

# Performance Status and Number of Metastatic Extra-cerebral Sites Predict Survival After Radiotherapy of Brain Metastases from Thyroid Cancer

LIESA DZIGGEL<sup>1</sup>, NIKLAS GEBAUER<sup>2</sup>, TOBIAS BARTSCHT<sup>2</sup>, STEVEN E. SCHILD<sup>3</sup> and DIRK RADES<sup>1</sup>

*Departments of <sup>1</sup>Radiation Oncology and Hematology and <sup>2</sup>Medical Oncology,  
University of Lübeck, Lübeck, Germany;*

*<sup>3</sup>Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, U.S.A.*

**Abstract.** *Background/Aim: Patients with brain metastases from thyroid cancer are extremely rare. This study evaluated clinical factors for survival following whole-brain radiotherapy (WBRT) alone. Patients and Methods: In six patients, the following factors were analyzed for survival: Regimen of WBRT (5×4 Gy vs. 10×3 Gy), gender, age (≤55 vs. ≥56 years), Karnofsky performance score (KPS) (60% vs. 70-80%), number of brain lesions (2-3 vs. ≥4) and number of extra-cranial metastatic sites (one vs. more than one). Results: KPS 70-80% (p=0.036) and involvement of only one extra-cranial site (p=0.018) were associated with better survival on univariate analysis. On Cox regression analysis, KPS (p=0.14) and number of extra-cranial sites (p=0.14) showed trends for association with survival. In patients with KPS 70-80% and only one extra-cranial site, 6-month survival was 100%, no patient with KPS 60% and more than one extra-cranial site survived to 6 months. Conclusion: KPS and number of involved extra-cranial metastatic sites were associated with survival and may be helpful for individualizing therapy in patients with brain metastases from thyroid cancer.*

Patients with brain metastases from thyroid cancer are extremely rare and represent fewer than 1% of all patients with metastasis from a solid tumor to the brain (1, 2). Therefore, only very little is known about this group of patients with cancer. The current study was conducted to add more data for patients with thyroid cancer who received

whole-brain radiotherapy (WBRT) alone for intracerebral metastatic lesions. The main goal of this study was identification of clinical factors associated with survival. Such factors could be used to tailor treatment, in particular the radiotherapy regimen for an individual patient, taking into account the most appropriate overall treatment time.

It is generally agreed that when considering treatment effect and potential toxicities, patients with a poor survival prognosis should preferentially receive a shorter course of WBRT and those with a more favorable prognosis a longer course of WBRT (2-4). It has been shown that factors predicting survival can differ considerably between various solid tumor types which lead to brain metastases (5-13). Therefore, studies performed to identify the significant predictors separately for each tumor entity are important.

## Patients and Methods

Six patients who received WBRT alone for more than one metastasis to the brain from thyroid cancer between 2000 and 2004 were included in this retrospective study and evaluated for survival. A total of six clinical factors were analyzed for a potential association with outcome following WBRT. The investigated factors included were the regimen of WBRT (5×4 Gy over 2 weeks vs. 10×3 Gy over 3 weeks), gender, age at the time of WBRT (≤55 vs. ≥56 years, median=55.5 years), the Karnofsky performance score (KPS of 60% vs. 70-80%, median=65%), the number of metastatic lesions to the brain (2-3 vs. ≥4, median=3) and the number of involved extra-cranial metastatic sites (one vs. more than one, median=1) (Table I). Initially, a univariate analysis of survival was performed using the Kaplan–Meier method supplemented with the log-rank test (14). Subsequently, those factors achieving significance on univariate analysis ( $p<0.05$ ) were investigated in a multivariate fashion (Cox regression model).

## Results

The median follow-up time was 8 months (range=1-18 months) for the entire cohort and 12.5 months (range=7-18

*Correspondence to:* Professor Dirk Rades, MD, Department of Radiation Oncology, University of Lübeck, Lübeck, Ratzeburger Allee 160, 23562 Lübeck, Germany. Tel: +49 45150045401, Fax: +49 45150045404, e-mail: rades.dirk@gmx.net

**Key Words:** Thyroid cancer, metastatic lesions to the brain, whole-brain radiotherapy alone, survival, predictive factors.

Table I. Distribution of the investigated clinical factors.

