Advances in Treatment of Metastatic Brain and Spine Tumors

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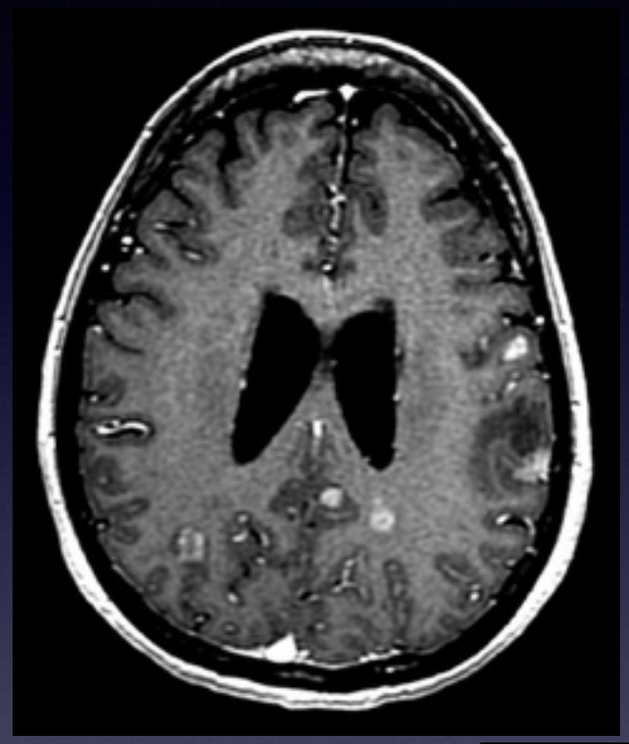
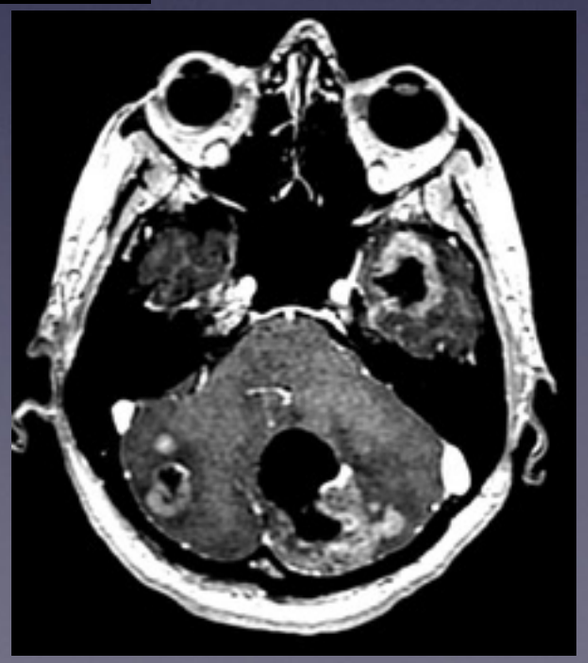
Disclosures

- No Financial Disclosures

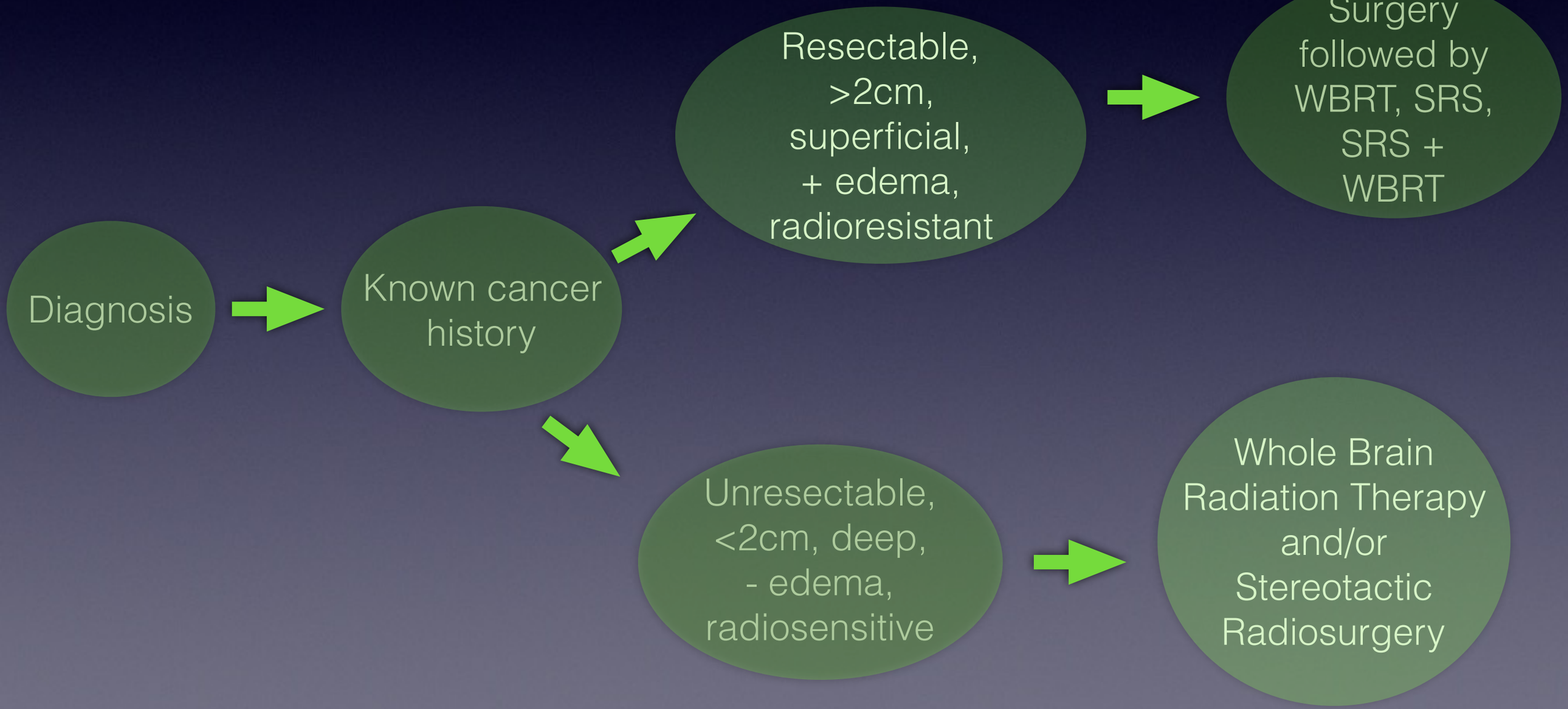
Metastatic Brain Tumors

- In the U.S. in 2016 according to American Cancer Society
  - Approximately 1.7 million new cancer cases
- Almost 1 in 4 cases will have metastases to the brain
  - ~ 400,000 cases

