CNS Metastasis: Evolving Multidisciplinary Tumor Board Conversations, Radiation Oncology

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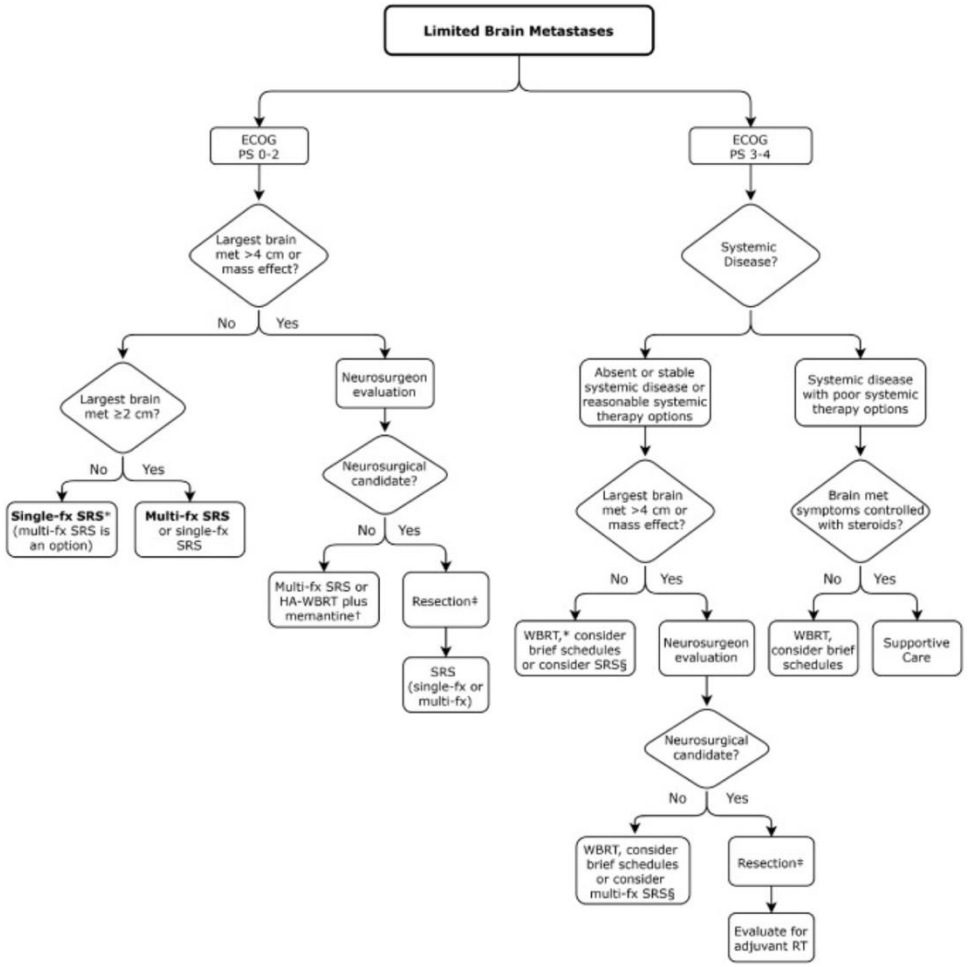
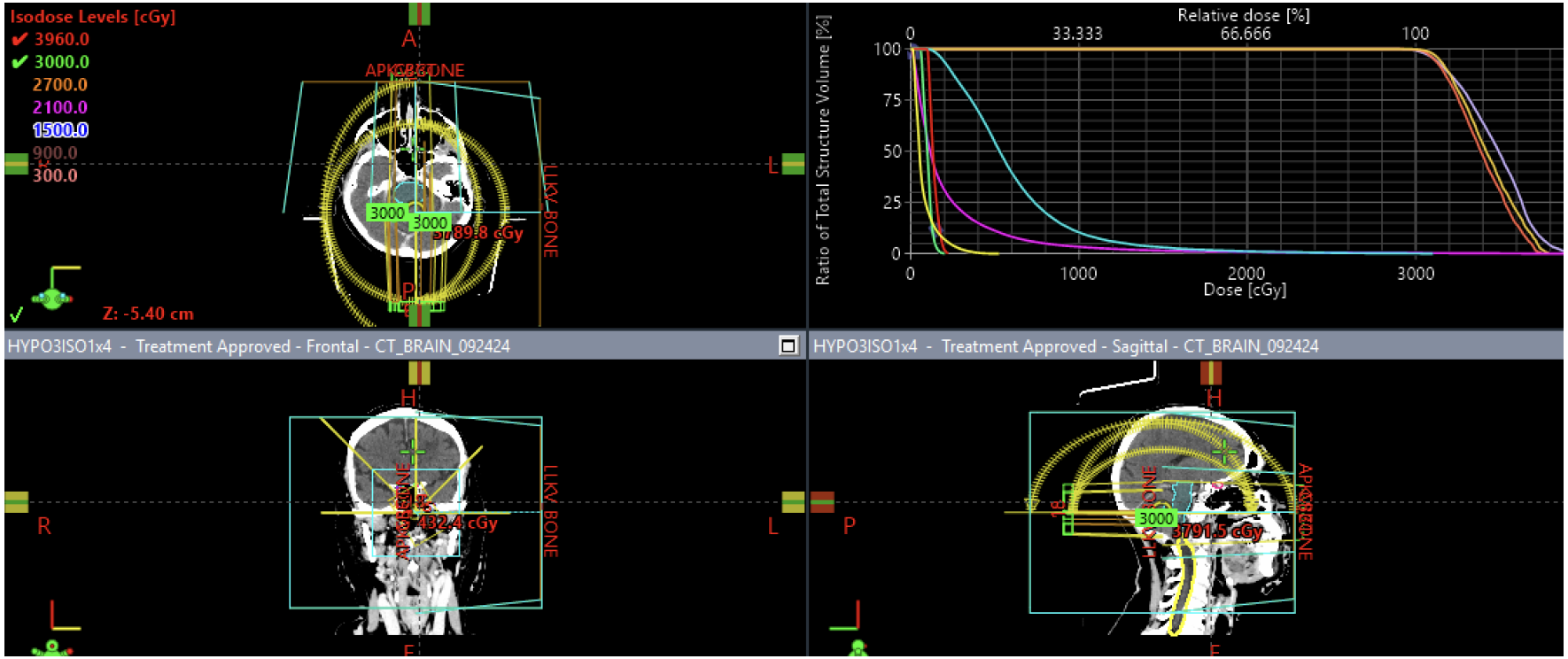
Multi-Disciplinary Consideration with Brain Metastases



