

# Congruence of Primary Brain Tumor Patient and Caregiver Symptom Report

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**BACKGROUND:** Evaluating the severity of symptoms in patients with primary brain tumors (PBTs) is important in clinical care and research but may be difficult due to patient neurocognitive (NC) impairment. This study was conducted to evaluate the congruence of symptom reporting in patient and caregiver dyads, examining potential impact of NC impairment and Karnofsky performance status (KPS). **METHODS:** PBT patients undergoing NC testing and their caregivers were included in this study. These dyads (paired patient and caregiver group) completed the MD Anderson Symptom Inventory-Brain Tumor Module prior to testing, and impairment was categorized based on NC test scores. Concordance and equivalency was then assessed using Bland-Altman analysis and 2 one-sided techniques. **RESULTS:** A total of 115 dyads participated. Median patient and caregiver age was 49 and 51 years, respectively, and 63% of patients were male (73% female caregivers). Most patients had a good KPS ( $\geq 90$ , 66%) but were classified as NC impaired (58%). Caregiver's report of patient symptoms are congruent to the self-report of the patient. Equivalency between patient and caregiver report were found using prespecified confidence intervals. KPS group (good,  $\geq 90$ ; poor,  $\leq 80$ ) comparisons of equivalency indicated no significant differences in symptoms and interference reporting between dyads (good = 0.49,  $P > .05$ ; and poor = 0.3,  $P > .05$ ) overall, but there was a tendency for higher report by caregivers if the patients had a poor KPS. **CONCLUSIONS:** Caregivers of PBT patients have similar assessments of symptom severity (highly congruent) with patient self-report regardless of NC function or KPS. These findings suggest that caregivers may serve as proxy report of symptoms for primary brain tumor patients. *Cancer* 2012;118:5026-37. © 2012 American Cancer Society.

**KEYWORDS:** brain tumor, symptoms, caregiver, neurocognitive status, patient-reported outcomes.

## INTRODUCTION

Symptoms such as headaches, poor cognition, and muscle weakness in patients with primary brain tumors (PBT) significantly impact functional status and need for assistance in daily care.<sup>1</sup> The majority of patients undergo a surgical procedure and other therapies, including radiation and chemotherapy,<sup>2</sup> and most will experience acute side effects of therapy as well as late sequelae.<sup>3</sup> Neurocognitive (NC) dysfunction associated with disease progression and/or adverse treatment effects often occurs and may limit the ability to self-report symptoms.<sup>4-7</sup> Therefore, evaluating the impact of both treatment and disease progression on the occurrence of symptoms requires adequate longitudinal measurement and may be hampered by the patient's inability to report as the disease progresses and NC symptoms become more severe.

The ability to collect data on the occurrence of multiple symptoms has important implications for patient care, because symptoms affect a variety of health outcomes in cancer patients, including functional status, disease progression, and survival.<sup>8-10</sup> Symptom clustering can occur and may result from a shared biologic mechanism.<sup>11,12</sup> Therefore, identifying symptom clusters in patients with PBT may have important implications for patient care and ultimately, development of effective treatment.

Medical care is primarily delivered in the outpatient setting, requiring that the report of symptoms come directly from the patient or a closely involved caregiver.<sup>13-15</sup> Based on shared experiences, caregivers' assessments of the patient's symptoms may be more accurate than the health care provider.<sup>16</sup> Several studies have explored the issue of use of caregivers as proxy to patient self-report related to quality of life,<sup>17-19</sup> with mixed results. To our knowledge, there are no studies in PBT patients related to patient and caregiver concordance in reporting symptom severity and the impact of NC and functional status. In other solid tumor patients, there is a bias of family caregivers to report more negatively than patients on the patients' symptom experiences, but the differences are often of small magnitude.<sup>20</sup> As a consequence, use of caregivers

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as proxy or complementary reporters in patients with cancer<sup>21</sup> and nonmalignant neurologic diseases<sup>22</sup> has been described.

In summary, patients with PBT experience significant symptoms, and NC symptoms may make self-report difficult. The purpose of this study was to determine whether the use of the MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT) module completed by a caregiver proxy is feasible, reliable, and valid, and if caregiver report correlates with the patient's own self-report of symptoms, regardless of functional and NC status.

## MATERIALS AND METHODS

### Study Population

This study population included adult PBT patients referred for formal NC testing as part of routine care. Subjects were screened and selected if they were  $\geq 18$  years of age and able to speak, read, and write English. The caregivers were  $\geq 18$  years of age and were able to speak, read, and write English, and were identified by the patient as individuals who are primarily involved in their care in the home setting (biological, legal, or functional relationship).

The investigators performed the human investigations after approval by the The University of Texas MD Anderson Cancer Center institutional review board. The investigators also obtained informed consent from each participant.

