cancer, HIV/AIDS, MS, neuromuscular conditions, spinal injuries, stroke, musculoskeletal conditions, and surgical procedures (Ware, 2000). It has also been used with different cancer populations.

The SF-36 provides information on 8 health-related concepts (physical health, role limitations due to physical or emotional problems, general mental health, general health perceptions, bodily pain, vitality) (Ware, 2000). It also has 2 higher order constructs, the physical and mental component summary scales (Dallmeijer et al, 2006). The Physical
Health Component is represented by 10 items: 4 Role-physical, 5 General Health, and 2 Bodily Pain (Ware, 2000). The Mental Health Component has 4 Vitality items, 2 Social Functioning items, 3 Role-Emotional items, and 5 Mental Health items (Ware, 2000). These items are then scored using norm-based scoring to standardize each of the 8 health concepts. There is also an item that is not scored in which the subject rates their health compared to a year ago.

There has been some question as to the appropriateness of use of all 8 domains for neurological diagnoses such as stroke, MS, Parkinson’s disease (PD), and ALS (5 of the domains met criteria for use in these populations, one- Mental Health- was borderline, two- General Health and Vitality- scored just below the suggested percentage of total variance of 60%) (Dallmeijer et al., 2006). Hobart, Freeman, Lamping, Fitzpatrick, and Thompson (2007) also raised questions about use of the SF-36 with the MS population, stating that as a health measure in multiple sclerosis summary scores should be reported with caution”. Jenkinson et al (2002) found high internal reliability across all domains but lack of statistical support for the two (Physical and Mental) constructs when tested with an ALS population. However, evidence also exists supporting use of the SF-36 with a reliability coefficient greater .80 (Ware et al., 1993). There has also been internal consistency between .8 and .9 for each subscale (Cusimano 1999). Brazier et al (1992) found the SF-36 had a reliability coefficient for each of the 8 individual domains (> .75) except for social functioning and evidence of “construct validity in terms of distinguishing between groups with expected health differences”. Jenkinson, Wright, and Coulter (1994) determined from a sample of 9332 persons between age 18-64 years with varying extents of illness that all domains of the SF-36 had alpha > .8 except for social
functioning (.76) and good criterion validity. The authors also theorize the lower social functioning score to be due to limited number (2) of items scored for this area. Lyons, Perry, and Littlepage (1994) had similar results with 216 adults aged 65 and older (internal consistency >.80 for each parameter) and good validity in determining those with and without identifiers of worse health. Reulen et al (2006) determined the Cronbauch’s alpha to be greater than the recommended value of >.70 (ranged from .73 to .96) across all domains for all types of cancer diagnoses in a study of 10,189 survivors of childhood cancer ages >16.

Overall the SF-36 has been used in a variety of disease-related studies; it has been documented in more than 4000 publications” (Ware, 2000). Its extensive use across populations indicates evidence for its validity (Cusimano, 1999). There is extensive research of the instruments’ reliability and appropriateness for use with neurological populations as well as “evidence of content, concurrent, criterion, construct, and predictive validity” (Ware, 2000; Brazier, 1992). Scott, Tobias, Sarfati, and Haslett (1999) calculated internal consistency reliability of .80 or greater for all domains as well as range of internal consistency scored for each item within domains to be >.60 with the exception of items pertaining to social functioning (ranged from .39 to .56) and bodily pain (ranged from .26 to .56) McHorney, Ware, and Raczek (1993) looked at the validity of both the physical and mental constructs. They determined that the SF-36 has both convergent and discriminant validity meaning it differentiates between physical and mental health with medical and psychiatric clients.

With respect to cancer populations, Fang, Tsai, Chien, Chiu, and Wang (2004) used the SF-36 with 66 oral cancer survivors after surgery and postoperative radiotherapy and
found that this population had significantly lower scores for all domains, especially those related to function, compared to a control group. Terrell, Nanavati, Esclamado, Bradford and Wolf (1999) found that 6 of the 8 domains were significantly worse in 97 head-and-neck cancer patients when compared to age appropriate US norms. Funk et al (1997) identified that outcomes of 180 head-and-neck cancer patients at 6 months or less post-treatment were significantly worse in most functional domains.

Rogers, Humphris, Lowe, Brown, and Vaughan (1998) performed a longitudinal study using the SF-36 with 50 oral cancer survivors and found that patients scored below the norms in all areas, especially in 3 of the 8 domains at the time the subjects presented to the physician. At 3 months post-surgery, the patients had significantly declined in 4 domains. By one year post-surgery, the patients were nearly at pre-treatment levels. Fang et al (2004) recommend more studies be done in this manner using QOL measures.