- Limited vs. extensive brain metastases
- Performance status
- Size/ NSG evaluation
- Size single vs. multifractionated SRS
- Systemic burden

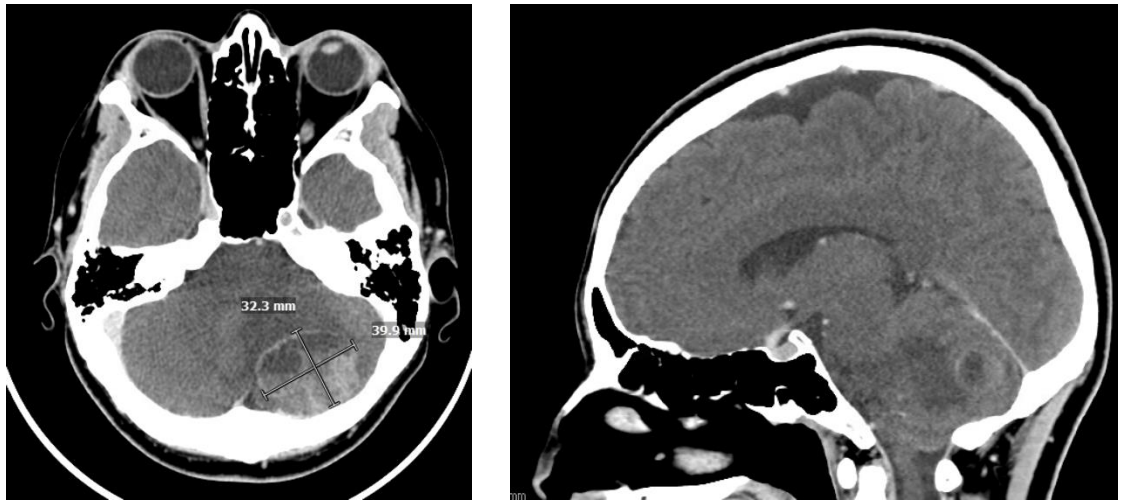
Stereotactic Radiosurgery

- Evolving role of SRS
- Single vs. multi-fractionated
- Radiation necrosis
- Role with CNS penetrating systemic therapy
- Evolving role
  - HA-WBRT
  - CSI



Case Presentation – Multi-Disciplinary management

- Case: 38 y/o with triple negative T2N1 breast cancer presented with nausea/vomiting headache



- CT brain: 4.2 x 3.4 x 2.5 cm hemorrhagic cystic left cerebellar mass with mass effect and edema, effacement of the 4th ventricle. Inferior displacement of the cerebellar tonsils

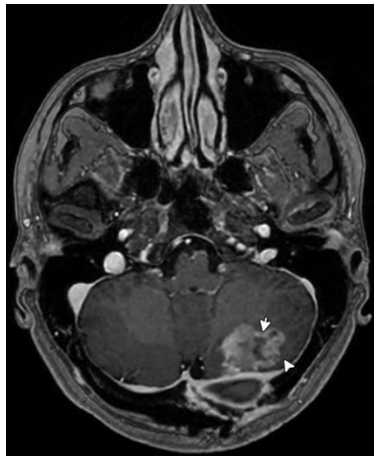
Management: Surgery and Post-operative SRS