The patient/caregiver dyad was approached about participation at the time of presentation for NC testing, consent was obtained, and the patient and caregiver were moved into separate rooms and questionnaires were completed. Prior to completing the MDASI-BT, the caregiver was read the following script, as developed by Lobchuk et al,<sup>23</sup> to invoke empathy with the patient:

*We have listed 22 symptoms and 6 interference items on the form in front of you. Please read each question carefully. We are asking for the severity of each item for the patient in the last 24 hours. While you are completing this questionnaire, please try to imagine how the patient feels and how these symptoms are affecting him/her. In your mind's eye, put yourself in the patient's shoes. Forget yourself. Try to picture how the symptom feels to the patient. Answer the question as you believe the patient would. Please tell us how severe the symptom is for the patient. If the patient would say he or she did not have the symptom, mark "0" or "not present." If it is the most severe he or she can imagine, mark it "10."*

This script is an approach that a clinician can use that is designed to assist the caregiver to "place oneself in

another's shoes," and simply instructs the caregiver to report the symptoms as they think the patient would, not the severity that they think the patient has. After completion of the questionnaires, the patient underwent NC testing.

### Instruments

The study instruments used included the MDASI-BT completed by both patient and caregiver proxy; a clinician-completed clinical checklist; a patient-completed demographic information sheet; a caregiver information sheet; and objective testing with a battery of NC tests (described in detail below). The MDASI-BT consists of 22 symptoms and 6 interference items rated on an 11-point scale (0 to 10) to indicate the presence and severity of the symptom, with 0 being "not present" and 10 being "as bad as you can imagine." Each symptom is rated at its worst in the 24 hours prior to completion.<sup>24</sup> Symptoms included on the instrument include those common in PBT patients and those associated with cancer therapies. The average time to complete the MDASI-BT is 5 minutes.<sup>25</sup> The caregiver version included the same questions, with the instructions adapted to ask the caregiver to rate the symptoms as perceived to be experienced by the patient.

Patient sex, ethnicity, race, age, level of education, marital status, and employment status were collected using a *demographic information sheet*. The *caregiver information sheet* was used to determine the caregiver's demographic characteristics and relationship to patient, time spent with the patient, and care needs provided for the patient. Information on tumor type and characteristics and Karnofsky performance status (KPS) was recorded on the *clinical assessment tool*.

All patients received the following tests as part of a larger comprehensive neuropsychological evaluation: Hopkins Verbal Learning Test-Revised (HVLTR)<sup>26</sup>; Digit Span subtest of the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III); and Trail Making Test (parts A and B).<sup>27</sup> The psychometric properties of these instruments are well documented, and adequate norms are available.<sup>26-28</sup> Scores obtained from these measures reflect aspects of attention, learning and memory, processing speed, and executive function.

### Statistical Analysis

Statistical analyses were conducted using Predictive Analytics Software, a component of the Statistical Package for the Social Sciences, version 17.0.<sup>29</sup> Descriptive statistics were used to describe the population of patients and caregivers in terms of disease and demographic characteristics.

### Psychometric evaluation of the MDASI-BT by patient and proxy

Feasibility, validity, and internal consistency of the patient-reported MDASI-BT has been reported.<sup>25</sup> We did assess test–retest reliability of the patient-completed MDASI-BT for a subset of patients, because this has not been previously reported. Patients were given the MDASI-BT again after completion of testing. This time point was chosen for convenience, and also allowing for at least 2 hours, with distraction of testing between assessments. A Spearman correlation coefficient was calculated.

Feasibility of the caregiver-completed MDASI-BT was assessed by evaluation of completion time and report of difficulty completing items. Reliability was assessed by calculation of Cronbach's alpha, with an a priori criteria set as 0.7.

### Describing symptom reports

Descriptive statistics were used to define patient and caregiver ratings of symptom severity, and symptom interference with daily function. Means, standard deviations (SDs), and ranges, as well as lower and upper confidence limits were computed. The 5 most severe symptoms were identified based on the ranking of average symptom severity. Following the methods of Serlin et al<sup>30</sup> and Mendoza et al<sup>31</sup> for pain and fatigue cutoffs, we categorized symptom severity and symptom interference into none/mild (0-4) and moderate/severe (5-10), to facilitate clinical interpretation. The proportions of patients and caregivers rating their symptoms at 7 or greater (on a 0-10 scale), a level indicative of severe symptom level, were also reported, as well as those who reported symptoms at moderate-to-severe levels (5 or greater). The degree of difference between patient and caregiver report of individual symptoms was then evaluated by determining whether the mean difference between caregivers and patient scores was significantly different than 0. This was assessed for each symptom using paired *t* tests with Bonferroni correction for multiple test.

### Examining congruency

The Bland-Altman approach was used to determine whether patients and caregivers were in agreement in reporting subscale items as well as individual items,<sup>32</sup> using 2 steps: first, a scatterplot of the caregiver and patient symptom ratings for MDASI-BT, symptom severity, and interference subscale was produced and evaluated to see how much the ratings deviated from the 45-degree line. Second, individual symptoms and interference items difference scores were examined as to whether they were within the 95% limits of agreement. We then plotted this

difference with the average scores. This is done to evaluate whether the magnitude of the score affects whether there is a relationship between the patient and caregiver report.

### Testing for group differences

To investigate the effect of disease severity and neurocognitive function (NCF) on the results of the comparison between patients and caregivers, we categorized the dyads based on these 2 factors. When patients had NCF test results below the norm, the dyad was classified as impaired; otherwise, they were considered not impaired. For disease severity, dyads were categorized in groups of good versus poor performance status, when the patients had a KPS score of 90 to 100, versus 80 or less, respectively. In several prior studies, a significant difference in symptom burden and interference has been demonstrated in patients with KPS of  $\leq 80$  compared with those with KPS of  $\geq 90$ .<sup>25,33-35</sup> Independent sample tests were used to compare dyads with poor KPS versus those with good KPS, as well as dyads categorized as having impaired versus unimpaired NCF. In addition, known group validity was assessed for caregivers and patients separately, using KPS and NCF.