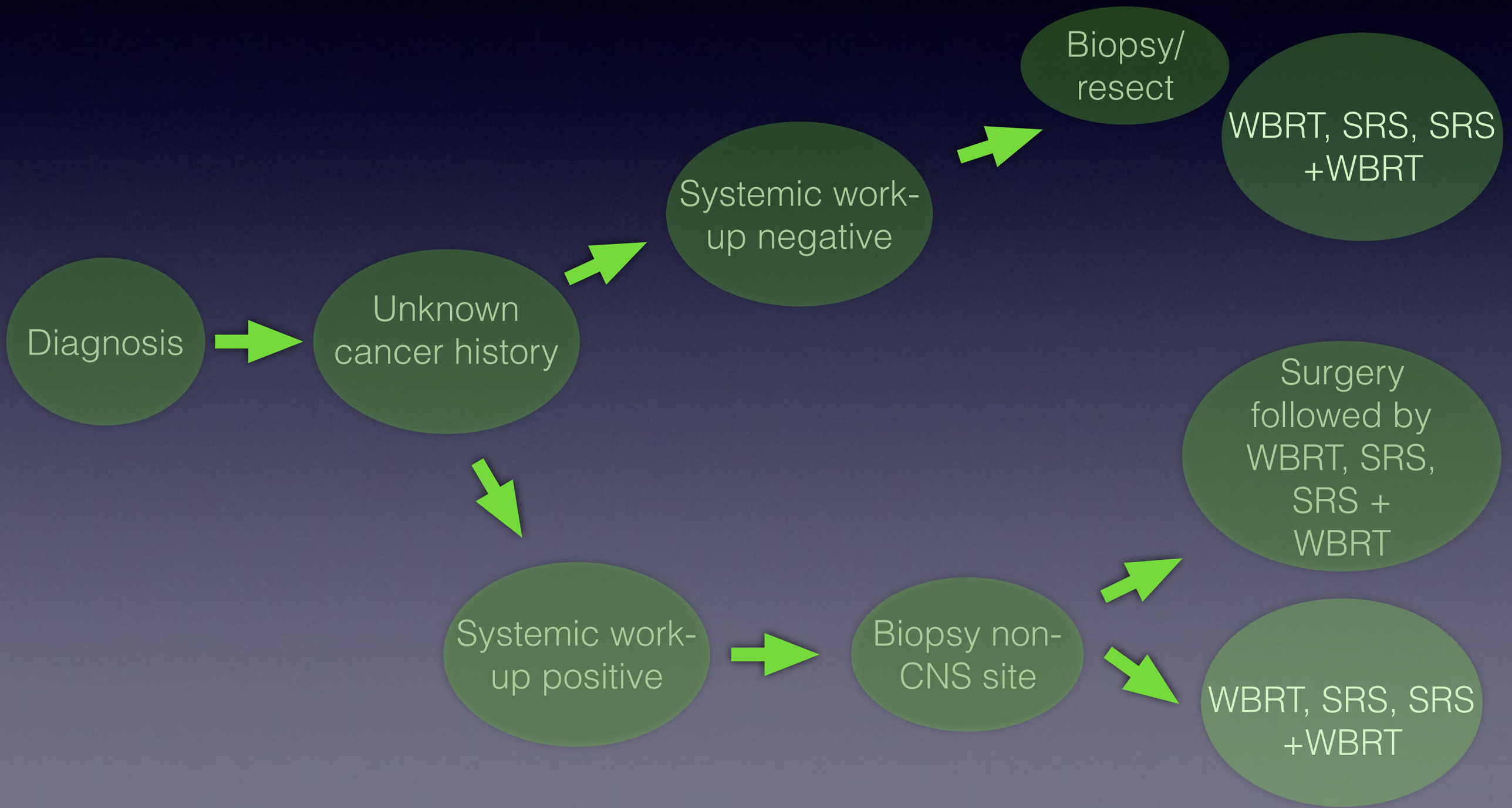




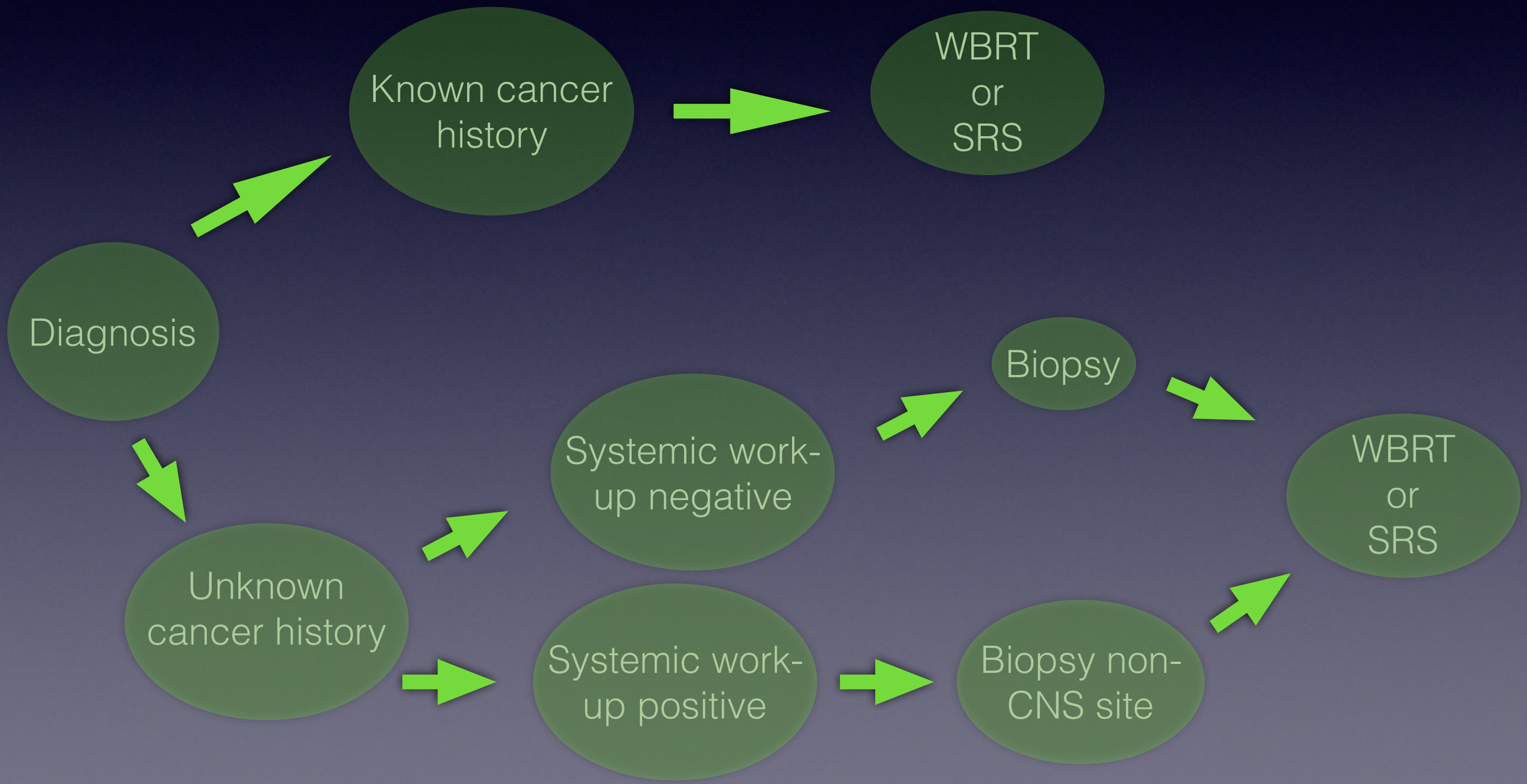
Solitary or Oligo Metastatic Brain Tumors (<3)