Finally, the SF-36 has been shown by Anderson, Laubscher, and Burns (1996) to be sensitive to mild functional deficits that affect the ability to live independently. The authors also state that the SF-36 “can detect higher levels of everyday physical functioning allowing a broader range of needs to be identified” as well as low levels of health functioning. This was demonstrated in a study by Garland, Ivanova, and Mochizuki (2007) where stroke patients with one-sided lower extremity paresis and balance problems demonstrated significant improvement in motor function, balance, and quality of life after 3 months though recovery was not complete. This overcomes a major concern of the KPS and supports the use of the SF-36 in QOL measurement.

It is the SF-36’s reliability in measurement of quality of life and the fact that its been used across multiple disease populations including neurologic conditions such as MS,
Parkinsons Disease, traumatic brain injury, and various cancers that make this an appealing instrument for this study. According to Ware (2000), the SF-36 “can also be used in repeated measures of the same patients over time” and Anderson et al (1996) mention that the instrument is sensitive to change and can be used as a pre- and post- test; the SF-36 will be employed in that manner here. Statistical analysis of the SF-36 will be completed to determine if significant change has occurred from pre-surgery to one week and/or three months post-surgery.

Finally, use of the SF-36 and other objective outcome measures is strongly advocated by Dr. Michael Cusimano who suggests that “use of scientifically sound and practical outcome measures” can influence and improve outcome after skull-based surgery for tumors (Cusimano, 1999).

*Physical Function Measures:*

While physical function is just one aspect of QOL, it is an important aspect that lacks much objective assessment in BT research. Giovagnoli (1999) points out that “functional impairments resulting from brain tumors can cause considerable distress…and thus impact QOL”. Two physical function items commonly assessed in other neurological populations are balance and walking ability, or ambulation.

The FIM is intended to be used with an inpatient population and has been the measure of choice for function when studying changes related to rehabilitation (see aforementioned studies on TBI, CVA, and BT clients). While the FIM has been shown to be a reliable and valid measure (Corrigan, Smith-Knapp, and Granger, 1997) the main complaint is its inability to detect small changes in function or changes in impairment. As
Flansbjer, Holmback, Downham, Patten, and Lexell (2005), many patients with stroke resume walking independently, but not at a speed or with the amount of endurance that permits them to participate in their daily activities. This type of change would not be perceived by the FIM. Also, a person may demonstrate significant deviation in walking and/or decreased gait speed but this also is not detectable with the FIM.

Another tool that has been used to assess BT patient function and outcome is the Karnofsky Performance Scale (KPS) (Ragnarsson and Thomas, 2003; Cusimano, 1999; Polin et al, 2005; Giovagnoli, 1999; Huang et al, 2001). A draw back to use of the KPS to measure function is its lack of specificity to physical function. The KPS has been used by medical personnel to rate the patient’s ability to perform daily activities including work, living at home, and performing self cares. It is scored in increments of ten from 0 (dead) to 100 (normal, no complaints, no evidence of disease) (Ragnarsson and Thomas 2003). Patients are scored, or place themselves, at various levels between 0 and 100 depending on the amount of assistance they require to perform these daily activities. The instrument does not account for why an individual requires assistance or what their specific physical impairments may be. The KPS is similar or possibly worse than the FIM in its inability to identify the quantity and severity of impairments. This measure has been used in multiple studies of patient physical function. But, as Huang et al (2001) found in their study of QOL and function following rehabilitation for BT, the KPS had diminished sensitivity as compared to the FIM or Disability Rating Scale (DRS) when “detecting change in functional status”. Chang and Hawes (1983) note that the KPS was not “sensitive enough to accurately assess rehabilitation improvements “ nor was it able to detect “subtle changes in patient’s disease course”.

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A third measure of function used in several BT studies is the Barthel Index (BI). This measure was designed for use with patients with chronic neurological conditions (Brazil et al., 1997). The BI is more complete than the KPS; it assigns scores for 10 specific items of physical functioning. Mobility items include stairs ambulation, transfers and overall mobility. Brazil et al (1997) demonstrated that the BI “was sensitive to change and reflected the degree of functional impairment” when applied to 107 high-grade glioma clients. The BI also addresses items such as bowel function, bladder function, grooming, toilet use, feeding, dressing, and bathing. The BI does not specifically quantify the level of physical impairments nor does it fully assess neurological function (Brazil et al., 1997). Mayo et al (1999) assessed disablement after stroke and noted that while the maximum score the BI was nearly achieved by three months (average of 94.4±10 out of a possible 100), 68% has slow mobility and 85% had impairment with gait speed. This indicates that the BI is not sensitive to gait and mobility impairment. The BI includes excellent items for assessment of activities of daily living (ADLs) but this study will focus solely on physical function and measurement of specific physical impairments.

There are many objective measures used with neurological patients but the two primary measures chosen for this study are the Timed-Up-and-Go (TUG) and the Tinetti Performance Oriented Assessment of Balance and Ambulation (Tinetti).