### Testing for equivalency

Equivalency in mean symptom severity and interference between patients and caregivers were explored using confidence intervals (CIs). Group differences of within 0.5 SD in symptom severity between groups were considered equivalent. This criterion was based on Sloan et al, who showed through their research that for any patient-reported outcome instrument, a difference of half an SD can be considered clinically significant.<sup>36,37</sup> Equivalency was declared if a 90% CI of the difference between patients and caregivers was inside our reference CI of  $(-0.5SD, +0.5SD)$ . This reference CI was constructed based on the SD of the mean scores for the patients used as reference group.

Equivalency testing involves performing 2 one-sided *t* tests. To establish equivalency, both 1-sided null hypotheses need to be rejected, but it is sufficient to perform only 1 test. Thus, we can perform the test without halving the typically used .05 significance level. This same logic was extended to the use of the CI. Hence, we used a 90% CI instead of a 95% CI.

### Effects of NC functioning and disease severity on equivalency

The effect of NCF and disease severity on the results of the comparison between patients and caregivers was

**Table 1.** Patient and Caregivers Sociodemographic Characteristics

Characteristics	Frequency (N = 115)			
	Patient		Caregiver	
<b>Demographic</b>				
Age, y, mean (range)	48.2	(18-80)	49.8	(20-80)
<b>Years of education</b>				
Mean (median)	14.6	(15)	14.6	(15)
12th Grade or less	28	(24.3)	24	(21.6)
	n	%	n	%
<b>Sex</b>				
Female	42	36.5	84	73
Male	73	63.5	31	27
<b>Marital Status</b>				
Divorced	9	7.8	5	4.3
Married	84	73	96	83.5
Separated	1	0.9	2	1.7
Single	17	14.8	11	9.6
Widowed	4	3.5	1	0.9
<b>Ethnicity</b>				
Asian or Pacific Islander	2	1.7	3	2.6
Black non-Hispanic	4	3.5	4	4
Hispanic	6	5.2	7	6.1
Native American or Alaskan Native	3	2.6	1	0.9
White non-Hispanic	98	85.2	100	87
Other (caucasian, white Hispanic)	2	1.7		
<b>Job status</b>				
Employed (full-time and part-time)	52	45.2	78	67.8
Retired	18	15.7	12	10.4
Homemaker	4	3.5	17	14.8
Unemployed due to diagnosis of tumor	20	17.4	1	0.9
Unemployed prior to diagnosis	7	6.1	2	1.7
Student	2	1.7	1	0.9
Other (disabled, family medical leave, student, homemaker)	12	10.4	4	3.5
<b>Relation to patient</b>				
Spouse			69	60
Child			10	8.7
Parent			17	14.8
Sibling			3	2.6
Unmarried partner			6	5.2
Other (cousin, employee, ex-spouse, friend)			10	8.7
<b>Caregiver income</b>				
Less than \$30,000			13	11.3
\$30,000 to \$39,999			5	4.3
\$40,000 to \$49,000			10	8.7
\$50,000 or more			83	72.2
Missing			4	3.5
			<b>Caregiving Assistance Provided to Patients</b>	
Years lived with patient (mean/SD)			19.2	13.7
			n	%
<b>Currently living with patient</b>				
Yes			91	79.1
No			24	20.9
<b>Moved in due to diagnosis</b>				
Yes			15	13
No			84	73

(Continued)

Table 1. (Continued)

Characteristics	Frequency (N = 115)	
	Patient	Caregiver
<b>Time spent prior to diagnosis (h/wk)</b>		
0-5 h	22	19.1
6-20 h	14	12.2
21-40 h	6	5.2
41-80 h	17	14.8
More than 80 h	56	48.7
<b>Time spent since diagnosis (h/wk)</b>		
0-5 h	3	2.6
6-20 h	9	7.8
21-40 h	10	8.7
41-80 h	7	6.1
More than 80 h	86	74.8
<b>Caring for household</b>		
Yes	65	56.5
No	50	43.5
<b>Cooking</b>		
Yes	68	59.1
No	47	40.9
<b>Eating</b>		
Yes	17	14.8
No	98	85.2
<b>Taking medications</b>		
Yes	59	51.3
No	56	48.7
<b>Driving</b>		
Yes	82	71.3
No	33	28.7
<b>Walking</b>		
Yes	26	22.6
No	89	77.4
<b>Grooming</b>		
Yes	18	15.7
No	97	84.3
<b>Bathing</b>		
Yes	13	11.3
No	102	88.7
<b>Total care</b>		
Yes	5	4.3
No	110	95.7

examined by comparing difference scores between dyads with impaired versus unimpaired NCF, and good versus poor KPS for the group overall and then separately for each group. An independent sample *t* test was used to conduct this comparison. In addition, a 2-factor analysis of variance test was conducted to investigate potential interaction effect between NCF and disease severity measured by KPS.

