SRS Using Multiple Isocenters

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Outline

1. Clinical Goals
2. Treatment planning
3. Conformality
4. Setup uncertainties
5. Conclusions
Clinical Goals

- SRS: Primary goal is geometric localization of the dose
- Single, ablative dose delivered to a highly localized area
- No (or limited) fractionation affects
- Minimize dose to normal brain and particularly to the optics, brainstem, and other regions determined by the physicians. Eg. Motor strip or hippocampus
- Avoid radionecrosis

![Graph showing cell survival and fractionation effects](image)

**Biologically:**
(8 Gy x 1) > (2 Gy x 4)

**Biologically: equivalent dose calc fails at high single fraction doses!**
Radionecrosis

Does Stereotactic Radiosurgery Have a Role in the Management of Patients Presenting With 4 or More Brain Metastases?

Stereotactic radiosurgery (SRS) and whole brain radiation therapy (WBRT) are effective treatments for management of brain metastases. Prospective trials comparing the 2 modalities in patients with fewer than 4 brain metastases demonstrate that overall survival (OS) is similar. Intracranial failure is more common after SRS, while WBRT is associated with neurocognitive decline. As technology has advanced, fewer technical obstacles remain for treating patients with 4 or more brain metastases with SRS, but level I data supporting its use are lacking.

Observational prospective studies and retrospective series indicate that in patients with 4 or more brain metastases, performance status, total volume of intracranial disease, histology, and rate of development of new brain metastases predict outcomes more accurately than the number of brain metastases. It may be reasonable to initially offer SRS to some patients with 4 or more brain metastases. Initiating therapy with SRS avoids the acute and late sequelae of WBRT. Multiple phase III trials of SRS vs WBRT, both current and ongoing, are directly comparing quality of life and OS for patients with 4 or more brain metastases to help answer the question of SRS appropriateness for these patients.

**KEY WORDS:** Brain metastases, Stereotactic radiosurgery, Whole brain radiation

**CLINICAL INVESTIGATION**

IRRADIATED VOLUME AS A PREDICTOR OF BRAIN RADIONECROSIS AFTER LINEAR ACCELERATOR STEREOTACTIC RADIOSURGERY

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Results: Sixty-three patients were reviewed, with a total of 173 lesions. Most patients (63%) had received previous whole-brain irradiation. Mean prescribed SRS dose was 18 Gy. Symptomatic RN was observed in 10% and asymptomatic RN in 4% of lesions treated. Multivariate regression analysis showed V8 Gy–V16 Gy to be the most predictive of symptomatic RN (p < 0.0001). Threshold volumes for significant rise in RN rates occurred between the 75th and 90th percentiles, with a midpoint volume of 10.45 cm³ for V10 Gy and 7.85 cm³ for V12 Gy. Conclusions: Analysis of patient and treatment variables revealed V8 Gy–V16 Gy to be the best predictors for RN using linear accelerator–based single-fraction SRS for brain metastases. We propose that patients with V10 Gy >10.5 cm³ or V12 Gy >7.9 cm³ be considered for hypofractionated rather than single-fraction treatment, to minimize the risk of symptomatic RN. © 2010 Elsevier Inc.

**TABLE 3. Rate of radionecrosis for V10 Gy and V12 Gy volumes**

<table>
<thead>
<tr>
<th>Volume (cm³)</th>
<th>Radionecrosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V10 Gy</td>
<td></td>
</tr>
<tr>
<td>&lt;1.6</td>
<td>4.7</td>
</tr>
<tr>
<td>1.6–2.6</td>
<td>11.9</td>
</tr>
<tr>
<td>2.6–4.5</td>
<td>34.6</td>
</tr>
<tr>
<td>&gt;4.5</td>
<td>68.8</td>
</tr>
<tr>
<td>V12 Gy</td>
<td></td>
</tr>
<tr>
<td>&lt;1.6</td>
<td>4.7</td>
</tr>
<tr>
<td>1.6–4.7</td>
<td>11.9</td>
</tr>
<tr>
<td>4.7–10.8</td>
<td>34.6</td>
</tr>
<tr>
<td>&gt;10.8</td>
<td>68.8</td>
</tr>
</tbody>
</table>

Abbreviations: V10 Gy, V12 Gy = volume of brain receiving 10 Gy and 12 Gy, respectively.