**Timed up-and-Go (TUG):**

**Procedure:** Test subjects started in a comfortable seated position in a standard arm chair (seat height of 46 cm, arm height 65 cm). When asked to do so, they stood up from the chair, walked a distance of 3 meters (approximately 10 feet) to a marker on the floor,
turned around, walked back to the chair, and sat down again. Participants were allowed to use assistive devices or wear orthotics but no physical assistance is provided. Those that fell or required assistance were not given a score (Podsiadlo and Richardson, 1999).

**Background:** This measure was developed by Podsiadlo and Richardson in 1991 through redesign of the Mathias et al’s “Get-up-and-go” (Mathias, Nayak, and Isaacs, 1986) when the timed element was added in lieu of the scoring aspect. The TUG requires very little time and is objective; it also requires little space or equipment. This tool measures skills required for daily activities: getting in-and-out of a chair, turning, and walking (Podsiadlo and Richardson, 1991). The TUG is not used to identify specific impairments such as decreased muscle strength or presence of abnormal muscle tone. The TUG has been studied with many populations including the fall-risk elderly and people with lower limb amputation and stroke, and has been established as a reliable and valid performance measure to establish fall risk in elderly individuals with Parkinson’s disease, stroke, lower-limb amputation, arthritis, and hip fracture. It has also been shown to be valid in quantifying functional mobility and is valuable for monitoring change in performance over time (Bennie et al 2003). Interrater reliability has been established as high as .98 in use with Parkinson’s and .99 overall.

Bischoff et al (2003) used the TUG with 413 community-dwelling and 78 institutionalized woman aged 65-85 and found times on the TUG significantly increased with the population having decreased mobility status. It also established that community-dwelling elderly should perform the test at or less than 12 seconds.
Shumway-Cook, Brauer, and Woollacott (2000) examined two populations of community dwelling elderly, one with history of falls and one without, and found the TUG to be a valid tool for identifying functional mobility status and fall risk in this population. Boulgarides, McGinty, Willett, and Barnes (2003) determined excellent inter and intrarater reliability (.99) for the TUG with a population of independent community elderly persons but found the instrument was not a good predictor of fall risk.

Steffen, Hacker, and Mollinger (2002) used the TUG to examining elderly individuals who had a variety of medical diagnoses including cancer and stroke but who were at the time high-functioning community-dwelling elderly. The authors found the TUG to have high test-retest reliability (intraclass correlation coefficient (ICC) = 0.97).

Podsiadlo and Richardson (1991) found that those who took less than 10 seconds on the TUG were independent while those who required >15 seconds had fall risk, but if still less than 20 seconds were independent with transfers and stair ambulation. Those who took >30 seconds were found to need assistance with transfers and activities of daily living and could not safely go out of their home alone. The authors also state that the TUG is valid in quantifying functional mobility and is valuable for monitoring change in performance over time. They also determined that the TUG had intrarater reliability of .99 and that it correlated well (.81) with the Berg Balance Scale (BBS), a scale very similar and found to correlate well with the Tinetti (Podsiadlo and Richardson, 1991).

Wall, Bell, Campbell, and Davis (2000) compared young healthy adults, elderly healthy adults and impaired elderly adults. Results indicated that there was significant difference in TUG times between both healthy groups (young averaged 7.36 sec, elderly averaged = 8.74 sec.) and the elderly group with history of falls (average of 18.14 sec.). The authors
concluded that the TUG is sensitive to functional impairments and that those independent in ADLs should be able to complete the test easily in under 10 seconds.

Bennie et al (2003) compared the TUG with known reliable and valid balance assessments, the Berg Balance Scale (BBS) and Functional Reach Test (FR). They found significant correlation with the BBS with $r = -0.47$ in all 20 subjects and correlation of $-0.67$ for the 11 subjects receiving balance therapy. There was no significance in correlation ($r = 0.39$) for the TUG and BBS in subjects not receiving balance treatment. The authors concluded that the TUG is a comparable balance assessment tool to the BBS and is much less time consuming to complete.

Brusse, Zimdars, Zalewski, and Steffen (2005) used the TUG as one of several balance and function measures with people who have PD. Their results indicated TUG scores (amount of time to complete the movement) were higher (subjects moved slower) than TUG scores for the community elderly. The TUG correlated well with other measures (Berg Balance Scale, comfortable and fast gait speeds), leading the authors to conclude that “mobility, ambulation, and balance are not mutually exclusive constructs” (Brusse et al., 2005). This supports the reasoning for selecting these measures for this study. Using the TUG and Tinetti together will provide a more complete picture of the subjects’ balance and mobility skills.

Ng and Hui-Chan (2005) found excellent test-retest reliability (ICC = 0.97) for the TUG. They also determined that the TUG differentiated well between two groups of subjects, one who had diagnosis of chronic stroke and one of healthy elderly. The authors suspected that decreased strength and increased spasticity/abnormal muscle tone and their resulting impact on activation time and duration of leg muscles would impact speed.
of performance on the TUG. While the increased abnormal tone, decreased strength and increased times for the stroke group would seem to support this, the authors found the TUG to correlate strongly with plantar flexion strength (.860) deficits but not as well with plantar flexion spasticity (.421). The literature is divided in this regard with correlation present in some studies but not in others.

