Hypofractionated Stereotactic Radiosurgery as Salvage Treatment of Brain Metastases

Daniel Rueß, Sergej Telentschak, Stefan Grau, Martin Kocher, Maximilian Ruge
Objectives: SRS in brain metastasis

- SRS is part of standard care in brain metastasis

- Limitations of single-fraction SRS:
  - large volume of lesions (e.g. diameter > 3 cm)
  - close proximity to critical structures (i.e. pontine)
Objectives: Hypofractionation

Fractionated Radiotherapy

Single fraction radiosurgery

preservation by fractionation

preservation by conformal target definition

Hypofractionated radiosurgery (hSRS)
Objectives: Current studies

Clinical Oncology

Original Article

Fractionated Stereotactic Radiotherapy using CyberKnife for the Treatment of Large Brain Metastases

T. Murai *, H. Ogino *, Y. Manabe *, M. H. Suzuki *, Y. Shibamoto *

Objectives:
Current studies

RESEARCH

Optimal hypofractionated conformal radiotherapy for large brain metastases in patients with high risk factors: a single-institutional prospective study

Hiroshi K Inoue, Hiro Sato, Yoshiyuki Suzuki, Jun-ichi Saitoh, Shin-ee Noda, Ken-ichi Seto, Kota Torikai, Hideyuki Sakurai and Takashi Nakano

Cyberknife hypofractionated stereotactic radiosurgery (HSRS) of resection cavity after excision of large cerebral metastasis: efficacy and safety of an 800 cGy × 3 daily fractions regimen

Radiation Oncology

RESEARCH

Radiosurgery or hypofractionated stereotactic radiotherapy for brain metastases from radioresistant primaries (melanoma and renal cancer)

Investigation of the efficacy and safety of CyberKnife hypofractionated stereotactic radiotherapy for brainstem metastases using a new evaluation criterion: ‘symptomatic control’

Masaki Nakamura, Hideki Nishimura, Hiroshi Mayahara, Haruka Uezono, Aya Harada, Naoki Hashimoto, Yasuo Ejima, Takeaki Ishihara.
# Objectives: Summary of current studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>n (patients/tumors)</th>
<th>median Tumor Volume (cm³)</th>
<th>Radiation schedule</th>
<th>median Follow-up (mo)</th>
<th>6 mos LC %</th>
<th>6 mos OS %</th>
<th>median OS (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesueur et al, 2018</td>
<td>35/106</td>
<td>4.2</td>
<td>27-33Gy/3 fr. IDL: 80%</td>
<td>7.4</td>
<td>83</td>
<td>69</td>
<td>9.6</td>
</tr>
<tr>
<td>Nakamura et al., 2017</td>
<td>20/26</td>
<td>0.3</td>
<td>18–30 Gy / 3-5 fr. IDL 70–80%</td>
<td>6.5</td>
<td>100</td>
<td>72</td>
<td>17</td>
</tr>
<tr>
<td>Murai et al., 2014</td>
<td>54/61</td>
<td>≥ 8 - &lt; 33 ≥ 33</td>
<td>18-30Gy / 3 fract. 21-35Gy / 5 fract.</td>
<td>-</td>
<td>77</td>
<td>52</td>
<td>6</td>
</tr>
<tr>
<td>Inoue et al., 2014</td>
<td>88/92</td>
<td>10 – 74.6 (median 16.2)</td>
<td>25-40Gy / 3-10 fr. IDL 57-55%</td>
<td>7</td>
<td>90.2</td>
<td>62</td>
<td>9</td>
</tr>
<tr>
<td>Wang et al., 2012</td>
<td>37/37</td>
<td>11.07–81.04 (mean 28.84±16)</td>
<td>8 Gy x 3 fr. IDL 74–91%</td>
<td>5.5</td>
<td>80</td>
<td>-</td>
<td>5.5</td>
</tr>
</tbody>
</table>
Methods: Cologne protocol for hSRS of brain metastasis

