# A Survival Score for Patients Receiving Stereotactic Radiosurgery Alone for Brain Metastases from Breast Cancer

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**Abstract.** *Aim: To generate a survival score for patients with breast cancer treated with stereotactic radiosurgery (SRS) alone for brain metastases. Patients and Methods: Seven factors were evaluated in 34 patients, namely age, performance score, number of brain metastases, maximum diameter of all brain metastases, location of brain metastases, extracerebral metastases and time between breast cancer diagnosis and SRS. The score was created from factors having a significant impact on survival. Points of 0 (worse survival) or 1 (better survival) were assigned. Factor scores were added to total prognostic scores for each patient. Results: A significant impact on survival was found for performance score ($p<0.001$), maximum diameter of cerebral lesions ($p=0.002$), and extracerebral metastases ($p=0.026$). Three groups were designated by score: 0-1, 2 and 3 points. One-year survival rates were 48%, 71% and 100%, respectively ($p<0.001$). Conclusion: This score contributes to appropriate selection of personalized treatment in patients with breast cancer with few cerebral metastases.*

Patients with breast cancer account for about 25% of patients with brain metastases and represent the second most common entity after lung cancer associated with metastases to the brain (1-3). Therefore, patients with breast cancer with brain metastases do require particular attention. The majority of these patients present with multiple cerebral lesions generally defined either as more than three or more than four lesions. These patients are generally treated with whole-brain irradiation (WBI) alone. The situation is more complex in case of a limited number of brain metastases, *i.e.* ≤3 or ≤4 lesions. Many of these patients receive local treatment such as neurosurgical resection or stereotactic radiosurgery (SRS), either alone or in combination with WBI (3). Resection is usually limited to patients with a single brain metastasis. However, previous studies have shown that SRS (although non-invasive) resulted in better local control of treated brain metastases than neurosurgical resection both in patients with very few lesions and patients with a single lesion (4). Thus, SRS has become more popular for the treatment of brain metastases for up to 3-4 cm in diameter, which is considered the maximum extension of cerebral lesions suitable for SRS (3).

Several studies have shown that the addition of WBI to SRS can improve the control of the treated lesions and more successfully prevent new cerebral lesions (5, 6). However, these improvements did not translate into better survival. Since many physicians are afraid of WBI-related neurocognitive deficits, a considerable number of patients with up to four cerebral lesions receive SRS alone (7).

During the past decade, individualized treatment has gained attention in oncology. To be able to optimally tailor anticancer treatment to an individual patient's situation, it is crucial to estimate the patient's remaining lifetime as precisely as possible. This can be considerably facilitated with survival scores. Several such scores already exist for patients with brain metastases (8-11). However, during recent years it has been recognized that it would be desirable to have separate survival scores for each tumor entity and, furthermore, for specific situations such as multiple or limited numbers of cerebral lesions and specific treatment approaches such as WBI alone or SRS alone. Therefore, this study was initiated to develop a survival score particularly for patients with breast cancer treated with SRS alone for a limited number of cerebral metastases.

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## Patients and Methods

In this study, the data of 34 female patients with breast cancer treated with 18-20 Gy of SRS alone for 1-3 brain metastases were retrospectively analyzed. The dose was prescribed to the margins of each metastasis, which represented the 75-85% isodose. Seven factors were evaluated for potential associations with survival. The seven factors included age at the time of SRS (≤58 *vs.* ≥59 years; median=58 years), Karnofsky performance score (70-80 *vs.* 90-100), number of brain metastases (1 *vs.* 2-3), maximum diameter of all brain metastases (≤15 *vs.* >15 mm), location of the brain metastases (strictly supratentorial *vs.* infratentorial involvement), presence of extracerebral metastases at the time of SRS (no *vs.* yes), and time between breast cancer diagnosis and SRS (≤48 *vs.* ≥49 months, median=48.5 months). The distribution of these factors is shown in Table I.

The factors that achieved significance ($p<0.05$) in the survival analysis (Kaplan–Meier method plus log-rank test) were included in the prognostic score. For each significant factor, points of 0 (worse survival) or 1 (better survival) were assigned. Subsequently, the factor scores were added to a total prognostic score for each of the 34 patients.

## Results

A significant positive association with survival was found for a Karnofsky performance score of 90-100 ($p<0.001$), a maximum diameter of all cerebral lesions of ≤15 mm ($p=0.002$), and lack of extracerebral metastases ($p=0.026$). The results of the entire survival analysis are summarized in Table II. Taking into account the points assigned to the three significant factors (Table III), the total prognostic scores for the patients were 0, 1, 2 or 3 points. The corresponding 1-year survival rates were 39%, 56%, 71% and 100%, respectively ($p=0.002$). Subsequently, three survival groups were designated: 0-1 points, 2 points, and 3 points. The 1-year survival rates of these groups were 48%, 71% and 100%, respectively ($p<0.001$); and the 2-year survival rates were 0%, 71% and 100%, respectively ($p<0.001$).