Flansbjer et al (2005) note very good reliability for the TUG (confidence interval for ICC = .96). The authors also noted that the TUG is meaningful to the patient, address a variety of aspects of daily walking (velocity, endurance, balance, transitions) and that it is sensitive to small changes. They recommend the use of the TUG for measuring changes in mobility over time.


JC Whitney, Lord, and Close (2005) calculated that the average TUG time in a population of 110 clinic patients who experienced falls was 25.3 seconds and stated that TUG times in a population at risk for falls/ having balance issues was slower than the “suggested normal” of 12 seconds. Newton (1997) established an average on the TUG at
15 seconds in 252 mostly minority adults aged 60-95. SL Whitney, Marchetti, Schade, and Wrisley (2004) used the TUG with 103 persons with vestibular issues between the ages of 14 and 90. They found that non-fallers scored an average of 11.2 seconds, persons with one fall in their history had a mean of 13.5 seconds, and those with multiple falls had an average of 13.9 seconds and identified a sensitivity of 80% when setting the cut-off at 11.1 seconds; those scoring >11.1 seconds were 5 times more likely to have had a fall in the prior 6 months. Other studies have identified the cut-off for fall risk to be anywhere in the 10-16 second range (Dite et al, 2002, Rose et al, 2002, SL Whitney, Poole, and Cass, 1998). This data at least helps us to distinguish the level of balance deficits in the brain tumor population; a TUG of >11 seconds would indicate balance issues. We should also see a change in the TUG score as balance changes characterized by an increase with decline in function and decrease with improvement.

Studies have also indicated strong concurrent validity with other tests of balance and function: .81 with BBS and .78 with Barthel (Escolar et al., 2001). This test is quick to administer and provides a clear picture of the patient’s balance and mobility skills. It also demonstrates change over time and “timed scores are objective, straightforward and more sensitive to change over time than ordinal measures” (SL Whitney et al., 2004). Due to its use with other neurological populations, it is appropriate to generalize this measure to individuals with brain tumor; the outcome of this study will be used to identify appropriateness for future use of the TUG with this population.
**Tinetti Performance-Oriented Mobility Assessment (Tinetti):**

*Procedure:* The Tinetti assesses balance during movements that are considered very functional, day-to-day movements: It is a standardized test that measures a person’s ability to balance while performing certain activities as well as their ability to walk. It consists of two components: a nine item balance portion and a seven item gait section. The nine maneuvers of the balance scale are: sitting balance, arises, attempts to arise, immediate standing balance (first 5 seconds), standing balance, sternal nudge balance, eyes closed standing balance, turning 360° in standing, and sitting down. Each item is scored utilizing a scale of 0 to 2 with 0 meaning an abnormal response, 1 equally an adaptive response, and 2 indicating a normal response except in the case of the sitting balance and eyes closed standing balance in which 0 means abnormal response and 1 indicates a normal response. A total score of 16 is possible on the balance section of the POMA. The seven items on the gait portion of the POMA include initiation of gait, step symmetry, step continuity, path, trunk, and walking time as well as step length and height. The step length and height is split between right swing foot and left swing foot and has 2 areas of scoring for each foot swing: step length and clearance of the foot from the floor during swing. The maximum score that can be achieved during the gait section is 12. Total score possible on the POMA is 28 (Tinetti, Speechley, and Ginter, 1988).

*Background:* The Tinetti was developed by Mary Tinetti (Tinetti et al., 1988). The measure includes both a balance and gait section. An overall score of 28 is possible, with <19 indicating a high fall risk (van Wieringen, 2006). The Tinetti has an interrater reliability of .85 (Lin et al, 2004) to .95 (Tinetti et al., 1993) and test-retest reliability of
This test was developed for the elderly population to predict fall risk, but has been used in neurological populations and also as a tool to monitor change over time or after intervention (Harada et al., 1995; SL Whitney et al., 1998). The Tinetti is one of the measures of balance most often used in the clinic (Bennie et al., 2003). The Tinetti is quick—takes 15 minutes (Harada et al., 1995) and easy to administer (SL Whitney et al., 1998) and its reliability and validity have scored well. Tinetti et al (1988) calculated inter-rater reliability for the balance section at .90, sensitivity as 80 and specificity at 74 when using a cut-off score of 10. Harada et al (1995) calculated the sensitivity (“chance that the test will be positive when applied to someone known to have the disease or disability under consideration”) as 68% and the specificity (“the chance that the test will be negative when applied to someone known to be disease-free”) as 78% for the balance portion of the Tinetti in 53 elderly adults living in residential care facilities. Kloos (2004) used the balance portion with 32 individuals with a diagnosis of Amyotrophic Lateral Sclerosis (ALS) and calculated ICC scores of >.90 for total test scores indicating very good reliability between raters. Persons with ALS have symptoms similar to people with other neurological involvement such as patients with primary brain tumor, including weakness and spasticity with resulting deficits in mobility and activities of daily living. Kloos (2004) goes on to say that clinicians at her facility utilize the Tinetti “to establish a baseline and stage progression of the disease (and) to assist in decision-making regarding treatment goals and interventions.”

