Implementing Novelties in the Clinic MO-D-Celestin-2

# Multiple Brain Metastases Stereotactic Radiosurgery - The current practice

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RETHINKING MEDICAL PHYSICS

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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.

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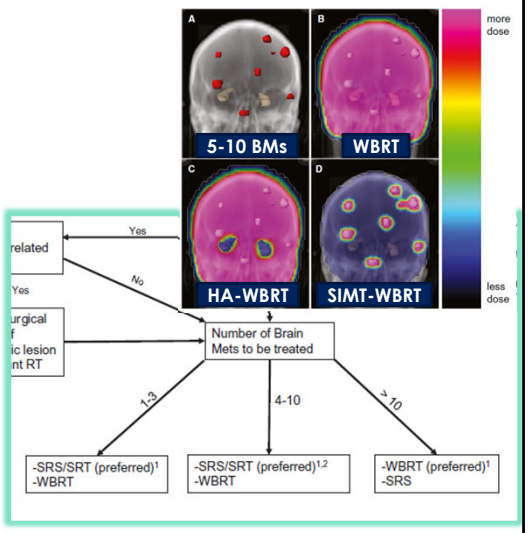
# Management of Brain Metastases

## SIMT

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




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

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# 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 $cm^3$

| Brain Metastasis volume | Dose Prescribed to Tumour Margin |
|---|---|
| Lesions < 4 cc | 22 Gy |
| Lesions 4-10 cc | 18-20 Gy |

| Brainstem Metastasis volume | Dose Prescribed to Tumour Margin |
|---|---|
| Lesions 4-10 cc | 14-16 Gy |
| Lesions 1- 4 cc | 16-18 Gy |
| Lesions < 1 cc | 18-20 Gy |

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## 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.

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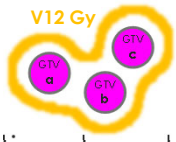
## CCTG CE.07 Phase III Trial

- **Total Brain:** the brain minus the summed volume of the GTVs
  - V12 Gy < 30 $cm^3$ (30 cc).
  - Adjacent lesions: V12 Gy < 8.5 $cm^3$.

    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 $cm^3$** (the brainstem minus GTV)

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# Recurrent BMs

Brain Metastasis Velocity

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

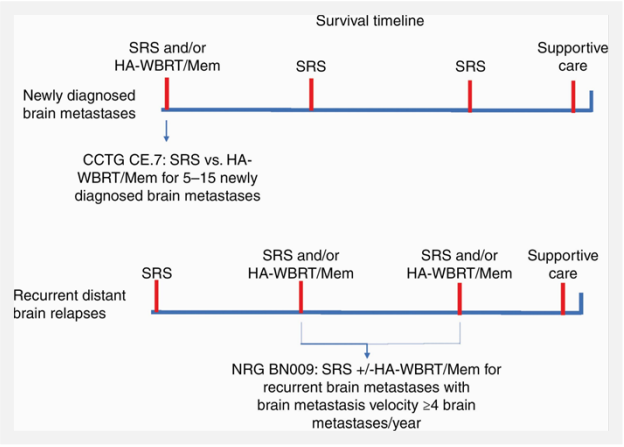
- Farris et al. 737 BM single institution + 2000 BM muti-institution validation
- BMV 4 ≥ BMs/year: 7-month shortening in median survival as compare to BMV of less than 4 BMs/year (*P*<.0001)
- BMV 4 ≥ BMs/year: optimizing intracranial control with combined HA-WBRT plus SRS may prevent neurologic death from being a primary contributor to survival.

v26 Neuro-Oncology Advances
3(S5), v26–v34, 2021 | https://doi.org/10.1093/noajnl/vdab126

**Advances in radiotherapy for brain metastases**

**Vinai Gondi, Jacquelyn Meyer, and Helen A. Shih**

*Northwestern Medicine Cancer Center Warrenville and Proton Center, Warrenville, Illinois, USA (V.G.); University of Wisconsin-Madison, Madison, Wisconsin, USA (J.M.); Department of Radiation Oncology, Massachusetts General Hospital, Boston, Massachusetts, USA (H.A.S.)*

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# HyTec

HyTEC Introduction

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

**Jimm Grimm, PhD,*,† Lawrence B. Marks, MD,‡ Andrew Jackson, PhD,§ Brian D. Kavanagh, MD,‖ Jinyu Xue, PhD,¶ and Ellen Yorke, PhD§**

Received Oct 2, 2020. Accepted for publication Oct 8, 2020.