## Discussion

Since the locoregional treatment of breast cancer has considerably improved in recent decades, more patients live longer and, therefore, are more likely to experience metastatic spread during the course of their cancer (12-14). This also applies to the development of brain metastases. Different treatment modalities are available, most of all radiotherapy including WBI with/without SRS. The use of SRS is generally limited to a few, generally three or four cerebral lesions (3). The optimal treatment approach for these patients still requires further research. One question that still needs to be answered is the use of SRS alone or in combination with WBI. A few studies including randomized trials have demonstrated that the addition of WBI to SRS improves local control of the treated lesions, provides freedom from new cerebral lesions, and overall intracerebral control (4-6). However, survival was not improved when WBI was added. Additionally, randomized trials have shown that the risk of decline in neurocognitive function significantly increases with the addition of WBI (7). Therefore, many treating physicians are hesitant regarding the combination of SRS and WBI, and SRS alone is becoming more frequently employed.

If SRS alone is chosen, physicians wish to deliver an individualized treatment approach that optimally meets a patient's individual needs. It is well known that such personalized approaches must take into account a patient's remaining lifespan to optimally balance several important factors, including efficacy of the treatment, treatment-related toxicities, and the burden of treatment for the patient. Therefore, survival scores have gained importance in recent years (15). Because every tumor entity has its specific characteristics, including tumor biology and the pattern of spread, it is important to have available specific scores for each tumor entity. To avoid a selection bias caused by the treatment approach (WBI alone, SRS alone, WBI plus SRS, neurosurgery alone, neurosurgery plus WBI), separate scores should ideally be developed in patient cohorts uniformly treated with one form of treatment (2, 11). Therefore, this study focused solely on patients with one to three brain metastases from breast cancer treated with SRS alone.

Three factors were identified that had a significant impact on survival in such patients, the Karnofsky performance score, the maximum diameter of all cerebral lesions and the presence or not of extracerebral metastases. Based on these factors, three survival groups were defined with significantly different 1-and 2-year survival rates. Patients with 0-1 points had the worst prognosis, with 1-year and 2-year survival rates of 48% and 0%, respectively. In this group, 15 patients died during the follow-up, seven patients from new distant brain metastases and eight patients from extracerebral tumor progression. Therefore, these types of patients would appear to benefit from intensification of systemic treatment in a timely manner. Patients with 2 points by this new score had a more favourable prognosis, with a survival rate of 71% at 1 year and 2 years. Two patients died during follow-up, one patient each from new distant brain metastases and from extracerebral progression. Therefore, such patients may not require WBI in addition to SRS, and systemic treatment should be balanced against potential risks of significant toxicities. Since all of the patients with 3 points were still alive 2 years following SRS without progression of disease, such patients should not receive WBI, and systemic treatment may be withheld until extracerebral progression of disease is detected. Close follow-up, particularly of these patients, is recommended.

In summary, the new survival score developed in this study for patients with breast cancer receiving SRS alone for few brain metastases contributes to the selection of individualized treatment approaches and personalized cancer care of this patient group.

Table I. *Distribution of the factors evaluated for survival in this study.*

| | Number of patients | Proportion of patients (%) |
|---|---|---|
| Age | | |
| ≤58 Years | 18 | 53 |
| ≥59 Years | 16 | 47 |
| Karnofsky performance score | | |
| 70-80 | 16 | 47 |
| 90-100 | 18 | 53 |
| Number of brain metastases | | |
| 1 | 27 | 79 |
| 2-3 | 7 | 21 |
| Maximum diameter of all cerebral lesions | | |
| ≤15 mm | 19 | 56 |
| >15 mm | 15 | 44 |
| Location of the cerebral lesions | | |
| Strictly supratentorial | 23 | 68 |
| Infratentorial involvement | 11 | 32 |
| Extracerebral metastases | | |
| No | 13 | 38 |
| Yes | 21 | 62 |
| Time from breast cancer diagnosis to SRS | | |
| ≤48 Months | 17 | 50 |
| ≥49 Months | 17 | 50 |

Table II. *Analysis of the seven factors with respect to survival in this study.*

| | Survival at 1 year (%) | Survival at 2 years (%) | *p*-Value |
|---|---|---|---|
| Age | | | |
| ≤58 Years | 76 | 31 | |
| ≥59 Years | 56 | 37 | 0.36 |
| Karnofsky performance score | | | |
| 70-80 | 41 | 0 | |
| 90-100 | 88 | 75 | **<0.001** |
| Number of brain metastases | | | |
| 1 | 65 | 49 | |
| 2-3 | 71 | 0 | 0.54 |
| Maximum diameter of all cerebral lesions | | | |
| ≤15 mm | 79 | 79 | |
| >15 mm | 51 | 0 | **0.002** |
| Location of the cerebral lesions | | | |
| Strictly supratentorial | 59 | 34 | |
| Infratentorial involvement | 80 | 39 | 0.32 |
| Extracerebral metastases | | | |
| No | 84 | 73 | |
| Yes | 54 | 18 | **0.026** |
| Time from breast cancer diagnosis to SRS | | | |
| ≤48 Months | 76 | 41 | |
| ≥49 Months | 57 | 32 | 0.47 |

Bold *p*-values indicate significant association with survival.

Table III. *Factors significantly associated with survival in this study and the corresponding scoring points.*

| | Scoring |
|---|---|
| Karnofsky performance score | |
| 70-80 | 0 |
| 90-100 | 1 |
| Maximum diameter of all cerebral lesions | |
| ≤15 mm | 1 |
| >15 mm | 0 |
| Extracerebral metastases | |
| No | 1 |
| Yes | 0 |

## Conflicts of Interest

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

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