# NRG CC009

## Phase III Trial of Stereotactic Radiosurgery versus Hippocampal Avoidant WBRT for Small Cell Lung Cancer Brain Metastases

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Rad Onc: Paul Brown, MD Comp Effectiveness: Mark Mishra, MD
Stats: Stephanie Pugh, PhD

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# Background

- Whole-brain radiotherapy is standard of care for small-cell lung cancer brain metastases
  - Prior brain metastasis trials of SRS vs WBRT or HA-WBRT did not include small-cell lung cancer
- Cognitive toxicity from WBRT
  - Mitigated with SRS, memantine, hippocampal avoidance
  - Historic objections to SRS in small-cell related to concern for short interval CNS progression impacting OS

# Background

- Emerging evidence re: SRS for SCLC brain mets
  - Serizawa et al[2]: SRS SCLC n=34 vs. NSCLC n=211
    Comparable OS, CNS control, neurologic death
  - Yomo, Hayashi[3]: SRS SCLC n=70 (46 without prior PCI/WBRT)
    Med OS 7.8 mos
  - NCDB[4]: N=200 SRS vs. WBRT for SCLC brain mets
    Favorable OS with SRS overall and in matched data
  - Cifarelli et al[5]: N=293 SRS (61 without prior PCI/WBRT)
    Median OS 7.5 mo with upfront SRS, necrosis rate 5%

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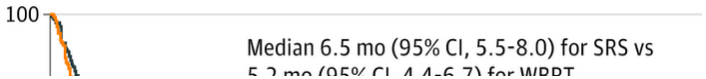
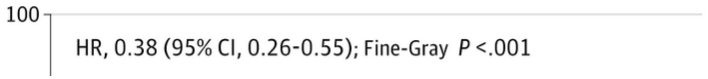
[1]Rusthoven, *JAMA Oncology* 2020 [2]Serizawa, *JNS* 2002,
[3]Yomo, *BMC Cancer* 2015, [4]Robin, *Lung Cancer* 2018, [5]Cifarelli, *Neurosurgery* 2019

# First-line Radiosurgery vs Whole-Brain Radiotherapy for Small Cell Lung Cancer Brain Metastases: The FIRE-SCLC Cohort Study

Rusthoven et al., *JAMA Oncology*. 2020 Jun 4




# Stereotactic radiosurgery versus whole brain radiotherapy in patients with intracranial metastatic disease and small-cell lung cancer: a systematic review and meta-analysis

*Karolina Gaebe, Alyssa Y Li, Amy Park, Ambica Parmar, Benjamin H Lok, Arjun Sahgal, Kelvin K W Chan, Anders W Erickson, Sunit Das*

## Summary

**Background** Patients with small-cell lung cancer (SCLC) are at high risk for intracranial metastatic disease (IMD). Although stereotactic radiosurgery (SRS) has supplanted whole brain radiotherapy (WBRT) as first-line treatment for IMD in most solid cancers, WBRT remains first-line treatment for IMD in patients with SCLC. We aimed to evaluate the efficacy of SRS in comparison with WBRT and assess treatment outcomes following SRS.

*Lancet Oncol* 2022; 23: 931–39
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https://doi.org/10.1016/
S1470-2045(22)00271-6

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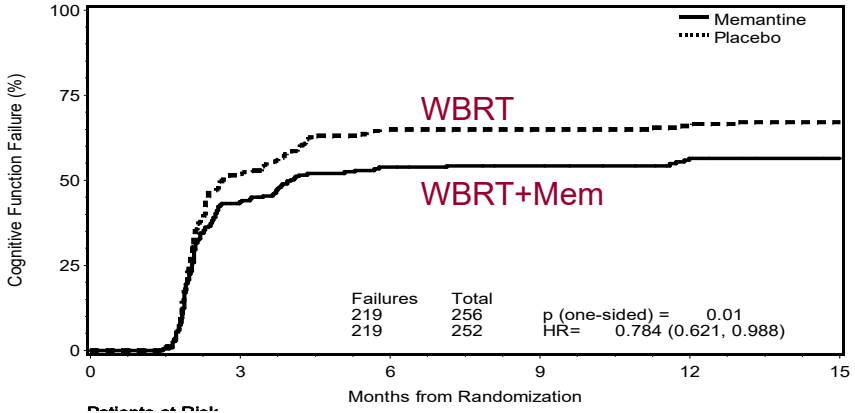
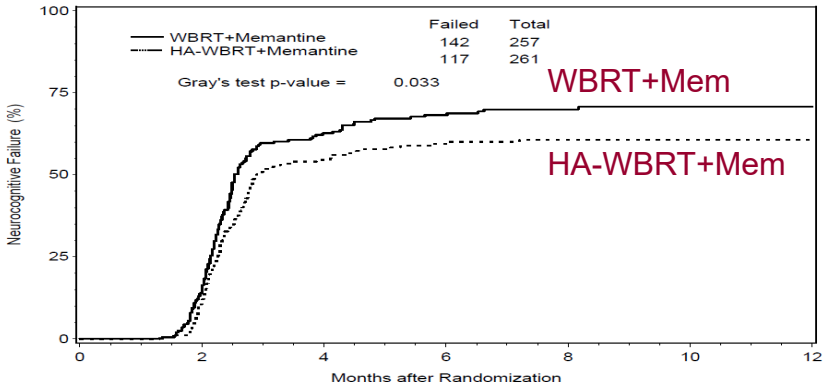
- After SRS, 34% underwent salvage SRS vs 16% salvage WBRT
- Leptomeningeal progression (10.8%), neurological mortality (12.4%)