Solitary or Oligo Metastatic Brain Tumors (<3)

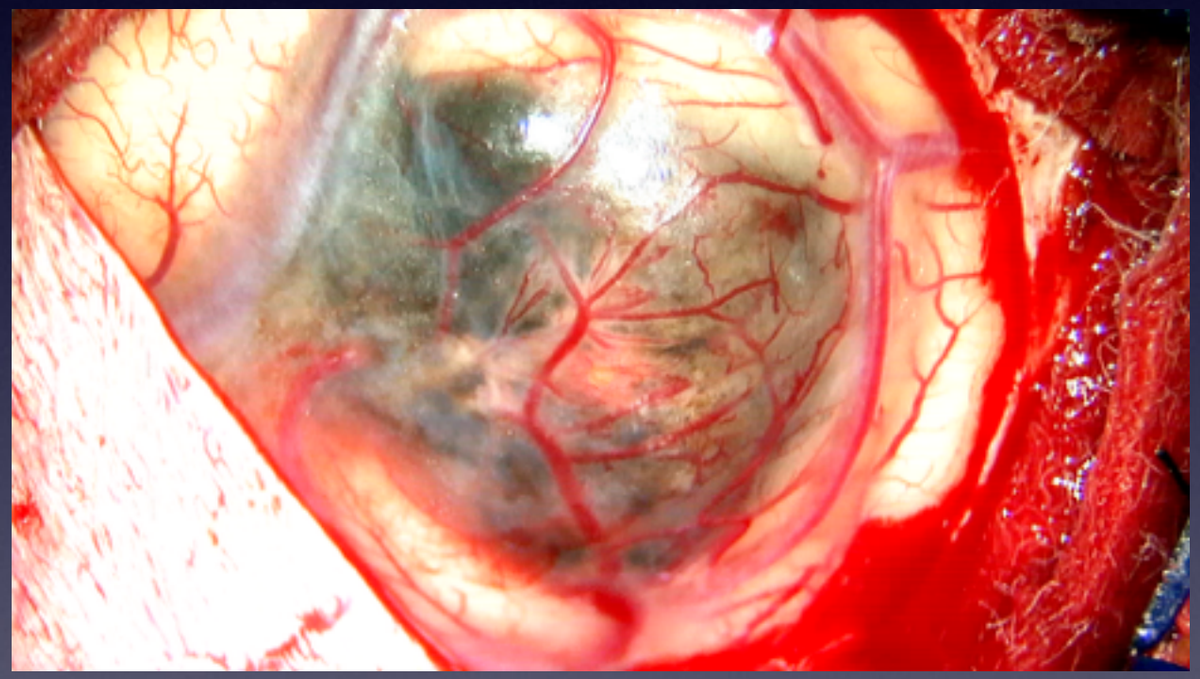


Multiple Metastatic Brain Tumors (>3)



Surgical Resection of Solitary Metastatic Brain Tumors

- Patchell et al. 1990, Vecht et al. 1993, Mintz et al. 1996.[1-3] - compared Surgery+WBRT vs. WBRT alone
  - Median survival (Patchell - 40 wks vs. 15 wks, Vecht - 10 mos vs. 6 mos, Mintz - 5.6 mos vs. 6.3 mos)
  - Rate of local recurrence (Patchell - 20% vs. 52%)
  - Maintained QOL KPS >= 70 (Patchell - 38 wks vs. 8 wks). Better functional independent survival with combined treatment (Vecht)
- Patchell et al. 1998 - compared Surgery vs. Surgery +WBRT[4]
  - Rate of local recurrence - 46% vs. 10%
  - Overall recurrence - 70% vs. 18 18%
  - Median survival - 43 wks vs. 46 wks



[1]Patchell et al. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med. 1990 Feb 22;322(8):494-500.
[2]Vecht et al. Treatment of single brain metastasis: radiotherapy alone or combined with neurosurgery? Ann Neurol. 1993 Jun;33(6):583-90.
[3]Mintz et al. A randomized trial to assess the efficacy of surgery in addition to radiotherapy in patients with a single cerebral metastasis. Cancer. 1996 Oct 1;78(7):1470-6.
[4]Patchell et al. Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. JAMA. 1998 Nov 4;280(17):1485-9.

Whole Brain Radiation Therapy versus Stereotactic Radiosurgery

- **WBRT Toxicity**
- Brown et al. for oligo-metastatic disease randomized SRS (111 pts) vs. SRS+WBRT (102 pts)[5]
  - Cognitive deterioration at 3 mos (63.5% vs. 91.7%)
  - QOL change from baseline at 3 mos (-0.1 pts vs. -12.0 pts)
  - 3 & 12 mos intracranial tumor control rate (75.3 %/50.5% vs. 93.7%/84.6%)
  - 3 & 12 mos local tumor control rate (89.%/72.8% vs. 96.8%/90.1%)
  - Medial overall survival (10.4 dos vs. 7.4 mos)

[5]Brown et al. Effect of Radiosurgery Alone vs Radiosurgery With Whole Brain Radiation Therapy on Cognitive Function in Patients With 1 to 3 Brain Metastases: A Randomized Clinical Trial. JAMA. 2016 Jul 26;316(4):401-9.

