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### Radiosurgery

# Brain stem metastases treated with radiosurgery: prognostic factors of survival and life expectancy estimation

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#### Abstract

**Background:** The objective of this study is to study prognostic factors of survival and 3 stratification systems for life expectancy estimation in patients with brain stem metastases treated with radiosurgery.

**Methods:** Between December 1999 and November 2006, 25 patients with 27 brain stem metastases were treated with Gamma Knife radiosurgery. The lesions' mean volume was 0.6 mL (0.013-3.6 mL). The mean marginal dose was 20 Gy (15-24 Gy). Univariate and multivariate studies were done to identify prognostic factors, and 3 patient stratification systems were applied for survival estimation: RPA, SIR, and BSBM.

**Results:** The primary tumor location was in the lungs in 12 patients, breast in 8, and other in 5. Fourteen lesions were located in the pons, 9 in the midbrain, and 4 in the medulla. All patients were followed clinically. Radiologic follow-up was available in 21 lesions (78%). Tumor control was achieved in all but one followed lesion (95%). There were no complications related to treatment. Median survival of patients with brain stem metastases was 11.1 months.

In multivariate analysis, KPS of 80 or more, control of the primary tumor, absence of radiotherapy, and a marginal dose higher than 18 Gy were associated with better survival. The BSBM in the univariate and multivariate analyses was the strongest predictor of survival (P < .0001).

**Conclusions:** The BSBM was the most useful tool for estimating survival. Rather than the brain stem location of an intracranial metastasis, the patient integral clinical status seems to be more important in determining survival.

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Keywords:

Radiosurgery; Brain stem; Metastases; Stratification; Survival

Abbreviations: BSBM, basic score for brain metastases; KPS, Karnofsky performance status; RPA, recursive partitioning analysis; SIR, Score Index for Radiosurgery in brain metastases; WBRT, whole brain radiotherapy.

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#### 1. Introduction

In the last 2 decades, there has been a continuous development on diagnosis and treatment of cancer disease with longer expectancy of life. This fact and the increasing knowledge of the effectiveness of radiosurgery for the treatment of brain metastases have allowed radiosurgery to be considered nowadays as a treatment of first line.

There are many articles in the literature demonstrating the use of radiosurgery for the treatment of brain metastases

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[1-3,11,13,15,17], but there is less information concerning the specific location in the brain stem [4,7-9,14,18].

For the indication of radiosurgery, it is crucial to estimate survival for selecting those patients with potential benefits. Three stratification systems have been used for estimating survival in patients with brain metastases treated with radiosurgery: the RPA [3,13], the SIR [17], and the BSBM [11]. All of these 3 systems have demonstrated to be useful for survival estimation in patients harboring brain metastases, but there is no consistent information in the literature regarding a detailed and systematic use of these systems in patients with brain stem metastases.

The aim of this study is to describe the results of a series of 25 consecutive patients with brain stem metastases treated with radiosurgery, focused on survival, prognostic factors of survival, as well as life expectancy estimation, using the 3 mentioned stratification systems.

#### 2. Materials and methods

The treatment was performed with a Leksell Gamma Knife model C (Elekta AB, Sweden).

The mean marginal dose was 20 Gy (range, 15-24 Gy), delivered at the median 50% isodose (range, 50%-70%), taking into account the lesion volume as well as the previous history of whole-brain radiotherapy. All treatments were

image guided with combined stereotactic magnetic resonance and computed tomography.

Clinical and radiologic controls by magnetic resonance were scheduled at 1, 3, 6, 12, 18, and 24 months after treatment. Follow-up was prospectively encoded. Treatment failure was defined as an increase in lesion volume of 25% or more during radiologic follow-up with a positron emission tomography with <sup>11</sup>C-methionine showing hypermetabolic activity compatible with tumor activity. Clinical follow-up was considered until the last clinical control for each patient.

Eleven general variables were studied for survival: sex, age (younger than 60 vs 60 years or older), primary tumor (lung, breast, and others), lesion location (medulla, pons, or midbrain), lesion volume (<0.2 vs  $\geq$ 0.2 mL), marginal dose ( $\leq$ 18 vs >18 Gy), whole-brain radiation therapy in any moment of the history of the patient, existence of other brain metastases, KPS (<80 vs  $\geq$ 80), control of the primary tumor, and the existence of extracranial metastases.

For those variables divided in 2 subgroups for statistical analysis, the breaking point was defined according to the best *P* value obtained in the univariate analysis.

Patients were stratified for their medical conditions using 3 different stratification systems: the RPA [3,5,6,13], the SIR [17], and the BSBM [11] (Fig. 1).

According to RPA [5,6], those patients with KPS of 70 or more, with controlled primary tumor, younger than 65 years,

#### Recursive Partitioning Analysis (RPA)

RPA	Patients characteristics
I	KPS 70 or more Age less than 65 years Primary tumor controlled No extracranial metastases
п	KPS 70 or more and any other such as: Age 65 or more Primary tumor uncontrolled Extracranial metastasis
ш	KPS less than 70

Score Index for radiosurgery in brain metastases (SIR)

Variable \ score	0	1	2
Age in years	60 or more	51-59	50 or less
KPS	50 or less	60-70	80-100
Systemic disease status	Progressive disease	Stable disease or partial remission	Complete clinical remission or No evidence of disease
Number of lesions	3 or more	2	1
Largest lesion volume in cubic centimeters	More than 13	5-13	Less than 5

#### Basic Score for Brain Metastases (BS-BM)

Variable \ Score	0	1
KPS	50 - 70	80 - 100
Control of primary tumor	NO	YES
Extracranial metastases	YES	NO

(KPS= Karnofsky performance status)

Fig. 1. The 3 stratification systems: RPA, SIR, and BSBM.

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