Lin et al (2004) compared the reliability and validity of the TUG and Tinetti balance measure as well as two other measures: One-leg Stand and Functional Reach in 1200 subjects over age 65. The results indicated that all four tools had exceptional test-retest
reliability and discriminant validity. The Tinetti showed better “discriminant, convergent, and predictive validities and responsiveness to ADL changes then the other three tests.” The TUG was moderately correlated with the Tinetti balance and gait scales (Kloos, 2004). The longer times on the TUG and lower Tinetti balance performance measures were significant predictors of falling and decreased ADL abilities. These two measures also showed improvements that occurred over time between initial and follow-up testing and following intervention thus demonstrating appropriateness for using these measures in this manner (Harada et al, 1995; SL Whitney et al, 1998).

**Correlation of functional measures and quality of life:**

Huang et al (2001) found that their functional measures (FIM, KPS, and DRS) did not correlate well with their OHS measure (FACT-BR) when analyzing the effects of rehabilitation in 10 clients with BT. The authors called for “further investigation…before correlations can be made between functional outcomes and (OHS)”. Other studies feel functional status correlates well with OHS; Osaba et al (1997) report that in a study of 105 people with malignant gliomas, patients with motor deficits “reported significantly lower levels of physical…and global (OHS) than did patients without these difficulties”. Specifically, presences of motor deficits significantly reduced physical, social, role, emotional and global OHS scores on the EORTC core Quality of Life Questionnaire (QLQ-C30) and “deterioration in neurological function is accompanied by significant deterioration in…global quality of life. This study will determine the correlation between
the TUG and Tinetti with the SF-36 to determine if physical function, especially when using impairment specific measures for balance and walking, correlate to OHS.

**Overall Testing Procedure:**

Prior to surgery for removal or debulking of the primary brain tumor and after informed consent was obtained, subjects were examined by the tester (one tester performed all scoring and examinations in this study).

Subjects completed the 2 trials of the TUG and scores were averaged and recorded. Subjects then completed the SF-36. They did this independently or with the assistance of their caregiver or the tester. Finally, the subject completed the Tinetti balance and gait assessments and these were scored.

The measures were repeated in this order following surgery once the subject was determined by the physician to be medically stable or on the day prior to discharging from the hospital.

The measures were repeated for the third and final time as part of the patient’s 3 month physician follow-up appointment; the tests were administered at this appointment by the original tester and were done in the same sequence.

**Statistical Methodology:**

Demographic characteristics (age, gender, tumor type) and outcome measures (TUG, Tinetti, SF-36) for all subjects were examined using descriptive statistics. Analysis of outcome measures was done for three time periods: pre-surgery to immediately post-
surgery, immediately post-surgery to 3 months post-surgery, and pre-surgery to 3 months post-surgery.

ANOVA with repeated measures over time was performed on measures obtained prior to and immediately after surgery. To examine the recovery from surgery on all outcome measures, a 2 X 2 repeated measures (group by time) ANOVA with repeated measures over time was performed on measures obtained immediately after surgery and three months post-surgery. To examine the overall effect of surgery on all outcome measures, a 2 X 2 repeated measures (group by time) ANOVA with repeated measures over time was performed on measures obtained prior to surgery and three months post-surgery. Statistical significance for all tests was accepted at p<0.05.

Results

Nine subjects (6m; 3f) participated in the study. Demographic variables are in Table 1.

Table 1.

Demographic Characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Race</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>49.2±10.1</td>
<td>3 female</td>
<td>9 Caucasian</td>
<td>3 gliomas</td>
</tr>
<tr>
<td></td>
<td>6 male</td>
<td></td>
<td>6 meningiomas</td>
</tr>
</tbody>
</table>

Note: All data represent means±SD

Comparison of Outcome Measures for All Subjects:

Because none of the demographic characteristics were statistically significant, no covariates were included in any ANOVA models. Repeated measures ANOVA
demonstrated significant differences in all outcome measures from pre-surgery to immediately post-surgery with OHS (SF-36: df=1, F=6.3, p=0.04) and physical functioning (TUG: df=1, F=6.4, p=0.05; Tinetti: df=1, F=7.2, p=0.03).

From immediately post-surgery to 3 months post-surgery, repeated measures ANOVA demonstrated significant differences in all outcome measures (SF-36: df=1, F=14.8, p=0.006; TUG: df=1, F=24.3, p=0.003; Tinetti: df=1, F=39.0, p<0.001).