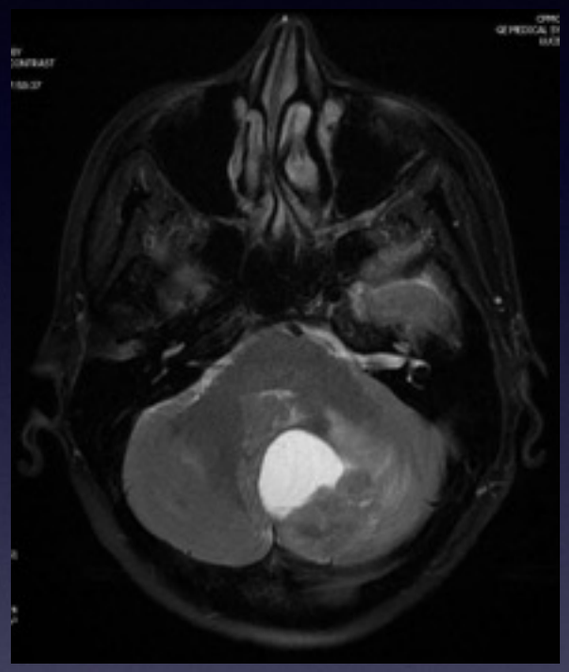
Surgery, WBRT, SRS - Maximizing benefit, minimizing harm

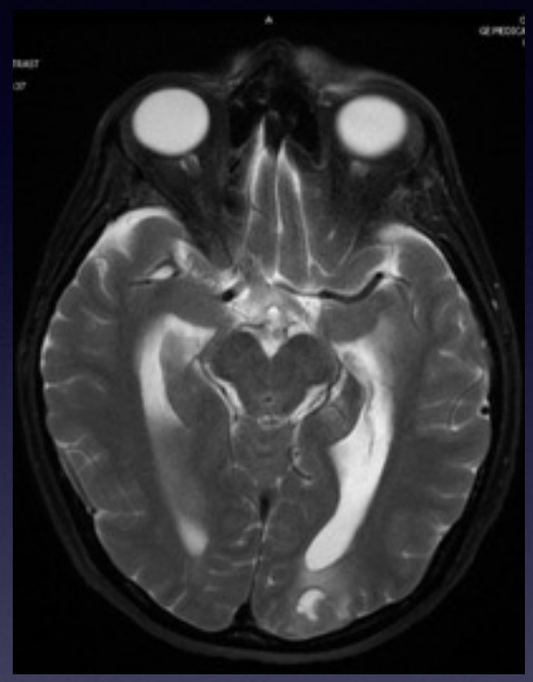
- Surgery - Part of combined therapy for local disease control and maintaining functional capacity

- WBRT - Primary/adjuvant therapy for CNS disease control. Negative neurocognitive effects

- SRS - Primary/adjuvant therapy for local disease control. Avoids neurocognitive effects of WBRT

What to do?

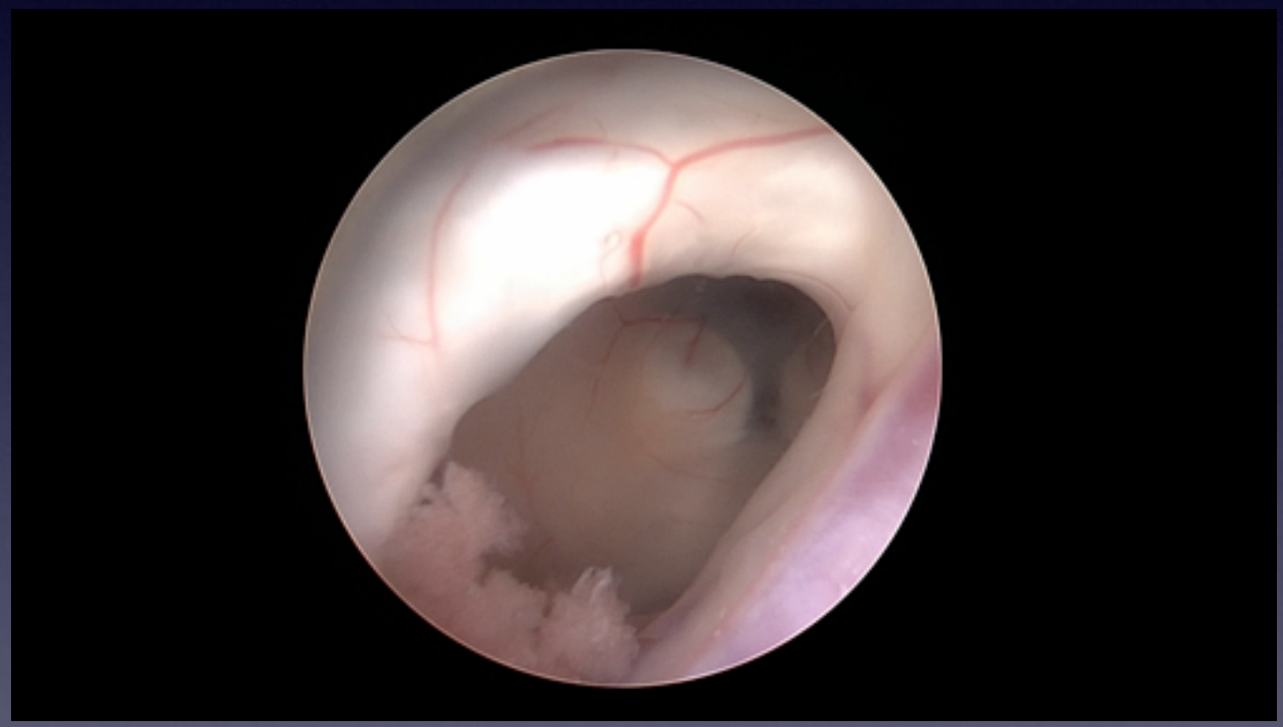




58 year old female with metastatic Breast Ca, 30-40 brain mets, large left cerebellar lesion with obstructive hydrocephalus

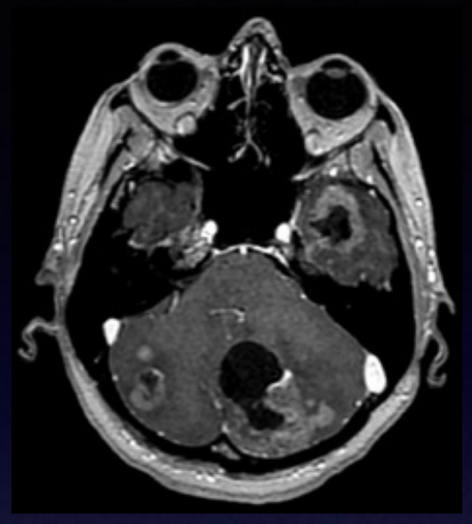
Endoscopic intraventricular surgery

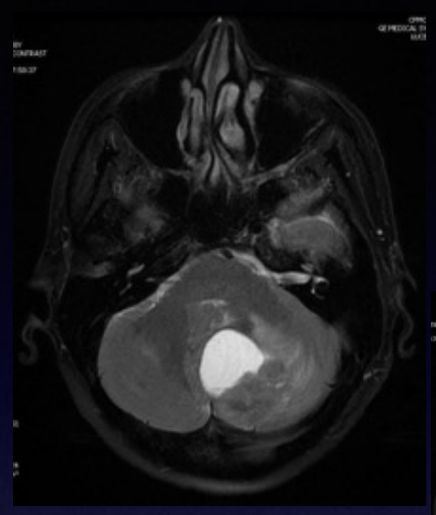
- Endoscope adapted from cystoscope
- Endoscopic treatment of hydrocephalus L'Espinasse and Kanavel first performed in 1910
- Mixter performed first endoscopic ventriculocisternostomy in1923
- 1960s significant improvement of endoscope by Hopkins reinvigorated technique