## RESULTS

### *Dyad Characteristics*

This study included 115 patient/caregiver dyads who were accrued between May 29, 2008, and December 14, 2009. Initially, 251 patients scheduled for NC testing were found eligible by initial screen, 121 patients were approached, of which 3 refused participation and 3 had incomplete data (unable to complete testing and

questionnaires due to impairment). Patients were primarily white (85%), males (63%), with a median age of 49 years. Caregivers were also white (87%), female (73%), spouses (60%), with a median age of 51 years. Demographic characteristics of patients and caregivers as well as caregiver attributes are presented in Table 1.

The most common diagnosis was glioblastoma (36%), and mean time since diagnosis was 1.7 years. The majority of patients had a good performance status (66%). Of the patients referred for NCF testing, 34% had known or suspected deficits; however, the majority (58%) were classified as exhibiting NC impairment as defined by the a priori criteria. Clinical characteristics are further outlined in Table 2.

### Psychometric Evaluation

#### Feasibility

The caregiver version of the MDASI-BT took on average 4 minutes to complete and there were no incomplete forms by the caregiver. Only 3 patient/caregiver dyads refused to participate in the study.

#### Reliability

Evaluation of internal consistency using Cronbach's alpha was completed with reliability for all 22 symptoms and 6 interference items for the caregiver of 0.949 and 0.942 for the patient. Reliability for the 22 symptoms was 0.924 for the caregiver and 0.925 for the patient and for the interference items, 0.917 for the caregiver and 0.905 for the patient.

Test-retest reliability was assessed in a subgroup of 21 patients. Patients completed the MDASI-BT before and immediately after NCF testing (approximately a 2-hour period between assessments). Spearman correlations between the 2 time points were computed and showed a very high level of correlation on repeated testing (mean symptom severity,  $r=0.952$ ,  $P<.0001$ ; mean interference,  $r=0.783$ ,  $P<.0001$ ).

#### Symptom Severity

All symptoms and interference items were reported through the full range of severity (0-10) by both patients and caregivers, with the exception of appetite (0-7) and vomiting (0-5) by caregivers, and pain (0-9) and vomiting (0-6) by patients. The 5 most severe symptoms reported by both patients and caregivers, in order of severity, were fatigue, difficulty remembering, drowsiness, distress, and sleep.

Descriptive statistics revealed mean severity subscale scores of 1.9 (SD = 1.56), and 1.7 (SD = 1.54) for caregivers and patients respectively, while average interference

**Table 2.** Patient Clinical Characteristics

Clinical Characteristics	Frequency (N=115)	
	n	%
Time since diagnosis, y, mean (standard deviation)	1.7	(3.5)
	n	%
Year 0	67	58.3
1 to 5 y	36	31.3
6 y or more	12	10.4
<b>Tumor grade</b>		
Astrocytoma/oligodendroglioma	39	33.9
Anaplastic astrocytoma/oligodendroglioma	15	13.0
Ependymoma/anaplastic ependymoma	2	1.7
Glioblastoma/gliosarcoma	44	38.2
Medulloblastoma	3	2.6
Other	12	10.4
<b>Tumor group (World Health Organization)</b>		
Grade: 1-2	35	30.4
Grade: 3-4	80	69.6
Most		
<b>Location</b>		
Side, left	64	55.7
Side, right	44	38.3
Midline	4	3.5
<b>Disease state</b>		
Newly diagnosed	76	66.1
Recurrence	39	33.9
<b>Reasons for testing</b>		
Preoperative	19	16.5
Postoperative follow-up	22	19.1
Deficits	39	33.9
Deficits follow-up	30	26.1
Protocol	5	4.3
<b>Karnofsky group</b>		
Poor: 60-80	39	33.9
Good: 90-100	76	66.1
<b>Current therapy</b>		
Chemotherapy	32	27.8
Radiation therapy	12	10.4
<b>Concurrent medications</b>		
Steroids	21	18.3
Anticonvulsants	68	59.1
Antidepressants	22	19.1
Stimulants	6	5.2
Opioids	15	13.0
<b>Neurocognitive testing</b>		
Overall patient performance		
Not impaired	42	36.5
Impaired	67	58.3
Missing	6	5.2

subscale scores were 2.73 (SD = 2.64), and 2.31 (SD = 2.43) for the same groups. Using the previously defined half SD rule, we derived confidence intervals of  $\pm 0.77$  and  $\pm 1.2$  for the severity and interference subscales