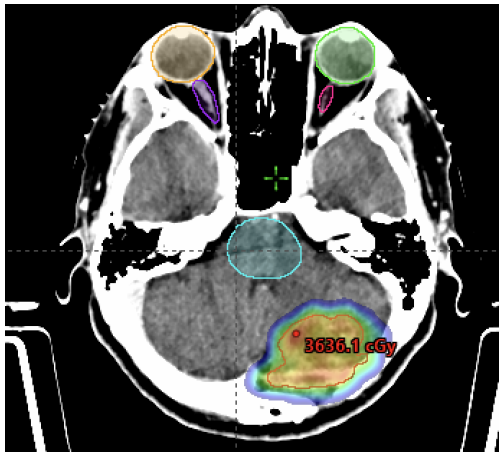
- Size / location / symptoms
- Pre-treatment edema/mass effect
- Cystic component
- Systemic therapy / Immunotherapy
- Hypofractionated treatment

Comparing Stereotactic Radiosurgery to Fractionated Stereotactic Radiosurgery for Patients with Cancer that has Spread to the Brain (NRG-BN013)

Case Presentation – Post-Operative RT

- 12 days post-operatively: Along the lateral surgical cavity, new more solid nodular heterogeneously enhancing lesion at 1.8 x 1.3 cm

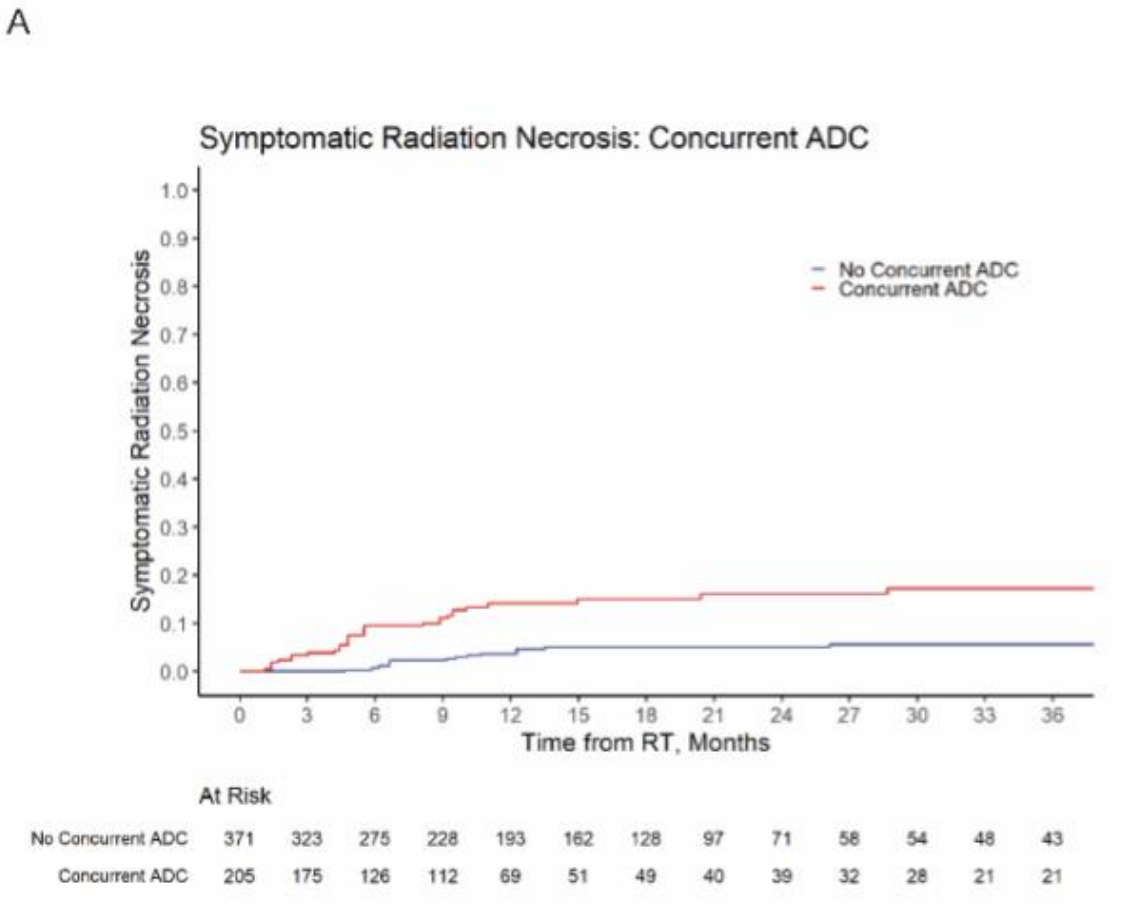




- Expedited post-operative SRS – 5 fractions
- Systemic therapy: Sacituzumab govitecan