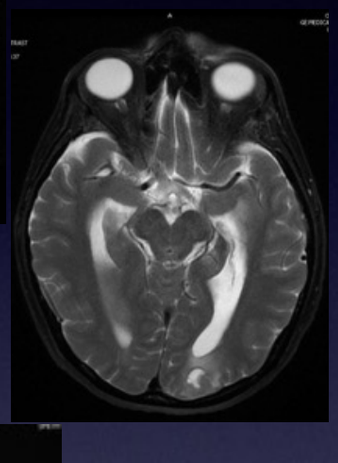


weill.cornell.edu/news/pr/2005/09/journey-to-the-center-of-the-brain.html

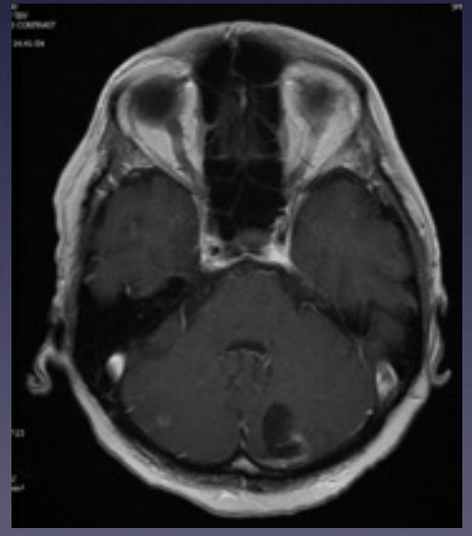
Temporary CSF Diversion and RT

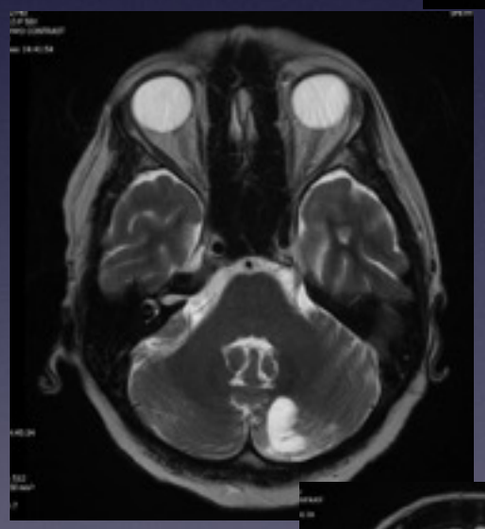


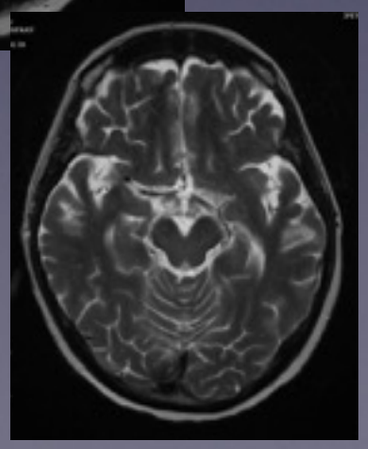




Preop







3mos Postop

58 year old female with metastatic Breast Ca, 30-40 brain mets, large left cerebellar lesion with obstructive hydrocephalus

- Endoscopic third ventriculostomy
- Whole Brain Radiation therapy POD#1
- Dc’ed to home POD#2

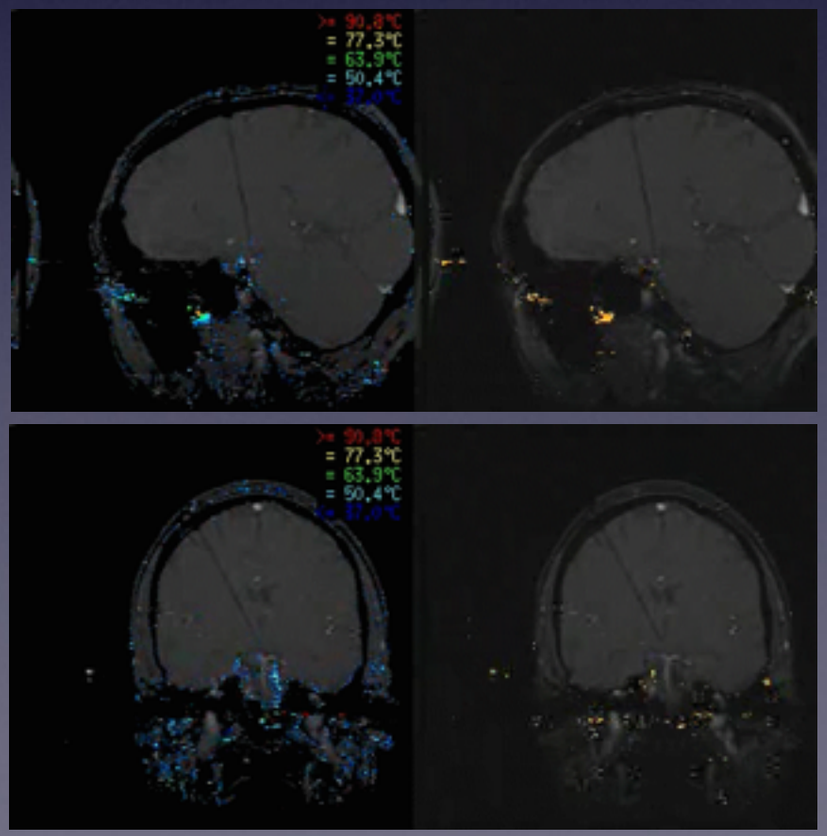
Laser Interstitial Thermal Therapy

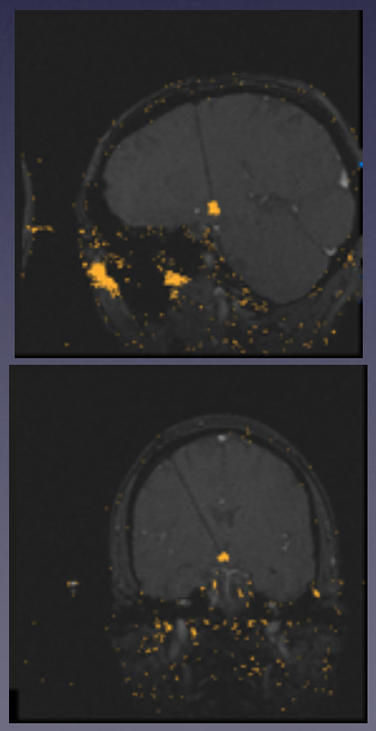
- Stereotactic image-guided technique using laser fiber to ablate lesion soft tissue
- Originally introduced in 1983
- Laser interstitial irradiation to produce thermal damage
    - Greatest degree of penetration in the near-infrared spectrum
    - Selective thermal injury of pathologic tissue
        - Sharp ablation zone border
- Early efforts confounded by ability to control thermal damage

Missios S1, Bekelis K, Barnett GH. Renaissance of laser interstitial thermal ablation. Neurosurg Focus. 2015 Mar; 38(3):E13.