# Reinventing the Wheel: Safer Delivery of WBRT

- Practice-changing evidence re: WBRT




RTOG 0614[1]:

Hazard ratio of memantine=0.78

NRG CC001[2]:

Hazard ratio of hippocampal avoidance added to memantine=0.74

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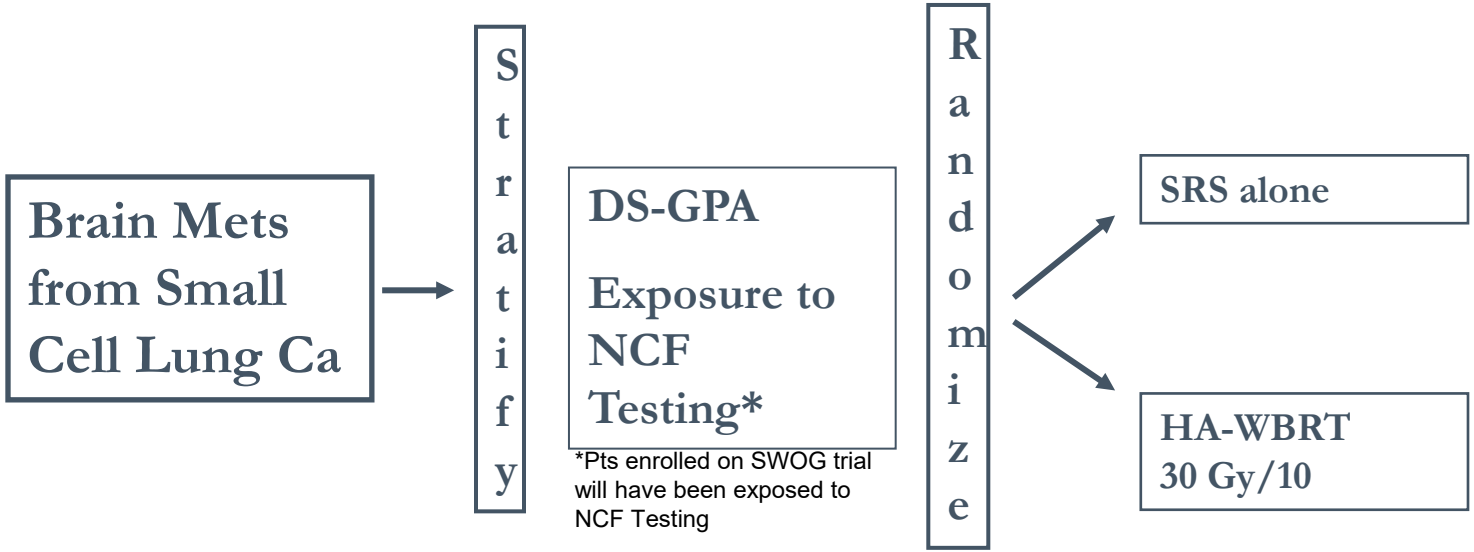
[1]Brown et al. Neuro-Onc 2013 [2]Brown, Gondi et al. JCO 2020

# NRG CC009: Phase III Trial Stereotactic Radiosurgery versus Hippocampal-Avoidant Whole-Brain Radiotherapy for 10 or Fewer Brain Metastases from Small Cell Lung Cancer

PIs: Chad Rusthoven (Univ of Colorado) + Vinai Gondi (Northwestern)

Basic Eligibility: Small cell lung cancer; ≤10 brain mets≤3cm; total vol 30cc; KPS≥70




Sample Size: 200 patients

Primary endpt: Time to cognitive failure--HVLT-R, COWA, and TMT A and B

Basic Statistical Design:
Cognitive fxn failure 58.8% at 6 mos with HA-WBRT+mem vs. 41.8% at 6 mos with SRS.
150 analyzable pts

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# Logistics and Trial Accrual

- Collaboration:
  - Support from SWOG, Alliance
  - SWOG MRI surveillance +/- PCI trial: brain met failures on observation arm can dual-enroll

**February 2021: Protocol Activated**
**As of 7/1/22, N=28 enrolled**
**N=15 in past 6 months (surpassed accrual in 2021)**

March 2022 (13 months after activation):
Trial activated at 77 sites, pending activation at 209 sites
NRG CC003: Trial activated 140 sites one year into activation

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