ZNS-Metastasen beim Mammakarzinom
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- **Versionen 2003–2017:**
  Bischoff / Diel / Fehm / Friedrich / Gerber / Huober / Loibl / Lück / Maass / Müller / Nitz / Jackisch / Jonat / Junkermann / Rody / Schütz / Witzel

- **Version 2018:**
  Müller / Stickeler

unter Mitarbeit von:
Petra Feyer und Dirk Rades (DEGRO)


Risk factors (see also references slide CNS incidence)


Brain metastases (BM) are more likely to be estrogen receptor negative, and overexpress HER2 or EGFR


There is no evidence for BM-screening in asymptomatic BC-patients

Graded Prognostic Assessment (GPA)  
Arbeitsblatt zur Abschätzung des Mortalitätsrisikos bei Hirnmetastasen (BM)

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPS</td>
<td>&lt; 50</td>
<td>60</td>
<td>70-80</td>
<td>90-100</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>subtype</td>
<td>Basal</td>
<td>n/a</td>
<td>LumA</td>
<td>HER2</td>
<td>Lumb</td>
<td></td>
</tr>
<tr>
<td>age, years</td>
<td>&gt; 60</td>
<td>&lt; 60</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>sum total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Median survival by GPA:
GPA 0-1.0 = 3.4 months
GPA 1.5-2.0 = 7.7 months
GPA 2.5-3.0 = 15.1 months
GPA 3.5-4.0 = 25.3 months

Subtype: Basal: triple negative; LumA: ER/PR positive, HER2 negative; LumB: triple positive; HER2: ER/PR negative, HER2 positive. ECM, extracranial metastases; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; KPS, Karnofsky performance score; LumA, luminal A; LumB, luminal B; PR, progesterone receptor.

Sperduto PW, J Clin Oncol 2012, 30:419-425

Breast-GPA


Prognostic Factors for Survival


Oligo-Hirnmetastasen

Alleinige Lokaltherapie: SRS (≤ 4 cm) oder FSRT
WBRT + Boost (SRS, FSRT)

Alleinige WBRT*
Hippocampuschonung

- Die Zahl der stereotaktisch sinnvoll zu bestrahlenden Metastasen ist von Lokalisation, Größe und anderen Faktoren abhängig
- WBRT zusätzlich zu SRS/FSRT verbessert die lokale Kontrolle und Symptomkontrolle, nicht aber das Überleben. Gleichzeitig scheint bei zusätzlicher WBRT eine größere neurokognitive Beeinträchtigung aufzutreten
- Bei einer limitierten Anzahl von Hirnmetastasen Präferenz zur stereotaktischen Bestrahlung

SRS = stereotactic radiosurgery (einzzeitig)
FSRT = fractionated stereotactic radiotherapy
WBRT = whole brain radiotherapy

* Patientinnen mit ungünstiger Prognose und/oder schlechtem Allgemeinzustand


Study design:
Patients with 1-3 brain metastases, each < 3 cm by contrast MRI, were randomized to SRS alone or SRS + WBRT and underwent cognitive testing before and after treatment. The primary endpoint was cognitive progression (CP) defined as decline > 1 SD from baseline in any of the 6 cognitive tests at 3 months. Time to CP was estimated using cumulative incidence adjusting for survival as a competing risk.*

Conclusion:
Decline in cognitive function, specifically immediate recall, memory and verbal fluency, was more frequent with the addition of WBRT to SRS. Adjuvant WBRT did not improve OS despite better brain control. Initial treatment with SRS and close monitoring is recommended to better preserve cognitive function in patients with newly diagnosed brain metastases that are amenable to SRS.

* Remark: No hippocampus-sparing was applied

### Adjuvant Whole-brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study

<table>
<thead>
<tr>
<th>2-year relapse rate after whole-brain radiotherapy (WBRT) versus observation after surgical resection or radiosurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>after surgical resection (n=160)</td>
</tr>
<tr>
<td>WBRT observation</td>
</tr>
<tr>
<td>Local recurrence</td>
</tr>
<tr>
<td>New lesions</td>
</tr>
</tbody>
</table>

- Only 12% of the patients had brain metastases from breast cancer.
- Overall survival was similar in the WBRT and observation arms (median, 10.9 vs. 10.7 months, respectively; P = .89).
- Intracranial progression caused death in 44% patients in the OBS arm and in 28% patients in the WBRT arm.

Kocher M. J Clin Oncol 2011, 29:134-141

Mögliche Entscheidungsfaktoren
Neurochirurgie vs. Stereotaktische Strahlentherapie

Pro Neurochirurgie:
- Histologische Sicherung nach z.B. langem rezidivfreiem Intervall
- Sofortige Dekompression notwendig, lebensbedrohliche Symptome
- Stereotaktische Radiotherapie (SRS oder FSRT) bei singulärer Metastase aufgrund der Größe nicht möglich

Pro primäre Radiotherapie*:
- Tumorlokalisaton nicht geeignet für chirurgische Resektion
- Mehr als eine Läsionen ohne die oben genannnten Kriterien

* Falls möglich stereotaktische Strahlentherapie bevorzugt


Radiochemotherapy


Re-Bestrahlung bei Rezidiv


2. Minniti, G., C. Scaringi, S. Paolin et al.: Repeated stereotactic radiosurgery for


**Chemotherapy**

1. Cortes, J., V. Dieras, J. Ro et al.: Afatinib alone or afatinib plus vinorelbine versus investigator's choice of treatment for HER2-positive breast cancer with


Anticonvulsants


Steroids


Trastuzumab intrathecal


MTX high dose