**Table 3.** Descriptive Statistics for the MDASI-BT (N = 115 dyads)

MDASI-BT	Group	Mean	SD	Range	% $\geq 5^a$	% $\geq 7^b$	% = 0 <sup>c</sup>
<b>Core symptoms (rank order)<sup>d</sup></b>							
Fatigue	Patients	3.45	2.85	0-10	35.1	14.9	16.7
	Caregivers	3.97	2.74	0-10	40.4	19.3	7.0
Difficulty remembering	Patients	3.22	2.91	0-10	30.4	18.3	17.4
	Caregivers	3.82	3.22	0-10	37.7	26.3	15.8
Drowsiness	Patients	2.77	2.76	0-10	21.9	11.4	24.6
	Caregivers	3.03	2.82	0-10	25.2	15.7	20.0
Distress	Patients	2.44	2.70	0-10	23.0	10.6	30.1
	Caregivers	3.32	2.93	0-10	35.1	21.1	23.7
Sleep disturbance	Patients	2.35	2.89	0-10	21.2	14.2	33.6
	Caregivers	3.03	3.18	0-10	32.7	17.7	31.9
Sadness	Patients	1.91	2.58	0-10	16.8	7.1	43.4
	Caregivers	2.56	2.94	0-10	25.4	13.2	36.8
Pain	Patients	1.61	2.34	0-9	15.8	5.3	54.4
	Caregivers	1.87	2.57	0-10	18.3	8.7	47.8
Dry mouth	Patients	1.58	2.38	0 – 10	14.9	5.3	55.3
	Caregivers	0.92	2.05	0 – 10	7.1	3.5	71.7
Lack of appetite	Patients	1.22	2.24	0 – 10	8.7	5.2	65.2
	Caregivers	0.98	1.93	0 – 7	7.8	3.5	71.3
Numbness	Patients	1.15	2.13	0 – 10	10.5	3.5	65.8
	Caregivers	1.14	2.18	0 – 10	11.5	5.3	65.5
Shortness of breath	Patients	0.79	1.99	0 – 10	6.1	4.3	75.7
	Caregivers	0.65	1.91	0 – 10	5.2	5.2	81.7
Nausea	Patients	0.75	1.83	0 – 10	3.5	3.5	75.2
	Caregivers	0.84	2.01	0 – 10	7.0	4.3	75.7
Vomiting	Patients	0.14	0.70	0 – 6	0.9	0.0	94.7
	Caregivers	0.11	0.56	0 – 5	0.9	0.0	93.9
<b>Module items (rank order)</b>							
Speaking	Patients	2.28	2.75	0 – 10	22.8	9.6	36.8
	Caregivers	2.20	2.84	0 – 10	20.0	10.4	40.9
Concentrating	Patients	2.16	2.48	0 – 10	17.7	8.8	28.3
	Caregivers	2.46	2.44	0 – 10	20.9	7.8	25.2
Irritable	Patients	1.96	2.47	0 – 10	15.0	8.8	36.3
	Caregivers	2.19	2.78	0 – 10	19.1	14.8	44.3
Weakness	Patients	1.86	2.98	0 – 10	19.1	13.0	56.5
	Caregivers	2.02	3.01	0 – 10	16.5	11.3	51.3
Understanding	Patients	1.71	2.43	0 – 10	21.2	12.4	42.9
	Caregivers	2.37	2.88	0 – 10	14.3	7.1	41.6
Vision	Patients	1.51	2.44	0 – 10	13.3	6.2	54.9
	Caregivers	1.80	2.92	0 – 10	17.1	10.8	57.7
Bowel pattern	Patients	1.29	2.52	0 – 10	10.5	7.0	63.2
	Caregivers	1.38	2.45	0 – 10	14.9	7.0	64.9
Appearance	Patients	0.74	1.72	0 – 10	5.3	2.7	73.5
	Caregivers	0.88	1.87	0 – 10	6.1	3.5	69.6
Seizure	Patients	0.26	1.21	0 – 10	2.6	0.9	92.1
	Caregivers	0.37	1.48	0 – 10	4.3	1.7	90.4
<b>Interference items (rank order)</b>							
Work, including housework	Patients	2.73	3.43	0 – 10	25.7	17.7	39.8
	Caregivers	3.33	3.65	0 – 10	34.8	26.1	34.8
Enjoyment of life	Patients	2.55	3.13	0 – 10	24.6	14.9	40.4
	Caregivers	2.89	3.13	0 – 10	30.7	21.1	33.3
General Activity	Patients	2.46	2.97	0 – 10	23.7	12.3	36.8
	Caregivers	3.18	3.27	0 – 10	33.9	21.7	31.3
Mood	Patients	2.37	2.69	0 – 10	20.5	9.8	32.1
	Caregivers	2.83	2.97	0 – 10	30.7	16.7	34.2
Walking	Patients	1.83	2.78	0 – 10	17.5	12.3	50.0
	Caregivers	2.06	3.11	0 – 10	20.9	15.7	56.5

(Continued)

Table 3. (Continued)

MDASI-BT	Group	Mean	SD	Range	% $\geq 5^a$	% $\geq 7^b$	% = 0 <sup>c</sup>
Relations with other people	Patients	1.80	2.48	0 – 10	14.9	8.8	47.4
	Caregivers	2.03	2.66	0 – 10	22.1	9.7	47.8
<b>Subscale Scores</b>							
Mean Severity (Core + BT)	Patients	1.70	1.54				
	Caregivers	1.90	1.56				
Mean Core (13 items)	Patients	1.81	1.64				
	Caregivers	2.02	1.58				
Mean BT (9 items)	Patients	1.54	1.59				
	Caregivers	1.74	1.70				
Mean interference (6 items)	Patients	2.31	2.43				
	Caregivers	2.73	2.64				
WAW (walk-activity-work)	Patients	2.36	2.74				
	Caregivers	2.86	2.97				
REM (relate-enjoy-mood)	Patients	2.26	2.44				
	Caregivers	2.59	2.69				

MDASI-BT indicates MD Anderson Symptom Inventory-Brain Tumor; SD, standard deviation.