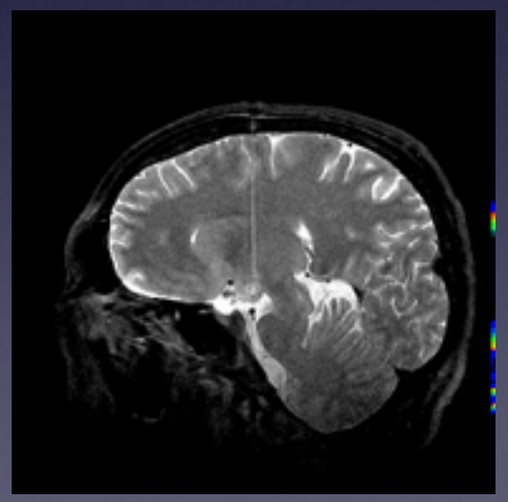
Laser Interstitial Thermal Therapy

- Development of real-time MR thermography to monitor treatment
- Coupled cooling mechanism over probe with feedback control mechanism and temperature limits
- Preliminary studies into malignant gliomas, cranial and spinal metastases, radiation necrosis, and epilepsy

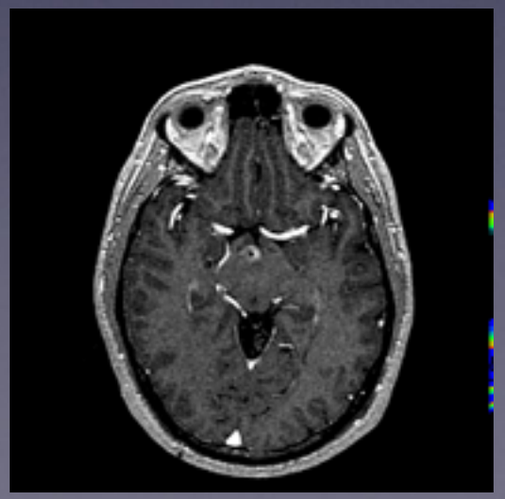




Damage model



Post-ablation Images



Tumor Treating Fields

Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma
A Randomized Clinical Trial

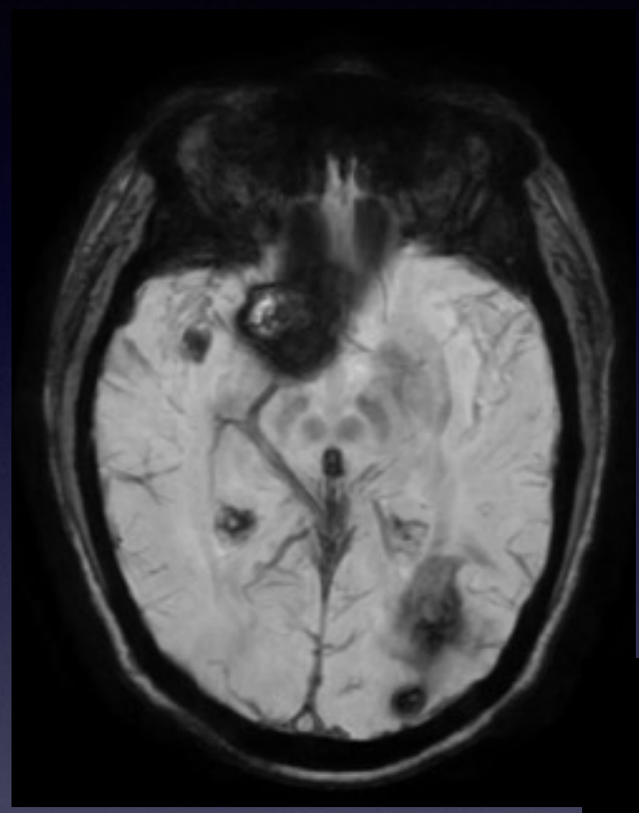
Roger Stupp, MD; Sophie Taillibert, MD; Andrew A. Kanner, MD; Santosh Kesari, MD, PhD; David M. Steinberg, PhD; Steven A. Toms, MD, FACS, MPH; Lynne P. Taylor, MD, FAAN; Frank Lieberman, MD; Antonio Silvani, MD; Karen L. Fink, MD, PhD; Gene H. Barnett, MD, MBA; Jay-Jiguang Zhu, MD, PhD; John W. Henson, MD, MBA, FAAN; Herbert H. Engelhard, MD, PhD; Thomas C. Chen, MD, PhD; David D. Tran, MD, PhD; Jan Sroubek, MD; Nam D. Tran, MD, PhD; Andreas F. Hottinger, MD, PhD; Joseph Landolfi, DO; Rajiv Desai, MD; Manuela Caroli, MD; Yvonne Kew, MD, PhD; Jerome Honnorat, MD, PhD; Ahmed Idbaih, MD, PhD; Eilon D. Kirson, MD, PhD; Uri Weinberg, MD, PhD; Yoram Palti, MD, PhD; Monika E. Hegi, PhD; Zvi Ram, MD

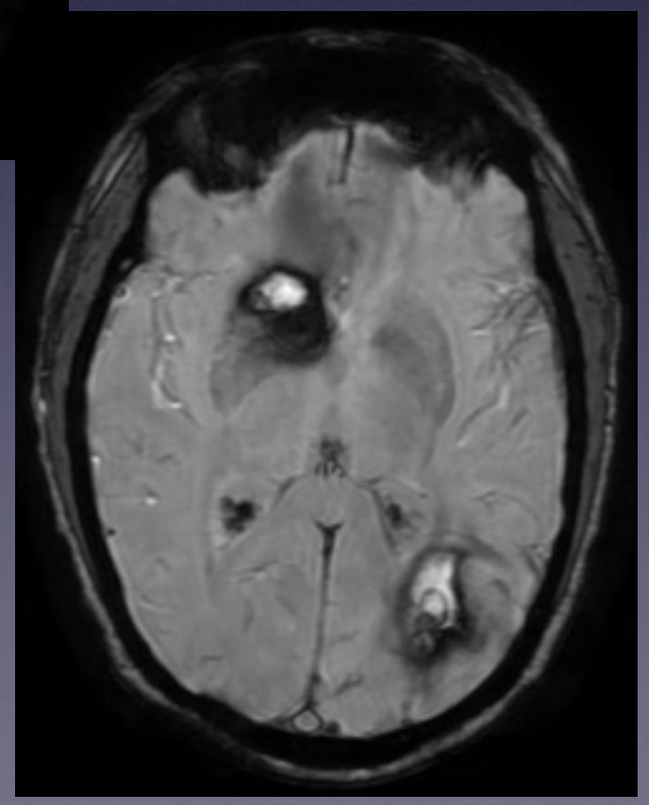
- Trial TTF + maintenance temozolomide vs TMZ alone[6]
  - Terminated early at interim analysis
  - PFS 7.1 mos vs 4.0 mos
  - Overall survival 20.5 mos vs 15.6 mos
- Application of Tumor-Treating Fields to other cancers
  - Ongoing Trials

[6]Stupp et al. Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma: A Randomized Clinical Trial. JAMA. 2015 Dec 15;314(23):2535-43.
Davies AM, Weinberg U, Palti Y. Tumor treating fields: a new frontier in cancer therapy. Ann N Y Acad Sci. 2013 Jul;1291:86-95.