**Table 2** Summary of NTCP estimates after SRS/SBRT from the HyTEC reports

| Organ | Volume segmented | Number of fractions | Endpoint | Dose (Gy) or dose-volume parameters | Rate (%) | Notes |
|---|---|---|---|---|---|---|
| Brain; for metastasis | Total brain including target | 1 | Symptomatic necrosis | $V_{12Gy} \leq 5\ cm^3$ | 10% | From Table 3 and Figs. 4 and 5 in paper. |
| | | 1 | Symptomatic necrosis | $V_{12Gy} \leq 10\ cm^3$ | 15% | Consistent with QUANTEC. |
| | | 1 | Symptomatic necrosis | $V_{12Gy} \leq 15\ cm^3$ | 20% | Prior whole brain RT appears to not markedly |
| | | 3 | Edema or necrosis | $V_{20Gy} \leq 20\ cm^3$ | ≤ 10% | increase risks in most reports (with the |
| | | 3 | Edema or necrosis | $V_{20Gy} \leq 30\ cm^3$ | ≤ 20% | exception of brain stem).† However, repeat |
| | | 5 | Edema or necrosis | $V_{24Gy} \leq 20\ cm^3$ | ≤ 10% | SRS/SBRS to the same area has been |
| | | 5 | Edema or necrosis | $V_{24Gy} \leq 30\ cm^3$ | ≤ 20% | associated with markedly increased risks. |

HyTEC Organ-Specific Paper: Brain and Eye

**Tumor Control Probability of Radiosurgery and Fractionated Stereotactic Radiosurgery for Brain Metastases**

**Kristin J. Redmond, MD,* Chengcheng Gui, BS,* Stanley Benedict, PhD,† Michael T. Milano, MD,‡ Jimm Grimm, PhD,§ J. Austin Vargo, MD,‖ Scott G. Soltys, MD,¶ Ellen Yorke, PhD,# Andrew Jackson, PhD,# Issam El Naqa, PhD,** Lawrence B. Marks, MD,†† Jinyu Xue, PhD,‡‡ Dwight E. Heron, MD, MBA,§§ and Lawrence R. Kleinberg, MD***

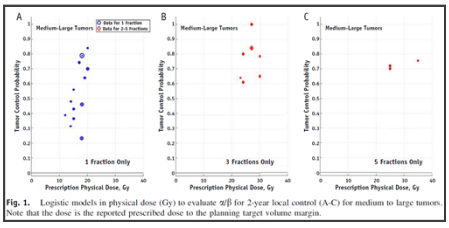


Fig. 1. Logistic models in physical dose (Gy) to evaluate α/β for 2-year local control (A-C) for medium to large tumors. Note that the dose is the reported prescribed dose to the planning target volume margin.

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# 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 $cm^3$
- 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

Advances in Radiation Oncology (2021) 6, 100760

advances in radiation oncology
www.advancesradonc.org

Scientific Article

**Outcomes in Patients With 4 to 10 Brain Metastases Treated With Dose-Adapted Single-Isocenter Multitarget Stereotactic Radiosurgery: A Prospective Study**

Grace J. Kim, MD, PhD,[a,*] Evan D. Buckley, MS,[b] James E. Herndon, PhD,[b] Karen J. Allen, NP,[a] Tyketra S. Dale, NP,[a] Justus D. Adamson, PhD,[a] Lam Lay, BA,[a] William M. Giles, PhD,[a] Anna E. Rodrigues, PhD,[a] Zhiheng Wang, PhD,[a] Chris R. Kelsey, MD,[a] Jordan A. Torok , Jr,MD,[a] Junzo P. Chino, MD,[a] Peter E. Fecci, MD, PhD,[c] John H. Sampson, MD, PhD, MBA,[c] Carey K. Anders, MD,[d] Scott R. Floyd, MD, PhD,[a] Fang-Fang Yin, PhD,[a] and John P. Kirkpatrick, MD, PhD[a,c]

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# 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.