<sup>a</sup>Percent moderate to severe.

<sup>b</sup>Percent severe.

<sup>c</sup>Percent of patients scoring at the floor (score = 0 on the 0-10 scale).

<sup>d</sup>Ranking based on patient's mean scores.

as reported by patients as a reference group compared to caregivers. These confidence intervals will also be used for further evaluation of equivalency described later. This study also indicated that both patients and caregivers similarly reported fatigue as the most prevalent symptom with 35% and 40% respectively, reporting fatigue at moderate to severe levels (5 or greater on a scale of 0 to 10). Table 3 outlines these results. Using a Bonferroni adjusted significance level of 0.002, only distress ( $P = .001$ ) and dry mouth ( $P = .002$ ) were significantly different between caregiver and patients (Table 4). In summary, symptoms were reported across a range of severity, and overall, patients and caregivers tended to report symptom and interference items similarly.

### Congruence

The Bland-Altman analysis indicates that the 90% limits of agreement between the caregiver and patient ratings ranged from  $-0.97$  to  $1.37$  at the item level. The caregivers and patients consistently provided similar ratings of symptoms. Figure 1 is a graphical display of the patient/caregiver congruence for the symptom and interference severity subscales of the MDASI-BT.

The next analysis of congruence involved determining if the difference scores and the average scores between caregivers and patients were significantly correlated (Fig. 2 shows representative plots). This test showed that the correlation between the difference and average scores between patients and caregivers is not significant for all items (Table 5). Therefore, because the 2 Bland-Altman

criteria were met, indicating congruency between patient and caregiver, we conclude that tests of congruency support that caregiver's report of patient symptoms are congruent and equivalent to the self-report of the patient.

### Testing for Group Differences

#### Effect of NC function

An independent sample  $t$  test comparing caregiver-patient discrepancy found no significant group differences between dyads considered impaired compared with those considered as nonimpaired. Mean differences from this comparison were  $0.23$  ( $P > .05$ ), and  $0.66$  ( $P > .05$ ) for the symptom and interference subscales respectively. The effect sizes were less than 0.5 SD units for both the symptom and interference subscales.

#### Effect of KPS

The impact of KPS on report by patient and caregiver was then assessed. For the entire sample, KPS group (good versus poor) level comparisons of caregiver-patient discrepancy indicated no significant differences for the symptom subscale. In this comparison, the mean differences were  $0.49$  ( $P > .05$ ), and  $0.3$  ( $P > .05$ ) for the symptom and interference subscales respectively. The effect sizes were all smaller than 0.5 SD units. In summary, there were no significant group-level differences in the similarity of patient and caregiver report.

#### Equivalency Test

The difference in average severity scores between caregivers and patients resulted in a difference of 0.21 with a



**Table 4.** Difference Scores Between Patient and Caregiver as Compared to 0

Difference Caregiver–Patient	Significance (2-Tailed)	Mean Difference	90% Confidence Interval of the Difference	
			Lower	Upper
Pain	.243	.26	-.11	.64
Fatigue	.021	.57	.17	.97
Nausea	.691	.08	-.25	.41
Sleep	.052	.60	.09	1.11
Distress	.001 <sup>a</sup>	.92	.47	1.37
Shortness of breath	.415	-.14	-.42	.14
Difficulty remembering	.061	.61	.08	1.15
Change in appetite	.284	-.23	-.60	.13
Drowsiness	.379	.27	-.24	.78
Dry mouth	.002*	-.63	-.97	-.30
Sadness	.032	.62	.14	1.09
Vomiting	.752	-.03	-.17	.11
Numbness	.916	-.02	-.30	.26
Weakness	.451	.16	-.19	.50
Difficulty understanding	.024	.62	.17	1.07
Difficulty speaking	.659	-.11	-.54	.31
Seizures	.474	.11	-.14	.35
Difficulty concentrating	.298	.28	-.17	.73
Change in vision	.210	.29	-.09	.68
Change in appearance	.538	.14	-.24	.52
Change in bowel pattern	.743	.09	-.36	.53
Irritability	.283	.26	-.14	.65
INTERFERENCE Activity	.030	.68	.16	1.19
Mood	.074	.47	.04	.90
Work	.192	.52	-.14	1.18
Relate	.537	.17	-.28	.62
Walk	.516	.17	-.26	.59
Enjoy	.305	.33	-.20	.85

<sup>a</sup>Significant results (corrected  $P = .002$ )

90% confidence interval (CI) of (-0.02, 0.43) for the symptom subscale. The test for the interference subscale produced a difference of 0.37 and a 90% CI of (-0.02, 0.75). Based on the half standard deviation rule, we found that both the CI for the symptom and interference subscales were within our reference CI of (-0.77, 0.77) and (-1.2, 1.2), respectively, thus supporting equivalency between patients and caregivers report.