Targeted Systemic Therapy

- Targeted inhibitors and immunotherapy may improve control of CNS metastatic disease
  - Melanoma
  - Breast Ca
  - NSCLC
- **CPMC experience**
  - 79 patients with metastatic melanoma to the brain treated with CTLA-4Ab, PD-1Ab or BRAF (+/- MEK) inhibitors
  - Historically, melanoma with brain mets OS ~ 5mos
  - Median OS from brain met dx <u>12.8 mos</u>
  - Median OS from stage IV dx <u>18.2 mos</u>



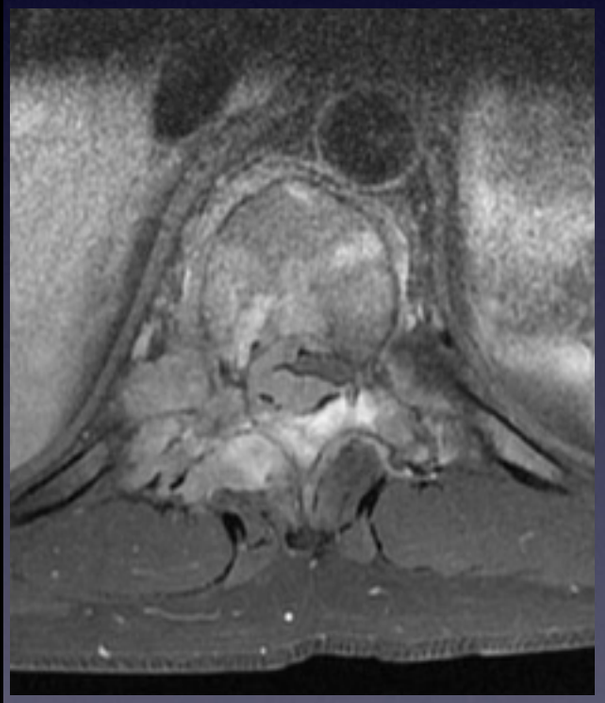


Metastatic Spine Tumors

- Bone is the 3rd most common site of cancer metastasis after lungs and liver

- Majority of bony metastasis are in the spine

- Up to 40% of patients with metastatic cancer will have spinal metastasis during the course of their disease



Surgical intervention for metastatic spine tumors

Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial

Roy A Patchell, Phillip A Tibbs, William F Regine, Richard Payne, Stephen Saris, Richard J Kryscio, Mohammed Mohiuddin, Byron Young

- Patchell et al. landmark 2005 study evaluating the role of surgery for metastatic spine tumors[7]
- Demonstrated benefit of surgery+RT over RT alone
    - Ambulating after Tx (84% vs 57%); Maintained ambulation (122 days vs 13 days); Regained ability to ambulate (62% vs 19%)

[7]Patchell et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet. 2005 Aug 20-26;366(9486): 643-8.

Surgical intervention for metastatic spine tumors

Laufer et al. 2013

- Laufer et al. study evaluated the outcomes of **“Separation Surgery”** approach using NOMS (Neurologic, Oncologic, Mechanical stability, Systemic disease) criteria[8]
- Resection of epidural tumor, creating “separation” of 2-3mm plus stabilization followed by single fraction or hypo fractionated SRS[9]
    - 1 yr local progression 16.4%
        - Low dose hypo-fractionated (30Gy in 5-6 fractions) 22.6% progression
        - High dose hypo-fractionated (27Gy in 3 fractions) 4.1% progression
        - Single-fraction (24Gy) 9% progression
- **“Minimally Invasive” Approach**

[8]Joaquim et al. An update in the management of spinal metastases. Arq Neuropsiquiatr. 2015 Sep;73(9):795-802.
[9]Laufer et al. Local disease control for spinal metastases following "separation surgery" and adjuvant hypofractionated or high-dose single-fraction stereotactic radiosurgery: outcome analysis in 186 patients. J Neurosurg Spine. 2013 Mar;18(3):207-14.