From pre-surgery to 3 months post-surgery, repeated measures ANOVA demonstrated no significant difference for all outcome measures (SF-36: df=1, F=2.3, p=0.18; TUG: df=1, F=0.03, p=0.86; Tinetti: df=1, F=3.4, p=0.11).

SF-36 scores for all subjects across all three measurement times are in Figure 1. TUG scores for all subjects across all three measurement times are in Figure 2. Tinetti scores for all subjects across the three measurement times are in Figure 3. Averages of the outcome measures for all subjects are shown in Table 4.

Table 2.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>SF-36</th>
<th>TUG (sec)</th>
<th>Tinetti</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-surgery</td>
<td>57.3±16.9</td>
<td>13.9±4.2</td>
<td>20.4±5.7</td>
</tr>
<tr>
<td>Immediately Post</td>
<td>48.9±17.4</td>
<td>18.8±7.1</td>
<td>14.4±8.2</td>
</tr>
<tr>
<td>3 months Post</td>
<td>69.2±21.2</td>
<td>13.0±5.7</td>
<td>23.6±4.6</td>
</tr>
</tbody>
</table>

Note: All data represent means±SD. SF-36=MOS Medical Outcome Study (MOS) 36-Item Short Form Health Survey. TUG=Timed-up-and-Go. Tinetti=Tinetti Performance-Oriented Mobility Assessment.
Table 3.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>SF-36</th>
<th>TUG (sec)</th>
<th>Tinetti</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-surgery to Immediately Post-surgery</td>
<td>-8.4</td>
<td>5.5</td>
<td>-6</td>
</tr>
<tr>
<td>Immediately Post-surgery to 3 months Post-surgery</td>
<td>20.34</td>
<td>-6.11</td>
<td>9.11</td>
</tr>
<tr>
<td>Pre-surgery to 3 months Post-surgery</td>
<td>11.89</td>
<td>-0.87</td>
<td>3.11</td>
</tr>
</tbody>
</table>

Note: All data represent differences of the means. SF-36=MOS Medical Outcome Study (MOS) 36-Item Short Form Health Survey. TUG=Timed-up-and-Go. Tinetti=Tinetti Performance-Oriented Mobility Assessment

Correlation of Outcome Measures:

Spearman’s correlations were conducted on all pre-surgery, immediately post-surgery, and 3 months post-surgery measurements. None of the pre-surgery measures significantly correlated with other measures except for the pre-surgery TUG and pre-surgery Tinetti (r=0.992 p=0.00). All other post-surgery scores significantly correlated with the other instruments post-surgery. This included the two physical functioning measures (TUG and Tinetti) immediately post-surgery (r=-0.833, p=0.01) and 3 months post-surgery (r=-0.966, p=0.0) (see Table 4) as well as the OHS and physical functioning measures: SF-36 and TUG (r=-0.762, p=0.028) and SF-36 and Tinetti immediately post-surgery (r=0.883, p=0.002); SF-36 and TUG (r=-0.845, p=0.004), and SF-36 and Tinetti 3 months post-surgery (r=0.849, p=0.004) (see Table 5). Figure 4 illustrates correlation of the average scores for all outcome measures over the three measurement points.
Table 4:

**Spearmans’s Correlations Between Physical Functioning Measures**

<table>
<thead>
<tr>
<th></th>
<th>Tinetti pre-surgery</th>
<th>Tinetti Immediately post-surgery</th>
<th>Tinetti 3 months post-surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TUG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre-surgery</td>
<td>-.992*</td>
<td>-.567</td>
<td>-.293</td>
</tr>
<tr>
<td>Immediately post-surgery</td>
<td>-.374</td>
<td>-.833*</td>
<td>-.872*</td>
</tr>
<tr>
<td>3 months post-surgery</td>
<td>-.176</td>
<td>-.800*</td>
<td>-.966*</td>
</tr>
</tbody>
</table>

Bolded items indicate correlations between items at same time points. TUG=Timed-up-and-Go. Tinetti=Tinetti Performance-Oriented Mobility Assessment

Table 5:

**Spearmans’s Correlations Between Overall Health Status and Physical Functioning Measures**

<table>
<thead>
<tr>
<th></th>
<th>TUG Immediately post-surgery</th>
<th>TUG 3 months post-surgery</th>
<th>Tinetti Immediately post-surgery</th>
<th>Tinetti 3 months post-surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SF-36</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately post-surgery</td>
<td>-.762*</td>
<td>-.817*</td>
<td>.883*</td>
<td>.828*</td>
</tr>
<tr>
<td>3 months post-surgery</td>
<td>-.719*</td>
<td>-.845*</td>
<td>.703*</td>
<td>.849*</td>
</tr>
</tbody>
</table>

Bolded items indicate correlations between items at same time points. TUG=Timed-up-and-Go. Tinetti=Tinetti Performance-Oriented Mobility Assessment. SF-36=MOS Medical Outcome Study (MOS) 36-Item Short Form Health Survey.