Radiation Necrosis Risk with Concurrent ADC

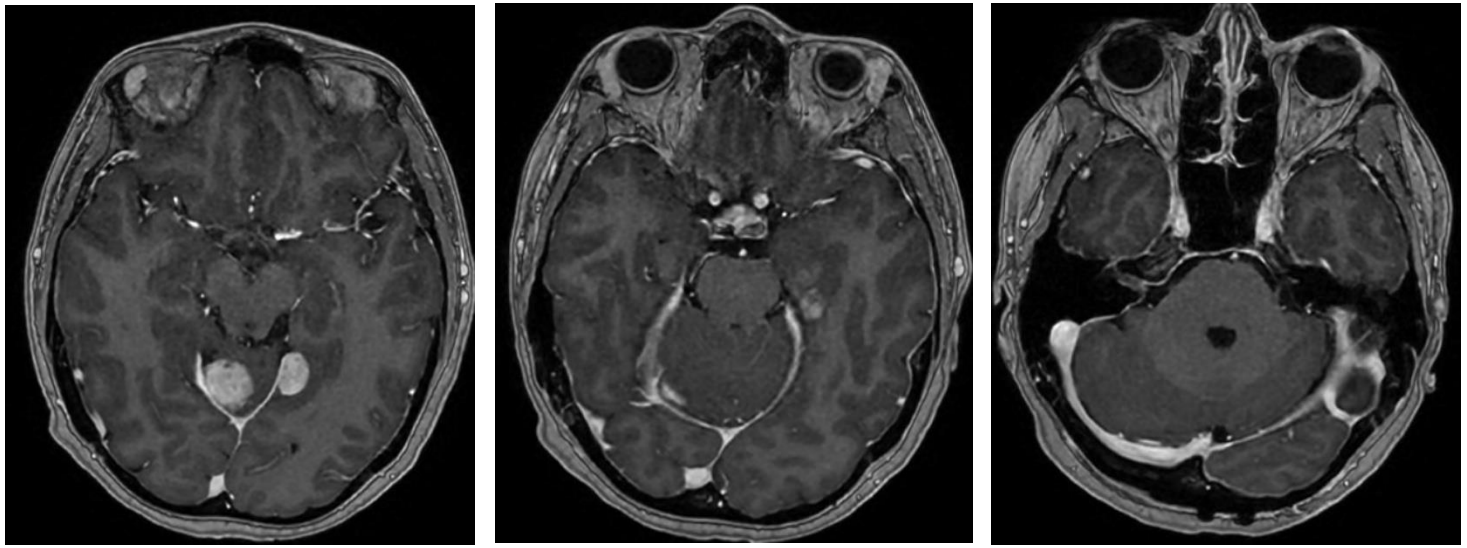
- n=101 patients treated by concurrent or sequential RT and ADC
  - Trastuzumab-deruxtecan (T-DXd)
  - Trastuzumab emtansine (T-DM1)
  - Sacituzumab govitecan (SG)
  - Enfortumab vedotin (EV)
- Concurrent ADC and RT symptomatic necrosis 11% vs. 5% at 24 months



Lebow et al Jama Onc 2023

Case Presentation – Pachymeningeal recurrence

- 5 weeks following post-operative SRS: Persistent headaches, nausea/vomiting



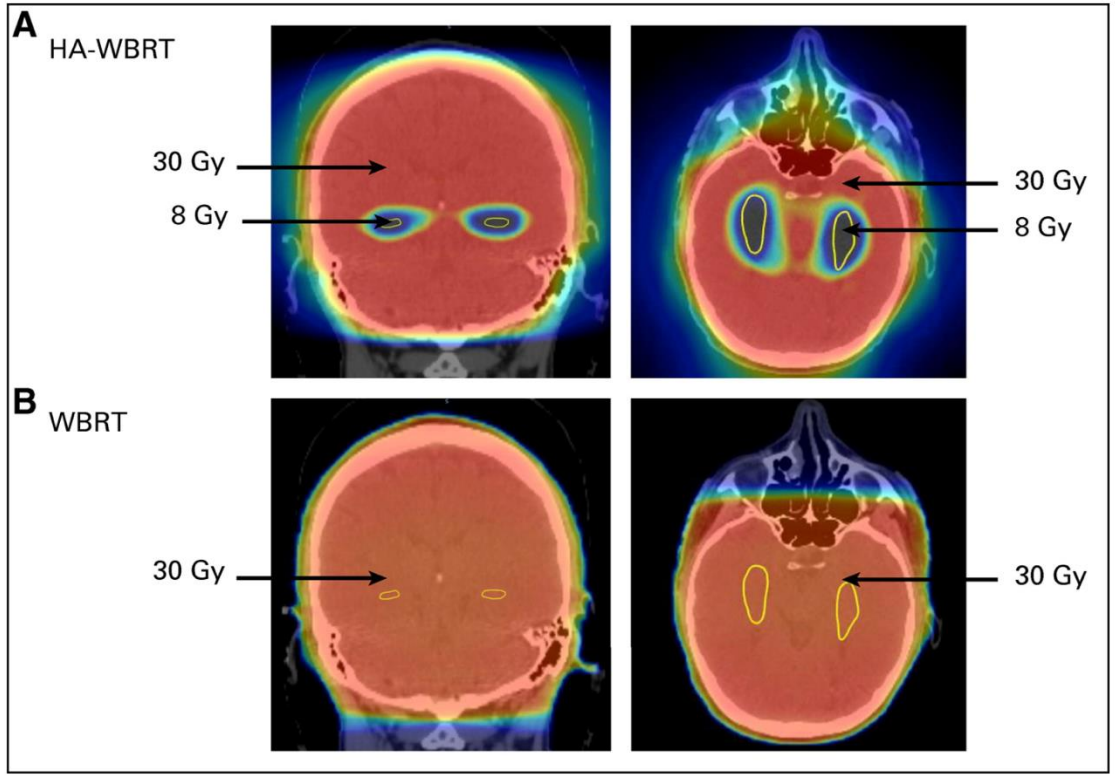
- Multi-focal dural metastases – contralaterall cerebellum, temporal lobe
- Superficial enhancement, R intenral auditory canal enhancement