#### Effect of NC function

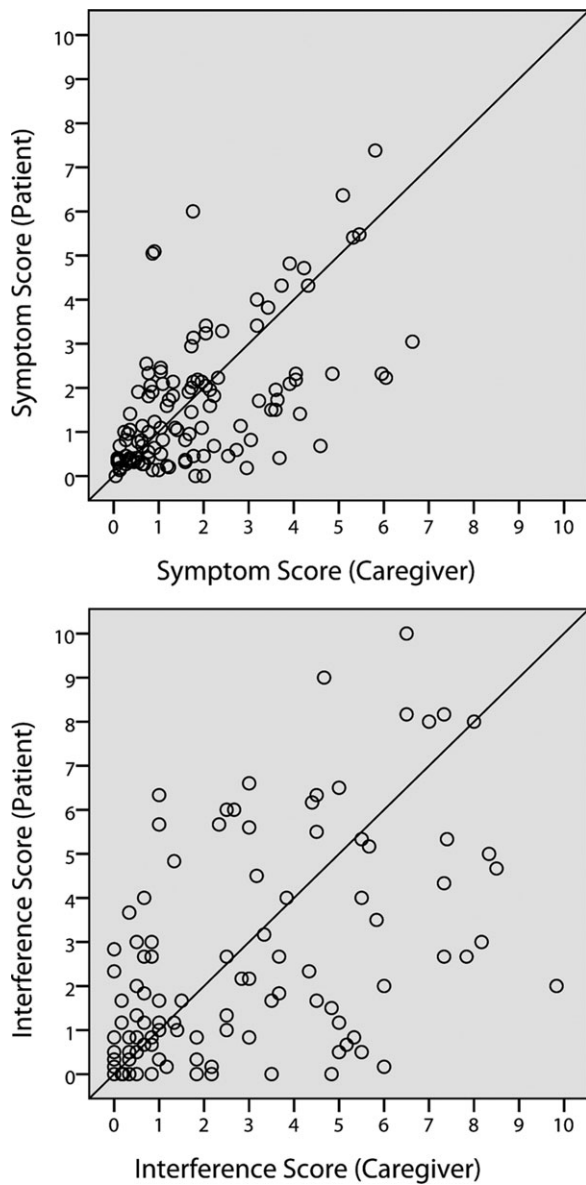
Mean differences in symptom and interference subscale scores among the nonimpaired group were 0.04 (-0.28, 0.35), and 0.09 (-0.65, 0.46), respectively. For the impaired dyads, the results of mean differences between patients and caregiver were 0.27 (-0.05, 0.59), and 0.57 (0.018, 1.12) for the symptoms and interference subscales respectively. This indicates that in this sample, caregivers' report of symptom severity was equivalent with report by both patients with NC dysfunction as well as those without NC dysfunction.

#### Effect of KPS on equivalency of symptom and interference subscale scores

The next step involved evaluating good versus poor KPS dyads separately. Patient versus caregiver comparisons conducted for dyads with good KPS revealed no significant differences (average between-group difference of 0.04 units [CI -0.22, 0.30] and 0.27 units [CI -0.11, 0.64] for both symptom and interference subscales, respectively). For dyads with poor KPS, significant differences were found for the MDASI-BT symptom score (mean differences between patients and caregivers of 0.53 units [CI 0.11, 0.95], and 0.57 units [CI -0.33, 1.47] for the symptom and interference subscales, respectively). These results indicate that caregivers are biased to report higher overall symptom and interference when the patient has a poor KPS.

#### Effect of KPS on individual symptom and interference report

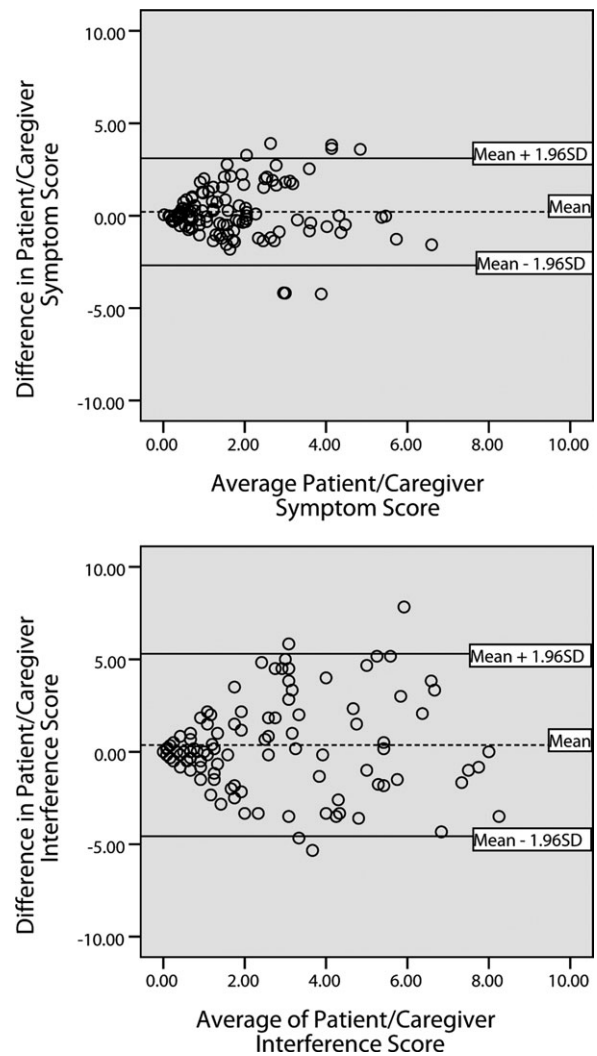
On an individual symptom level, dyads with good KPS were equivalent for all symptom and interference



**Figure 1.** Representative Bland-Altman plots compare mean symptom and interference severity between patient and caregiver.

items, except distress. For those dyads in which the patient had a poor KPS, there was lack of equivalency for 7 core items (pain, disturbed sleep, distress, problem remembering things, lack of appetite, drowsiness, and sadness); 7 brain tumor module items (difficulty understanding, seizures, difficulty concentrating, vision, appearance, bowel pattern, irritability); and all interference items, with caregivers reporting higher symptoms compared to patient self-report.