Discussion

The primary goal of this study was to examine recovery from surgery in patients with brain tumors. Contrary to this study’s main hypothesis, it was found that there was no overall improvement in function from pre-surgery to 3 months post-surgery when subjects were analyzed as a group. A second goal of this project was to examine the
utility of multiple functional assessments in this population and to determine the level of agreement among the instruments. Statistical analysis demonstrates that the instruments used in this study were appropriate to the population and correlated well with each other.

Regarding the primary goal, no change occurred in the primary brain tumor subjects from pre-surgery to 3 months post-surgery with regard to overall health status and functional skills, specifically mobility and balance. Factors that may have influenced subject outcomes and thus the overall response to treatment include type and location of the tumor, tumor size, use of adjuvant medical treatments, postoperative complications, and participation in rehabilitation or therapies. Tumor type would influence outcome depending on the aggressiveness and possible recurrence of the tumor. This appeared to be a major factor here as two subjects had aggressive gliomas which caused a decline in function over the three months. Location of the tumor may significantly impact the presence of and level of neurological deficits. Also, these deficits may be worsened due to surgery and not be a direct result of the tumor itself. Adjuvant therapies may play a role in improving overall patient abilities and especially survival time, but these, especially radiation, can cause a worsening of neurological deficits (Black, 1991). Postoperative complications may delay improvement, though at three months, these complications and their affect on function should have been overcome. However, complications may influence the data gathered immediately following surgery. These factors were not specifically analyzed in this study. A sufficiently powered study that includes these variables in the analysis is needed in order to draw definitive conclusions.

With regard to evaluating the relationship among the measures, strong correlations were observed among the outcome measures used in this study. The TUG and Tinetti
have been found reliable and valid for use in the stroke population. The neurological and mobility deficits and pattern of recovery of BT and stroke patients have been found similar (Haut et al, 1991; Black, 1991; Tang et al., 2008). Likewise, the measures utilized here have been determined valid and reliable for the stroke population. Therefore the use of the same measures for BT seems suitable. In this study, no correlations were noted between the SF-36 and either the TUG or Tinetti at baseline. This finding supports the differences between OHS measures and functional measures. They are not measuring the same things. However, after surgery (immediately after as well as 3 months post-) significant correlations were noted among all the measures. It can be concluded that as physical status changed, so did the subjects’ self-perception of their OHS. While there are many aspects to OHS, physical status appears to play a significant role.

Correlation of the measures also supports use of the measures used in this study for future research. As the SF-36 has been established as an appropriate measure for the brain tumor population, its correlation with the TUG and Tinetti here would further indicate that these are also appropriate measures for the BT population. Further supporting this is the TUG data when compared to values calculated by Mayo et al (1999) in a study of the course of recovery of 111 stroke patients in the first three months post-stroke. The average TUG for patients just after stroke is twice the rate of the TUG scores we noted with BT patients (39.3±16.8 versus 18.8±7.1). However, the TUG in Mayo et al’s study was reduced to 18.1±14.8 one month later. At three months, the TUG scores between studies were virtually the same (stroke patients = 15.2±11.2 and BT patients = 13.0±5.7), thus reinforcing the similarities between the stroke and BT populations with regard to health status and functional abilities.
Based on the strong correlations at baseline, immediately post- and 3-months follow up between the TUG and Tinetti, it could be suggested that either test could be used in lieu of the other. Both are measures of mobility and balance, and despite the fact that the Tinetti is a much more comprehensive assessment, and provides some specifics regarding gait, the TUG may be more practical to administer. In other words, where time is limited, use of the TUG would be appropriate and would provide adequate information regarding functional constructs of balance and ambulation.

Finally, clinically relevant observations can be made by examining raw scores using the Minimal Detectable Change (MDC). This is the amount of change on the score of an instrument that indicates a clinically relevant improvement or decline; in other words, a change that is observable and demonstrates a change in function.