Management Options

- Leptomeningeal work-up negative?
  - SRS to dural based disease
  - Hippocampal sparing whole brain RT
  - Presume radiographic leptomeningeal disease?
- Leptomeningeal disease
  - Whole brain + involved field RT
  - Proton CSI

Hippocampal sparing whole brain

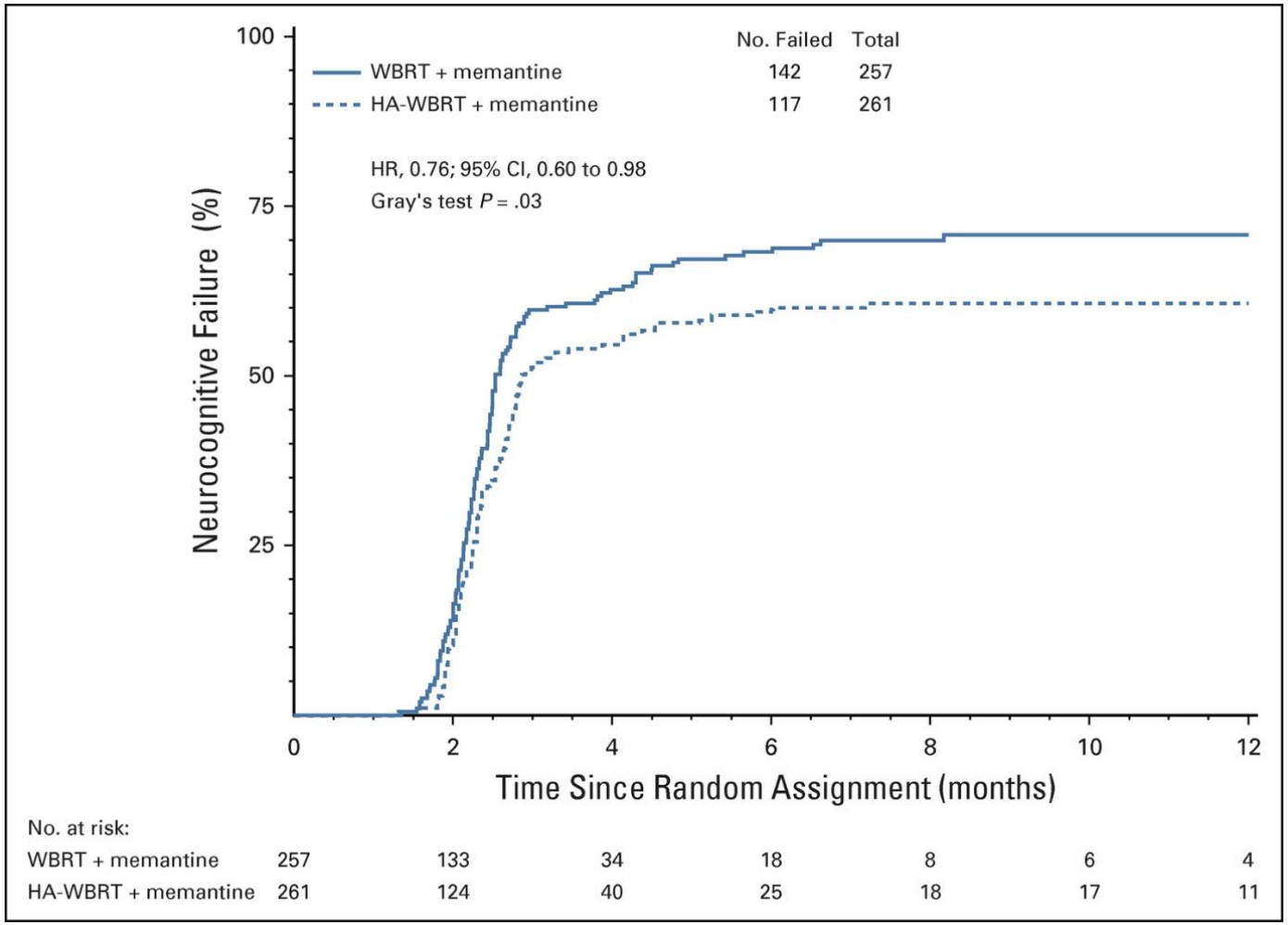
- Palliative whole brain radiotherapy provides intracranial control, however long-term deficits include:
  - Hippocampus is a source of neurogenesis – stem cells are radiosensitive
  - Short-term memory, learning, processing rely on hippocampal function
  - NRG CC001 – IMRT Hippocampal avoidance (HA) during whole-brain radiotherapy (WBRT) evaluated cognitive preservation