In summary, the dyads reported items similarly if the patient had a good KPS. For those in which the patient had a poor KPS, average differences of less than



**Figure 2.** Representative Bland-Altman plots show mean symptom and interference severity average and difference scores.

one point were found between the patient and caregiver rating. Because of this small magnitude of difference, the clinical significance of these differences is not known, but indicate a consistent bias for caregivers to report more severe symptom and interference caused by symptoms when the patient has a poor KPS. Further analyses using 2-factor analysis of variance test found no significant main effect or interaction for NCF or KPS. Parameters ranged from 0.04 to 0.8 with no statistical significance ( $P > .05$  and all CIs included the value 1). Therefore, the impact appears to be primarily in those patients with poor KPS.

**DISCUSSION**

To our knowledge, this is the first report evaluating the congruence between PBT patient and caregiver report of

**Table 5.** Correlation Between Difference and Average Scores Between Patient and Caregiver

MDASI-BT Symptom Item	Pearson Correlation	P
Pain	0.11	0.231
Fatigue	-0.03	0.732
Nausea	0.10	0.290
Sleep	0.08	0.386
Distress	0.09	0.319
Shortness of breath	-0.05	0.565
Difficulty remembering	0.11	0.258
Change in appetite	-0.16	0.093
Drowsiness	0.02	0.807
Dry mouth	-0.17	0.078
Sadness	0.14	0.137
Vomiting	-0.22	0.018
Numbness	0.03	0.743
Weakness	0.01	0.891
Difficulty understanding	0.19	0.043
Difficulty speaking	0.03	0.722
Seizures	0.22	0.021
Difficulty concentrating	-0.01	0.875
Change in vision	0.21	0.027
Change in appearance	0.10	0.310
Change in bowel pattern	-0.03	0.730
Irritability	0.15	0.110
Symptom Interference Items		
Activity	0.10	0.288
Mood	0.11	0.251
Working	0.06	0.553
Relationship with others	0.04	0.652
Walking	0.11	0.236
Enjoyment of life	0.00	0.959

MDASI-BT indicates MD Anderson Symptom Inventory-Brain Tumor

patient symptoms which also evaluates the impact of KPS and NCF. Overall, the caregiver's report of symptom severity and interference were correlated and congruent with patient report. This congruence remained whether the patient was classified as having impaired cognition or not. There was a consistent bias of caregivers to report more severe symptoms and interference of symptoms if the patient had a poor KPS, but the magnitude of this difference was small (less than 1).

One reported bias is that the patient and caregiver can have conflicting beliefs about the illness which influences the caregiver's ability to report patient's symptoms.<sup>23,38,39</sup> How the clinical question is posed to the caregiver may influence the reliability and validity of the response<sup>16,23,40</sup> and there are numerous theories on the best approach when prompting someone to describe another's experience.<sup>16</sup> Extant theory states that perspective-taking is an "interpersonal empathic process" involving a conscious effort in differentiating one's view from the view of another that can bring the caregivers' viewpoints in closer alignment with patients' viewpoints.<sup>41(p330)</sup> Using methods to assist the caregiver to

"place oneself in another's shoes" is an approach that a clinician can take to help this empathetic process,<sup>23</sup> that has been shown to improve congruence when the caregiver imagines the illness from the patients' perspective and not their own.<sup>16,41-43</sup> The current study used the prompt developed by Lobchuk to encourage the caregiver to report as they believe the patient would report and not how they themselves would rate the symptoms. The trend for caregivers to report higher symptoms and interference severity for those patients with poor performance status, may indicate that as functional status declines, either the patient has difficulty accurately reporting the impact of symptoms or the caregiver may include their own assessment of the impact when reporting. This finding requires further investigation, including assessment of caregiver characteristics which may influence this higher report and has implications for reporting for those patients with very poor functional status.

These results provide preliminary support for the use of the MDASI-BT by proxy for report of symptom severity. Caregivers of PBT patients appear to have assessments of symptom severity that are highly congruent with patient self-report in this select sample of patients. The utility in patients with more extensive NC deficits or worse KPS cannot be reported and requires further investigation. Future analyses will evaluate the congruence between patient and caregiver report of cognitive dysfunction and objective testing. In addition, evaluation of the method of introduction of proxy reporting was not assessed in this cross-sectional study, nor can the relationship of proxy group to specific patient populations be ascertained. The implications of this report on the use of proxy for other patient-reported outcome measures (ie, quality of life) or those instruments that measure report over a longer period than 24 hours are not known.

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The authors made no disclosure.

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