For the TUG, MDC has not been clearly established with values ranging from 2 to 15 seconds. The 15 second value was with a population of patients with arthritis and may have been a result of the large standard deviation of 17 seconds (Steffen and Seney, 2008). For three studies with neurological diagnoses the MDC was 2, 5, and 11 seconds in patient’s with Parkinson’s Disease (Lim, van Wegen, and de Goede, 2005; Nordin, Rosendahl, and Lundin-Olsson, 2006; Campbell, Rowse, Ciol, and Shumway-Cook, 2003). In a study of stroke patients, Flansbjer et al (2005) determined that this score for TUG should be 23% times the average baseline score which translates to 3.1 seconds for our BT group. Using a conservative cut-off here of 5 seconds as value for MDC, it is noted that from pre- to 3 months post-surgery, 3 of 9 subjects improved their TUG time and 2 subjects had a worse TUG time beyond the MDC. The 4 other subjects all improved their TUG scores but not beyond the MDC threshold.
The MDC for the Tinetti has been established as 5 points (van Wieringen, 2006). From pre-surgery to 3 months post-surgery, 5 subjects improved while 2 declined beyond the clinical threshold; one subject improved 4 points, from 24 to the maximum possible score of 28 and one subject stayed the same scoring the maximum of 28 both prior to and at 3 months post-surgery. This trend was expected in order to achieve the results presented earlier. But it is interesting to note from a clinical perspective the amount of change being seen in BT patients over time and to be able to compare this to a clinically relevant number, one meaningful to health care professionals.

It is important to look at the subjects individually using the MDC for each measure in addition to as a group. This is due to several factors which may have influenced the data from a group perspective. First, there were a limited number of subjects; having just 9 subjects allowed extreme scores by one or two subjects to skew the overall outcome. Secondly, there may have been ceiling effects, especially with the Tinetti, which limit the amount of improvement which can be demonstrated. For instance, a subject may score from 19-24 on the Tinetti despite while demonstrating balance impairments. These impairments may resolve at the 3 month point, but the score can only improve several points due to the maximum possible score being 28. Likewise, several subjects were included despite having little in regard to physical deficit. These subjects would have little room to demonstrate overall improvement. Finally, the overall group score may have been influenced by tumor type. Some subjects had aggressive tumors which recurred following surgery and progressed, thus causing a decline in function. This was evident in two subjects with gliomas. When comparing the scores as a group, the scores of these two individuals may well have offset the improvement noted in the other subjects.
resulting in the limited change seen in the subjects as a group from pre- to 3 months post-
surgery. This limitation is important to note for future research design.

Based on the aforementioned, the following interpretations may be drawn. These interpretations are made conservatively in recognition of the small number of subjects, a limitation of this study. The current study provides useful information. First is in the use of measurable, validated overall health status and functional mobility measures and the correlation this study found between these. Few studies have objectively measured functional mobility in this population prior to this study. This study supports the use of these measures in future studies of subjects with brain tumor as the measures were found to be appropriate instruments for use in this population. Secondly, is the determination that physical functioning significantly correlates with self-perceived health status. This further contributes to the literature supporting this determination (Dekkers et al., 2006). It may be concluded that physical functioning is a major factor in how people perceive their overall health. Thirdly, the very strong correlation of the TUG and Tinetti demonstrate that they measure similar, if not the same, things. Thus it can be advocated that the TUG can be used alone, especially as its an easy and quick test which can be carried out in the clinical setting. Lastly, we identify factors influencing outcome in the BT population, of which there are many, but especially of note is tumor type.

Implications for Future Research

A larger study is recommended, in regard to number of subjects. Data analysis should include comparison of age, tumor type, tumor size, tumor location, postoperative complications, surgical management (technique and amount resected), use of adjuvant
therapies, subject participation in rehabilitation and therapy, gender and recurrence. Pain is an additional aspect that has been researched to some extent and should be included in future studies as it pertains to effects on mobility and OHS. It would also be worthwhile to note whether physical and mobility deficits are present pre-surgery or not and to group these individuals separate from those with significant pre-surgery deficits to minimize ceiling effects.

Specific comparison may be difficult due to the sheer number of variables, but an extensive examination of balance, mobility, and OHS is possible, especially utilizing the measures used in this study, as they are not only reliable and valid, but quick and easy. The TUG (and Tinetti) as well as use of the SF-36 make up a quick clinical battery which can be performed with help of the physician or a therapist at the initial exam or follow-up. In fact, from a clinical standpoint, we recommend use of the TUG instead of both. Use of these would provide ongoing assessment of balance and walking skills with the BT patient so as to help determine functional status and change over time.

Summary

Functional recovery following surgery for brain tumor was not significant overall. When examined individually, a majority of subjects demonstrated improvement of a clinically relevant nature. Limitations of the study included 1) sample size, which limited the inferences that could be drawn regarding the response to surgery for all participants, 2) potential ceiling effects owing to the fact that nearly half (4 of 9) presented with relatively little in the way of motor deficits or functional impairment prior to surgery, and
3) the effect of tumor type. The rapid progression of the two gliomas led to decline in function which may have influenced the data due to the low subject number of this study.
Appendix A

Figures 1-4

Figure 1.

SF-36 Scores for all subjects across the three measurement/time points.

![Bar graph showing SF-36 Scores](image)

Figure 2:

TUG scores for all subjects across the three measurement/time points.

![Bar graph showing TUG Scores](image)
Figure 3.

Tinetti scores for all subjects across the three measurement/time points.

Figure 4.

Correlation: Average scores on all three outcome measures for all subjects across the three time points.