Brown et al JCO 2020

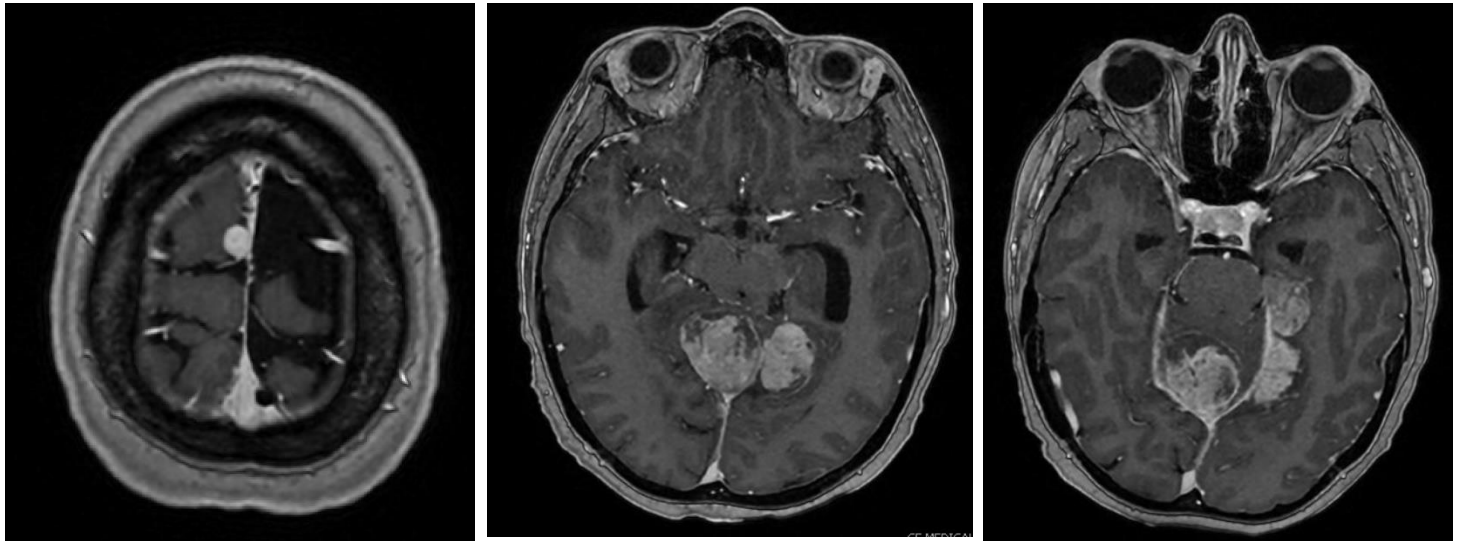
NRG-CC001: HA-WBRT + Memantine

- Primary end point was time to cognitive function failure
- HA-WBRT plus memantine better preserves cognitive function and patient-reported symptoms, with no difference in intracranial PFS and OS