Radiotherapy and Oncology 159 (2021) 168–175

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journal homepage: www.thegreenjournal.com

ELSEVIER

Original Article

Distance to isocenter is not associated with an increased risk for local failure in LINAC-based single-isocenter SRS or SRT for multiple brain metastases

Johannes Kraft[a,b,*], Janita E. van Timmeren[a], Michael Mayinger[a], Simon Frei[a], Kim Borsky[a], Luisa Sabrina Stark[a], Jerome Krayenbuehl[a], Mariangela Zamburlini[a], Matthias Guckenberger[a], Stephanie Tanadini-Lang[a], Nicolaus Andratschke[a]

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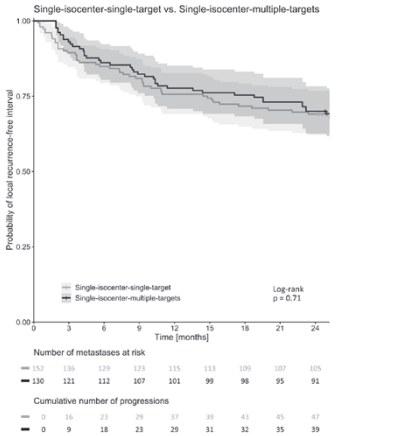


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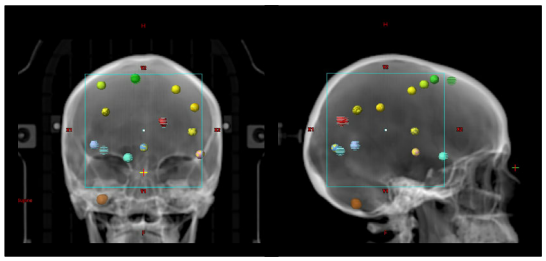
# Example SIMT Timeline

- 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***



Single isocenter for 14 multiple metastases

| | | | |
|---|---|---|---|
| HyperArc | 8:40 min | 22 Gy (7555MU) | 1 HA PTV1.2 1:53:02 PM; 1 CWG180.1C0 1:53:02 PM; 2 CCWG179C45 1:55:21 PM; 3 CCWG0C315 1:56:56 PM; 4 CWG180.1C270 1:58:21 PM |

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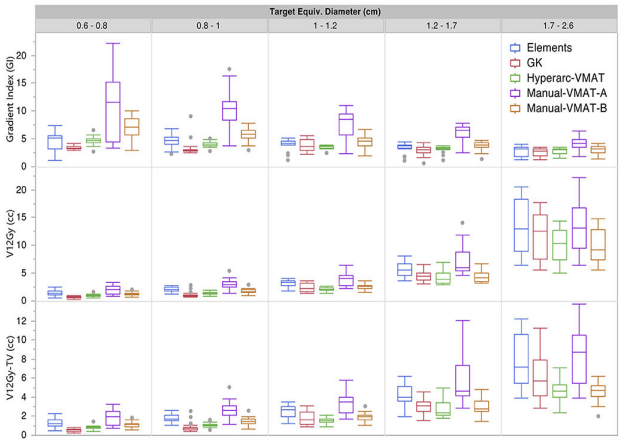
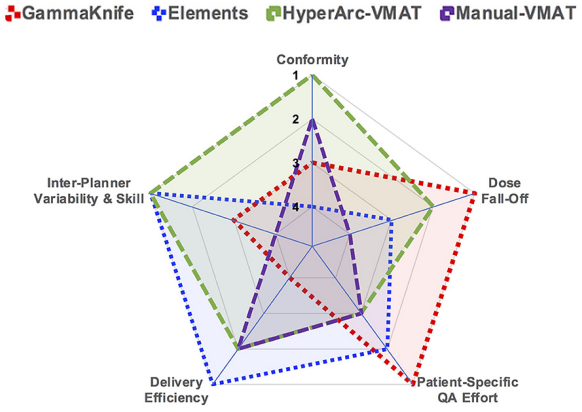
# Quality Metrics




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

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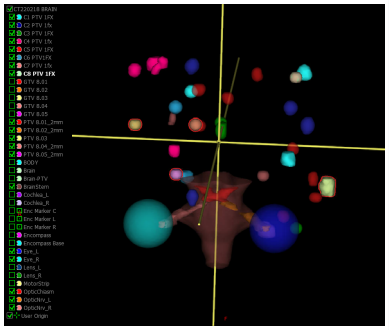
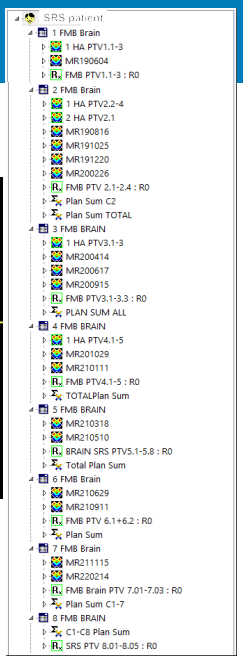
# Workflow

- 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



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

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