The cumulative volume of brain receiving 12 Gy (V12) is consistently used as a predictor of radiation necrosis after SRS (Table 2). The type of lesions treated across multiple series included patients with arteriovenous malformations, brain metastases, benign brain tumors, and patients who had received previous WBRT. Radiation necrosis occurs at a median of 10 to 12 mo after initial SRS. Most of the data in these series were generated from patients with a small number of brain metastases, in whom a dominant metastasis represented the largest portion of the V12. Solitary metastases with a V12 of less than 8 to 10 cc have low rates of radiation necrosis (<10%). Beyond this threshold, rates of radiation necrosis increase, approaching 20% to 50%. In the setting of multiple small metastases that sum to a volume of >10 cc, the rate of radiation necrosis may be significantly less, compared to a dominant lesion that occupies the majority of the treated volume. The upcoming CE.7 randomized trial limits any contiguous V12 to less than 8.5 cc, but constrains the cumulative brain V12 to 30 cc.24
Treatment planning

- Treatment planning can be performed with:
  - Cones
  - MLC
  - DCA
  - IMRT
  - VMAT
- For $n = 1: \text{num lesions}$
  - treatment planning
  - paperwork/documentation
- End
How to select modality

- Size and shape of lesions
- Planning constraints
  - OARs in close proximity
  - Dose uniformity
- SIB
Cones

- Classic forward (manual) optimization
- Cone size
- Arc angles
- Couch angles
- Beam weights
- Templates/scripting

Planning times can be fast for simple spheres, longer for multiple isocenters or regions of avoidance.
Linac IMRT and VMAT

DCA: less homogeneous dose

IMRT to Cavity with SIB

VMAT
Cones vs VMAT

- Hsu et al Rad Onc 2017
- Single lesion comparison
Multiple Targets and Isocenters

- Repeat the planning process for each target
- Small, spherical mets are most common for 3+ lesions → Cones most common
- Planning is incremental
- Scripting and templates can help with the more general planning steps
- Proton SRS is outside the scope of this talk…
Comparisons: DCA vs VMAT

DCA
Multi Iso

VMAT
Multi Iso

VMAT
Single Iso

Gavaert, et al 2016 Rad Onc
Comparisons: GK vs VMAT/HA

Vergalasova et al, Front Onc 2019
Comparisons: GK vs VMAT/HA
All data so far has assumed equal dose uncertainties for multiple isocenters versus a single.

Uncertainties that change little between single and multi-isocenter:
- Planning, CT, Segmentation
- Setup uncertainties can vary due to rotational uncertainties
- Immobilizations have a limit of uncertainties
- Dose model commissioning?

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### Uncertainties

<table>
<thead>
<tr>
<th>Dimension</th>
<th>mGTC</th>
<th>Intrafraction VMP</th>
<th>UJS</th>
<th>mGTC</th>
<th>Interfraction VMP</th>
<th>UJS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral (LAT), mm</td>
<td>-0.12±0.37</td>
<td>-0.11±0.29</td>
<td>-0.11±0.28</td>
<td>-0.04±0.55</td>
<td>0.58±0.61</td>
<td>0.69±0.78</td>
</tr>
<tr>
<td>Ant/Post (AP), mm</td>
<td>-0.09±0.37</td>
<td>-0.03±0.21</td>
<td>0.01±0.26</td>
<td>0.09±1.29</td>
<td>0.40±0.48</td>
<td>0.46±0.78</td>
</tr>
<tr>
<td>Cran/Caudal (CC), mm</td>
<td>0.11±0.41</td>
<td>0.13±0.30</td>
<td>0.05±0.58</td>
<td>0.09±1.13</td>
<td>-0.47±0.95</td>
<td>-0.01±1.47</td>
</tr>
<tr>
<td>Pitch (about LAT), °</td>
<td>0.14±0.20</td>
<td>-0.02±0.14</td>
<td>-0.05±0.48</td>
<td>0.07±1.07</td>
<td>-0.42±0.38</td>
<td>-0.41±0.95</td>
</tr>
<tr>
<td>Yaw (about AP), °</td>
<td>0.10±0.50</td>
<td>0.06±0.27</td>
<td>0.02±0.46</td>
<td>-0.08±0.51</td>
<td>0.06±0.38</td>
<td>0.18±0.80</td>
</tr>
<tr>
<td>Roll (about CC), °</td>
<td>0.06±0.25</td>
<td>-0.02±0.15</td>
<td>0.02±0.49</td>
<td>0.05±0.59</td>
<td>-0.03±0.40</td>
<td>0.21±0.70</td>
</tr>
</tbody>
</table>

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*Winey et al JACMP 2015*
Single vs Multiple Isocenters: VMAT

- Prentou et al JACMP 2020
- 10 patients, 36 lesions
Conclusions: multiple isocenters

- Can be more conformal
- No PTV
- Less integral dose
- Cones have less QA (no moving parts)
- Repeat QA for each isocenter (likely same for both techniques)
- Patient time on the treatment table can be long — increased discomfort and potential for motion
- Treatment planning time can be longer, particularly when running multiple optimizations
- Repeated paperwork and plan checks
- Machines are more accurate with the ability to check intrafraction position
- And! newer algorithms, machines, and delivery techniques