Rapid intracranial progression

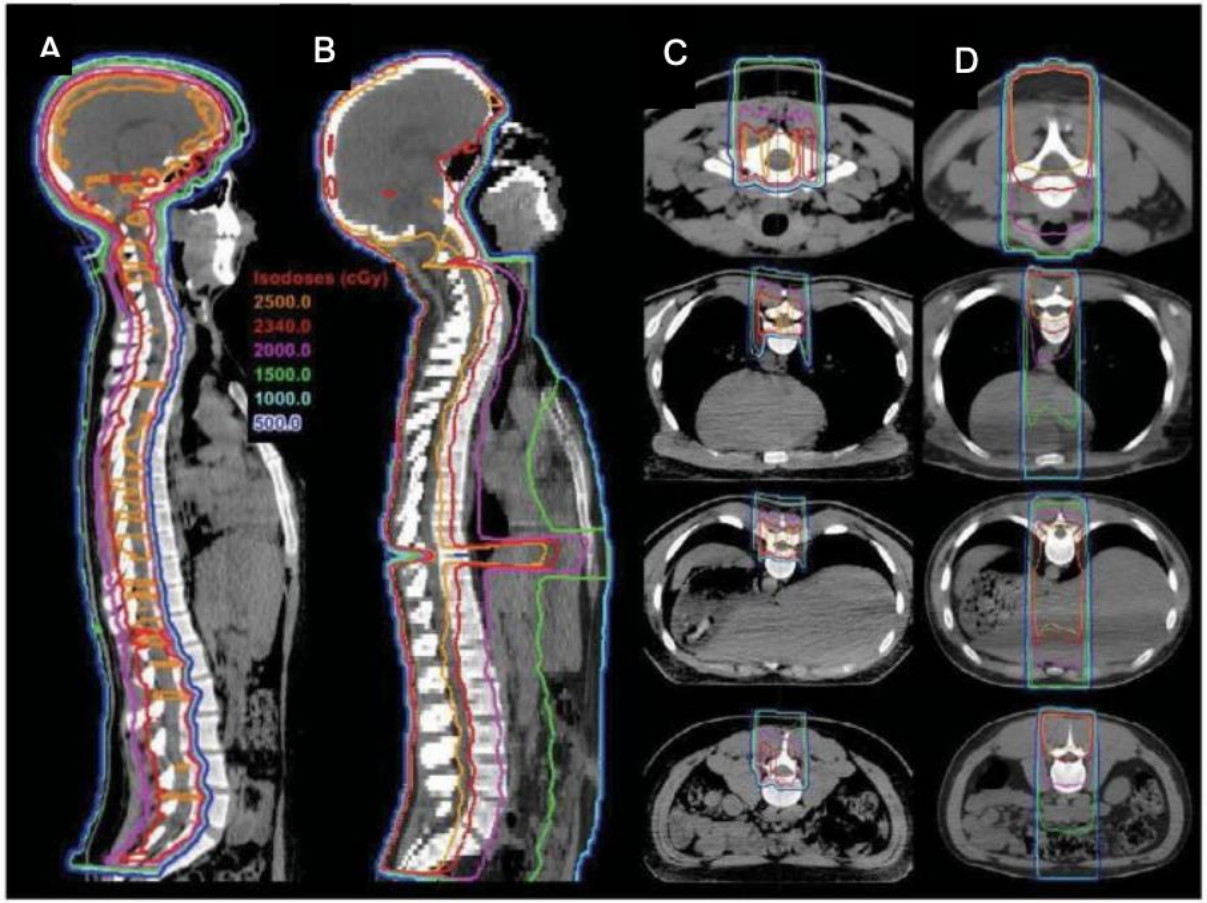
- 5 weeks following post-operative SRS



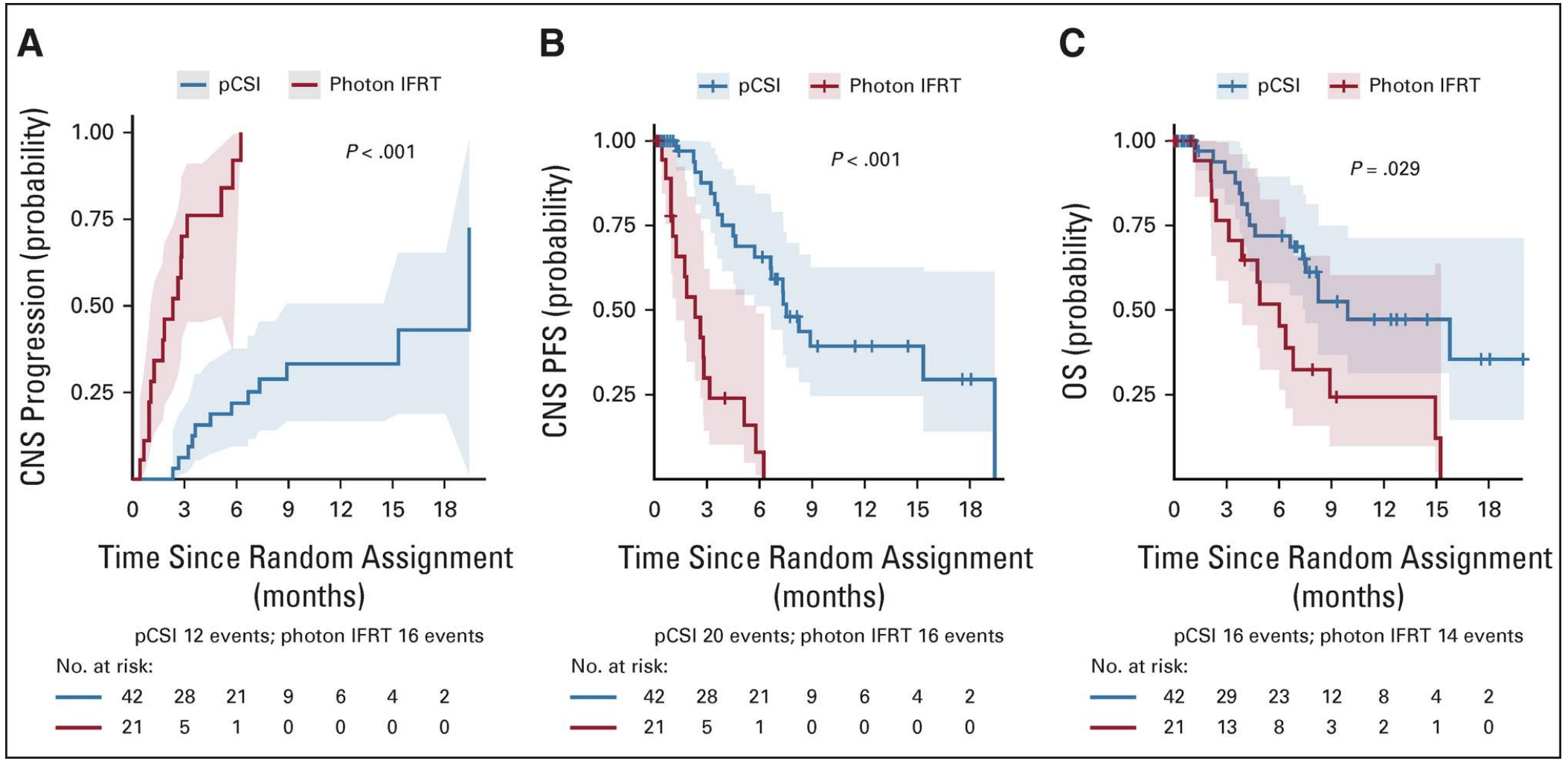
- Multi-focal dural metastases – contralateral cerebellum, temporal lobe
- Superficial enhancement, R internal auditory canal enhancement
- Diploplia, facial droop