	Number of patients
Regimen of WBRT	
5x4 Gy over 2 weeks	3
10x3 Gy over 3 weeks	3
Gender	
Female	2
Male	4
Age at WBRT	
≤55 Years	3
≥56 Years	3
Karnofsky performance score	
60%	3
70-80%	3
Number of metastatic brain lesions	
2-3	3
≥4	3
Number of extra-cranial metastatic sites	
1	4
>1	2

WBRT: Whole-brain-radiotherapy.

months) for the patients who were alive at their last follow-up. For the entire cohort, the survival rates at 6 and 12 months were 67% and 44%, respectively. On univariate analysis, a KPS of 70-80% (*vs.* 60%,  $p=0.036$ ) and involvement of only one extra-cranial metastatic site (*vs.* more than one site,  $p=0.018$ ) were significantly associated with survival (Table II). In the subsequent Cox regression analysis, both KPS ( $p=0.14$ ) and number of extra-cranial metastatic sites ( $p=0.14$ ) showed trends for associations with survival.

The importance of these two clinical factors is further supported by the finding that patients with a KPS of 70-80% and involvement of only one extra-cranial metastatic site achieved a 6-month survival rate of 100%, whereas those patients with a KPS of 60% and involvement of more than one extra-cranial metastatic site had a 6-month survival rate of 0%.

## Discussion

Thyroid cancer is considered an important disease, and considerable research has been performed to improve the prognoses of these patients. Clinical studies have been reported on surgical techniques, novel systemic treatments and multidisciplinary approaches (15-17). Another field of research aims to identify prognostic factors that allow clinicians to better judge a patient's prognosis, which is important for designing individualizing therapy. Prognostic factors have already been identified for treatment of the

Table II. Univariate analyses: survival rates at 6 and 12 months following WBRT.

	At 6 months, %	At 12 months, %	<i>p</i> -Value
Regimen of WBRT			
5x4 Gy over 2 weeks (n=3)	67	0	0.36
10x3 Gy over 3 weeks (n=3)	67	67	
Gender			
Female (n=2)	100	100	0.11
Male (n=4)	50	25	
Age at WBRT			
≤55 Years (n=3)	67	67	0.50
≥56 Years (n=3)	67	0	
Karnofsky performance score			
60% (n=3)	33	0	<b>0.036</b>
70-80% (n=3)	100	100	
Number of metastatic brain lesions			
2-3 (n=3)	33	33	0.79
≥4 (n=3)	100	50	
Number of extra-cranial metastatic sites			
1 (n=4)	100	67	<b>0.018</b>
>1 (n=2)	0	0	
Entire cohort	67	44	

WBRT: Whole-brain-radiotherapy, significant *p*-values are shown in bold.

primary tumor and also for metastatic disease (18-23). However, to our knowledge no study exists focusing on patients with thyroid cancer who require treatment for metastases to the brain. The most frequently used treatment modality for brain metastases is WBRT, either alone or combined with focal therapies such as neurosurgical resection and stereotactic radiosurgery (2). This study focused particularly on patients treated with WBRT alone.

In this study, two predictors of survival, namely the KPS and number of extra-cranial metastatic sites, were identified on univariate analyses. The prognostic value of the performance status for patients receiving treatment for brain metastases has been described for other tumors and was found to be prognostic for this cohort. The prognostic impact of the number of extra-cranial metastatic sites has been found prognostic in a few studies, mainly in patients with brain metastases from breast cancer or lung cancer (24-27).

Taking into account the retrospective design of the present study and the small number of patients evaluated, the results of the present study may serve to guide clinicians when they aim to tailor the radiation treatment to a patient with metastases to the brain from thyroid cancer. Since no patient with a KPS of only 60% and metastatic involvement of more than one extra-cranial site survived longer than 4 months, these patients appear good candidates for short-course

WBRT with 5×4 Gy over 1 week, which has shown to be non-inferior to longer-course WBRT programs with 30-40 Gy over 2-4 weeks (3). In contrast, patients with the most favorable survival prognosis (KPS >60% and involvement of maximum one extra-cranial site) could benefit from longer-course WBRT programs with higher total doses in terms of better intracerebral control and survival (4). Patients of the latter group with a limited number of cerebral lesions may also be good candidates for focal therapies (2).

In conclusion, in this study, the KPS and the number of involved extra-cranial metastatic sites were identified to be associated with survival in patients receiving WBRT alone for brain metastases from thyroid cancer. Although this study was small, these two factors could be used for personalization of care for this patient group.

### Conflicts of Interest

On behalf of all Authors, the corresponding Author states that there is no conflict of interest related to this study.

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