- **Dose prescription:** 27 Gy / 3 fractions / 65% isodose

- **PTV = CTV (GTV + 1-2 mm)**

- **Follow-up interval:** MRI every 3 months

- **Local control failure:**
  - RANO Brain Metastases Criteria (2015)
  - Contrast Enhancement ≥ 30%
  - preferably proven by FET-PET / biopsy
### Results: Patient characteristics

- **total no. of treated patients**: 34
  - 1 brain metastasis: 16
  - 2 brain metastases: 6
  - 3 brain metastases: 5
  - 4 brain metastases: 3
  - 5 brain metastases: 4

- **gender (m : f)**: 13 : 21

- **median age (range, years)**: 55.5 (35 – 84)

- **median follow-up (range, months)**: 8.0 (3 – 28)
Results: Tumor characteristics

- total no. of tumors: 75
- median tumor vol. (range, cm$^3$): 4.6 (0.03 - 24.8)
- median diameter (range, cm): 2.0 (0.4 – 4.3)
Results: Indications for hSRS of brain metastasis

<table>
<thead>
<tr>
<th>Indications</th>
<th>n (patients)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain metastases (≥3 cm)</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>Eloquent localization (close to critical structures)</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Shortening irradiation after surgery</td>
<td>1</td>
<td>2.9</td>
</tr>
<tr>
<td>Multiple lesion with confluent isodose</td>
<td>1</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td><strong>34</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Results: hSRS as salvage treatment

- hSRS as salvage treatment in 29.5% (n=10)

<table>
<thead>
<tr>
<th>Pre-treatment modality</th>
<th>n (lesions)</th>
<th>%</th>
<th>n (patients)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressiv &amp; new lesions after WBRT</td>
<td>24</td>
<td>32</td>
<td>8</td>
<td>23.5</td>
</tr>
<tr>
<td>Recurrence after SRS</td>
<td>1</td>
<td>1.3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Recurrence after 125-Iodine Seed Brachytherapy</td>
<td>1</td>
<td>1.3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>34.6</td>
<td>10</td>
<td>29.5</td>
</tr>
</tbody>
</table>
Results: Kaplan-Meier analysis

Overall survival (OS):

- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%
Results: Kaplan-Meier analysis

Overall survival (OS):
- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%

Progression free survival (PFS):
- 3 mo = 36%
- 6 mo = 28%
- 12 mo = 17%
Results: Kaplan-Meier analysis

Overall survival (OS):
- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%

Progression free survival (PFS):
- 3 mo = 36%
- 6 mo = 28%
- 12 mo = 17%

Local control rate (LC):
- 3 mo = 93%
- 6 mo = 84%
- 12 mo = 75%
Results: Complications

- Radiogenic edema (CTCAE Grade 1-3) \(\frac{3}{34}\) (9%)
- Expansion of tumor cyst / stereotactic puncture (CTCAE Grade 3) \(\frac{3}{34}\) (9%)
## Results: Comparison with literature

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<th>median Tumor Volume (cm³)</th>
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<th>median Follow-up (mo)</th>
<th>LC 6 mo (%)</th>
<th>median OS (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cologne hSRS data 2014-2017</td>
<td>34/75</td>
<td>4.6</td>
<td>27Gy/3 fr. IDL: 65%</td>
<td>7.4</td>
<td>84</td>
<td>6</td>
</tr>
<tr>
<td>Cited studies 2012-2018</td>
<td>234 / 322</td>
<td>12.3 (0.3 – 81.0)</td>
<td>18–40 Gy / 3-10 fr. IDL: 55–91%</td>
<td>6.6  (5.5-7.4)</td>
<td>86</td>
<td>9.4 (5.5-17)</td>
</tr>
</tbody>
</table>
Conclusion

- reasonable results for local tumor control

- promising salvage treatment option for brain metastasis:
  - with large volumes
  - in eloquent areas
  - after irradiation
Thank you for your attention!