Role of Proton Craniospinal Irradiation in Breast Cancer

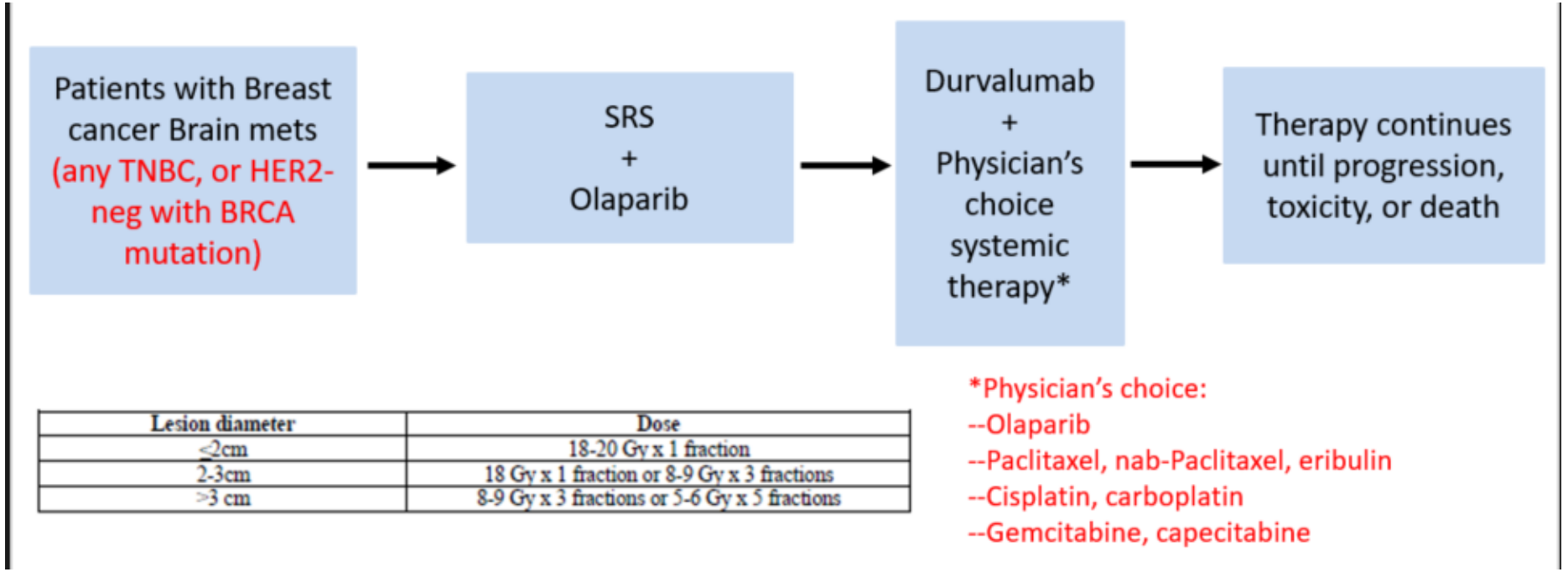
- Protons use ionizing radiation to damage DNA, however protons deposit majority of energy at the end of their range – allows for no significant dose distribution beyond the neuraxis
- Randomized (2:1) phase II multicenter trial in patients with Breast or NSCLC leptomeningeal disease
  - pCSI
  - Involved filed RT



Proton CSI


A
pCSI
Photon IFRT
CNS Progression (probability)
1.00
0.75
0.50
0.25
P < .001
0 3 6 9 12 15 18
Time Since Random Assignment (months)
pCSI 12 events; photon IFRT 16 events
No. at risk:
42 28 21 9 6 4 2
21 5 1 0 0 0 0
B
pCSI
Photon IFRT
CNS PFS (probability)
1.00
0.75
0.50
0.25
P < .001
0 3 6 9 12 15 18
Time Since Random Assignment (months)
pCSI 20 events; photon IFRT 16 events
No. at risk:
42 28 21 9 6 4 2
21 5 1 0 0 0 0
C
pCSI
Photon IFRT
OS (probability)
1.00
0.75
0.50
0.25
P = .029
0 3 6 9 12 15 18
Time Since Random Assignment (months)
pCSI 16 events; photon IFRT 14 events
No. at risk:
42 29 23 12 8 4 2
21 13 8 3 2 1 0

Multi-Modal Therapeutic Approaches - SOLARA



Lesion diameter	Dose
≤2cm	18-20 Gy x 1 fraction
2-3cm	18 Gy x 1 fraction or 8-9 Gy x 3 fractions
>3 cm	8-9 Gy x 3 fractions or 5-6 Gy x 5 fractions

Multi-Center Phase I-II study of SRS with concurrent Olaparib followed by Durvalumab with physician's choice chemotherapy in breast cancer brain metastases.

- TNBC or HER2 neg BC with BRCA mutation
- 1-15 brain metastases (at least 1 intact, surgical sub-study also available)
- Excluding: leptomeningeal disease, prior whole brain, prior combination DRI/immune checkpoint inhibition