Multiple Brain Metastases Stereotactic Radiosurgery - The current practice

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Learning Objectives

• Learn the current practice of the mBMs radiosurgery management
• Learn safe, optimal and efficient mBMs SRS strategies
• Learn AI-based planning and follow-up software development for mBMs SRS.
Management of Brain Metastases

**SIMT**

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Improved treated metastasis control</td>
<td>• Increase rate of new CNS metastases</td>
</tr>
<tr>
<td>• Delivered over 1-5 days</td>
<td>• Complex treatment planning</td>
</tr>
<tr>
<td>• Decreased dose to normal brain</td>
<td>• Requires advanced technology</td>
</tr>
<tr>
<td>• Avoids hippocampi</td>
<td>• Increased daily treatment delivery time vs WBRT</td>
</tr>
<tr>
<td>• Less neurocognitive function decline vs. WBRT</td>
<td>• Complex patient setup</td>
</tr>
<tr>
<td></td>
<td>• Treatment planning requires MRI</td>
</tr>
<tr>
<td></td>
<td>• Challenges with insurance coverage</td>
</tr>
</tbody>
</table>

Moravan et al., Current Multidisciplinary Management of Brain Metastases, Cancer, April 1, 2020, 1390-1406

**CCTG CE.07 Phase III Trial**

- STEREOTACTIC RADIOSURGERY COMPARED WITH WHOLE BRAIN RADIOTHERAPY (WBRT) FOR **5-15 BRAIN METASTASES**
  - The largest target < 2.5 cm dia.
  - Total Volume ≤ 30 cm³

<table>
<thead>
<tr>
<th>Brain Metastasis volume</th>
<th>Dose Prescribed to Tumour Margin</th>
<th>Brainstem Metastasis volume</th>
<th>Dose Prescribed to Tumour Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions &lt; 4 cc</td>
<td>22 Gy</td>
<td>Lesions 4-10 cc</td>
<td>14-16 Gy</td>
</tr>
<tr>
<td>Lesions 4-10 cc</td>
<td>18-20 Gy</td>
<td>Lesions 1-4 cc</td>
<td>16-18 Gy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lesions &lt; 1 cc</td>
<td>18-20 Gy</td>
</tr>
</tbody>
</table>
CCTG CE.07 Phase III Trial – Target definitions (ICRU50, 62)

- **Gross Tumour Volume (GTV):**
  - the contrast enhancing tumour on T1 with contrast scans.
  - Surrounding blood and edema will be excluded
  - Numbering GTV1, GTV2, GTV3 from the most cranial axial and from to back in same slice

- **Clinical Target Volume (CTV):** No additional margin

- **Planning Target Volume (PTV):**
  - 1 mm isotropic margin can be added when non-invasive immobilization is used for multiple-isocenter SRS for 6D setup. whereas 2 mm margins can be used with 3D setup correction.

- **Total Brain:** the brain minus the summed volume of the GTVs
  - V12 Gy < 30 cm³ (30 cc).
  - Adjacent lesions: V12 Gy < 8.5 cm³.
    If this volume is exceeded, the prescription doses to the adjacent metastases must be lowered until this constraint is met.
  - Median brain dose < 8 Gy.

- **Optic structures:** The maximum point dose < 9-10 Gy

- **Brainstem:** V12 Gy < 1 cm³ (the brainstem minus GTV)
Recurrent BMs

Brain Metastasis Velocity

\[ \text{BMV} = \frac{\text{Total number of new brain metastases since upfront SRS}}{\text{Time interval (in years) since upfront SRS}} \]

- Farris et al. 737 BM single institution + 2000 BM multi-institution validation
- BMV \( \geq 4 \) BMs/year: 7-month shortening in median survival as compared to BMV of less than 4 BMs/year (\( P < 0.0001 \))
- BMV \( \geq 4 \) BMs/year: optimizing intracranial control with combined HA-WBRT plus SRS may prevent neurologic death from being a primary contributor to survival.

HyTec

HyTec Introduction

High Dose per Fraction, Hypofractionated Treatment Effects in the Clinic (HyTec): An Overview

Jimn Grinn, PhD, Lawrence E. Marks, MD, Andrew Jackson, PhD, Brian D. Kavanagh, MD, Jinyu Xue, PhD, and Ellen Yorke, PhD


Table 2 Summary of NCT13志 estimates after SRS/WBRT from the HYTEC report

<table>
<thead>
<tr>
<th>Occurrence</th>
<th>Volume ( \leq 5 \text{ cm}^3 )</th>
<th>Volume ( \leq 10 \text{ cm}^3 )</th>
<th>Volume ( &gt; 10 \text{ cm}^3 )</th>
<th>Rate ( ^\circ )</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Tumor</td>
<td>50%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>10%</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Side-effect</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Intraocular</td>
<td>25%</td>
<td>30%</td>
<td>35%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Extraglandular</td>
<td>35%</td>
<td>40%</td>
<td>45%</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Extranodal</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Metastasis</td>
<td>20%</td>
<td>25%</td>
<td>30%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Ocular</td>
<td>25%</td>
<td>30%</td>
<td>35%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Retina</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>

UC San Diego Health
Dose-Adapted Approach SIMT

- Group 1: 1fx vs. Group 2: 5fx
- Decision Conditions for 5fx:
  - any PTV > 3 cm in max dimension or in brainstem
  - After 1fx plan V12 > 20 cm³
- Report
  - Survival, local and distant control
  - Toxicity
  - Neurocognition
- Conclusion
  - Demonstrates the dose-adapted SIMT SRS strategy can be used to effectively & efficiently tx 4-10 mets

UC San Diego Health

SIMT

- Purpose: Evaluate the impact of the distance on SIMT vs. local failure
- Total 315 Pts (1087 BM): SIMT SRS/SRT: 140 Pts (708 BM)
- Median follow-up:
  - 13.9 months for SIMT
  - 11.9 months for SIST
- One-year freedom from local recurrence
  - 94% in SIMT
  - 87% in SIST
- Median distance to isocenter 4.7 cm
- Conclusion
  - SIMT achieved high local control rates irrespective of distance to the isocenter, supporting efficacy of SIMT.
Example SIMT Timeline

- Optimization & calculation after the target delineation: **5-10 min**
- No limit for # of targets and off-axis distance
- Collision check is pre-configured
- Treatment from CBCT: **< 10-30 min**

<table>
<thead>
<tr>
<th>HyperArc</th>
<th>8:40 min</th>
<th>22 Gy (7SSMU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.5 MU</td>
<td>1 T2-360.1C0</td>
</tr>
<tr>
<td>2</td>
<td>23.5 MU</td>
<td>2 T2-360.1C0</td>
</tr>
<tr>
<td>3</td>
<td>23.5 MU</td>
<td>3 T2-360.1C0</td>
</tr>
<tr>
<td>4</td>
<td>23.5 MU</td>
<td>4 T2-360.1C0</td>
</tr>
</tbody>
</table>

Single isocenter for 14 multiple metastases

Quality Metrics

Vergalasova et al., Multi-Institutional Dosimetric Evaluation of Modern Day Stereotactic Radiosurgery (SRS) Treatment Options for Multiple Brain Metastases, Frontiers in Oncology, 2019, Vol. 9, Article 483
Workflow

- Dedicated workflow with enforce safety barriers
- Standardized nomenclature
  - TG263 structures
  - Target labelling
  - Previous tx targets
- Standards & Guideline including treatment approach for the SIMT
- Handling the follow-up MRI
- Task Group No. 362 - Multi-lesion Stereotactic Radiosurgery – on-going

Manger et al., Medical Physics, 42 (5), 2449-2461 (2015)