Metastatic Spine Tumors

Diagnosis

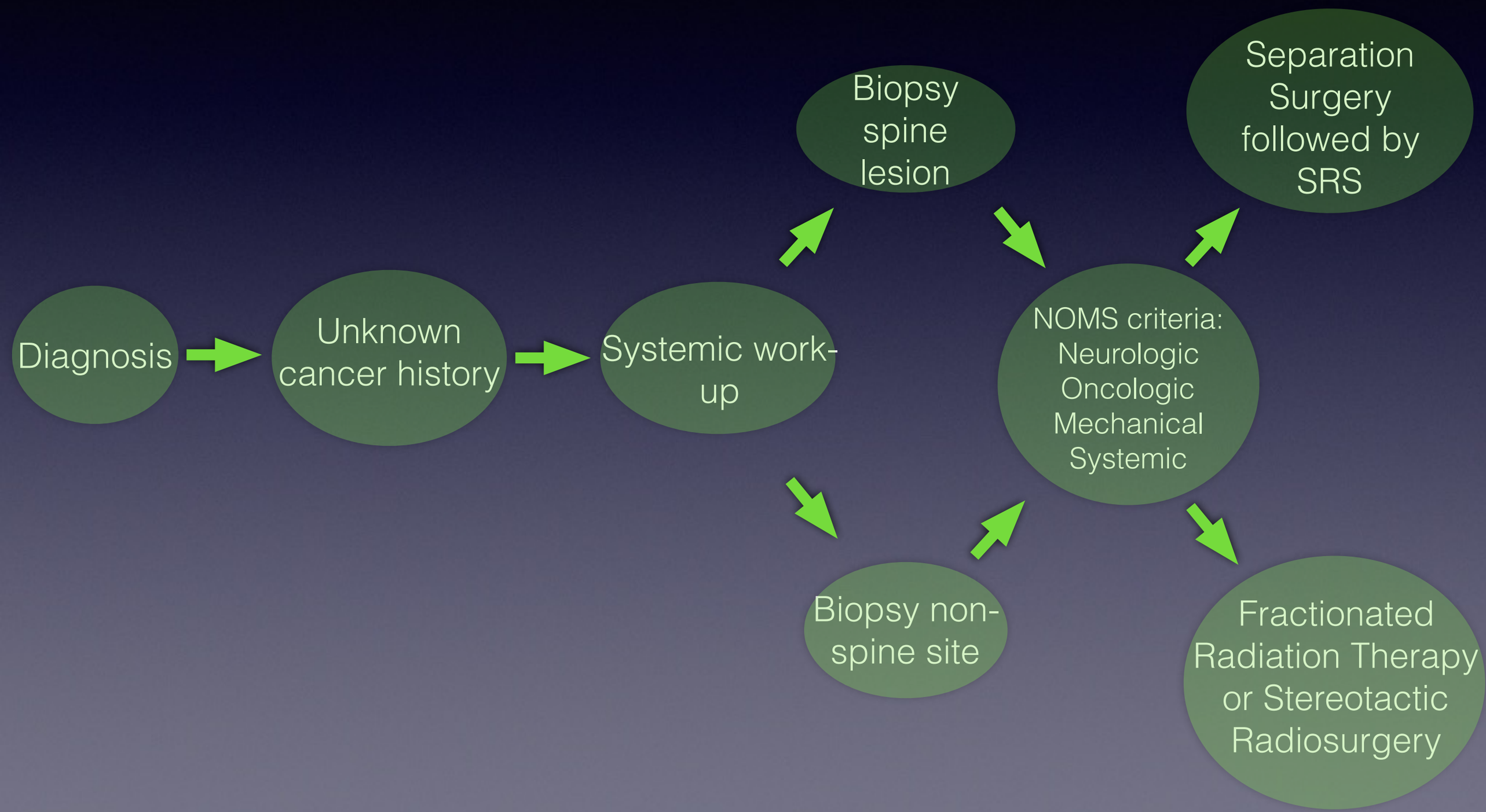
Known cancer history

NOMS criteria:
Neurologic
Oncologic
Mechanical
Systemic

Separation Surgery followed by SRS

Fractionated Radiation Therapy or Stereotactic Radiosurgery

Metastatic Spine Tumors



Minimally invasive surgery for metastatic spine tumors

Comparison of minimally invasive surgery with standard open surgery for vertebral thoracic metastases causing acute myelopathy in patients with short- or mid-term life expectancy: surgical technique and early clinical results

Massimo Miscusi, MD, PhD,[1] Filippo Maria Polli, MD, PhD,[2] Stefano Forcato, MD,[2]
Luca Ricciardi, MD,[1] Alessandro Frati, MD, PhD,[2,3] Marco Cimatti, MD, PhD,[2]
Luca De Martino, MD, PhD,[2] Alessandro Ramieri, MD,[4] and Antonino Raco, MD[2]

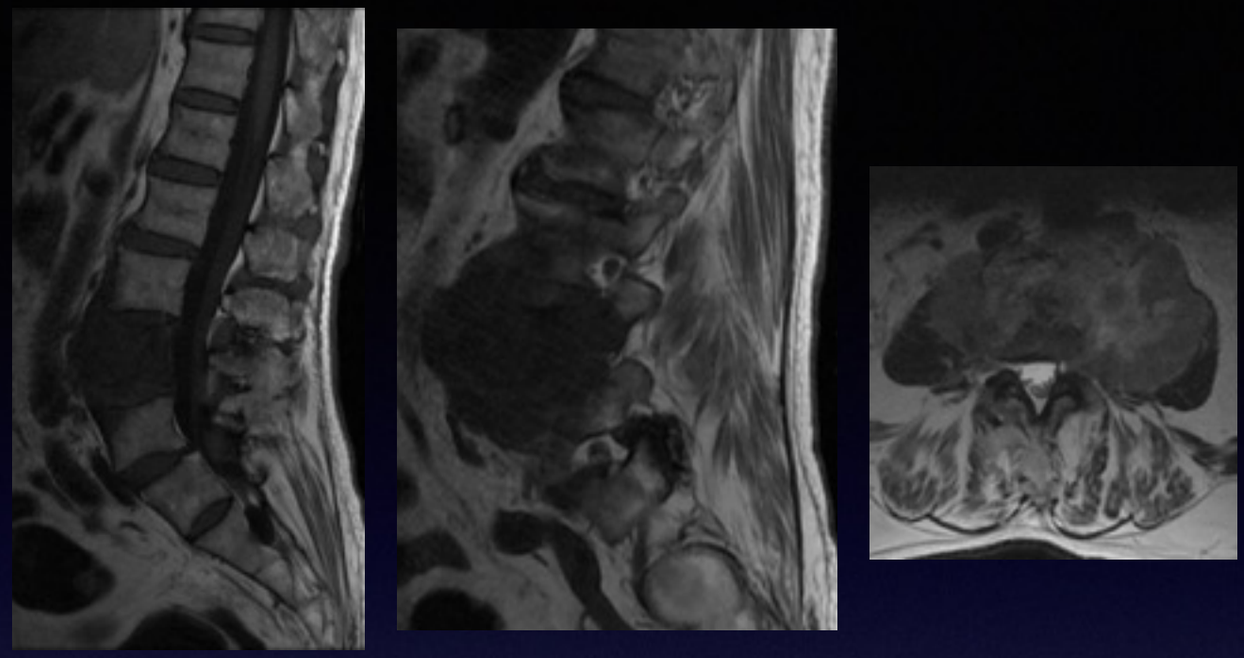
- Retrospective comparison between MIS (23 patients) vs traditional open surgery (19 patients)[10]
  - Pathology included Lung, Breast, Myeloma, Renal, Melanoma, Prostate, Ovarian, Thyroid
  - MIS vs Open: OR time (2.2 hrs vs 3.2 hrs), EBL (240ml vs. 900ml), Postop transfusions (0 pts vs 12 pts), Postop bedres (2 d vs 4 d), LOS (7.2 d vs 9.25 d), EORTC QOL-C30 improvement (13.6 vs. 9.8), QLQ-BM22 improvement (14.07 vs. 4.65)

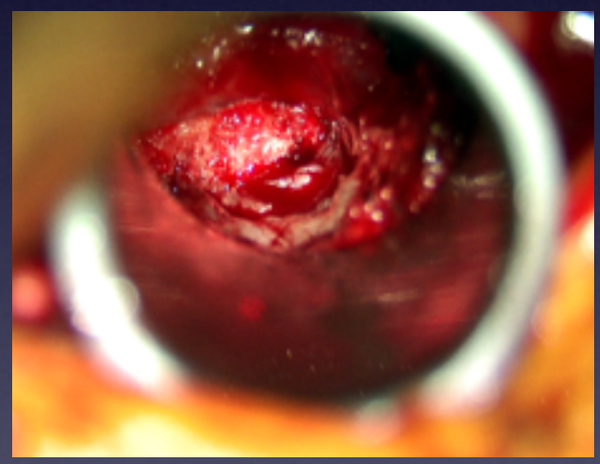
[10]Miscusi et al. Comparison of minimally invasive surgery with standard open surgery for vertebral thoracic metastases causing acute myelopathy in patients with short- or mid-term life expectancy: surgical technique and early clinical results. J Neurosurg Spine. 2015 May;22(5):518-25.

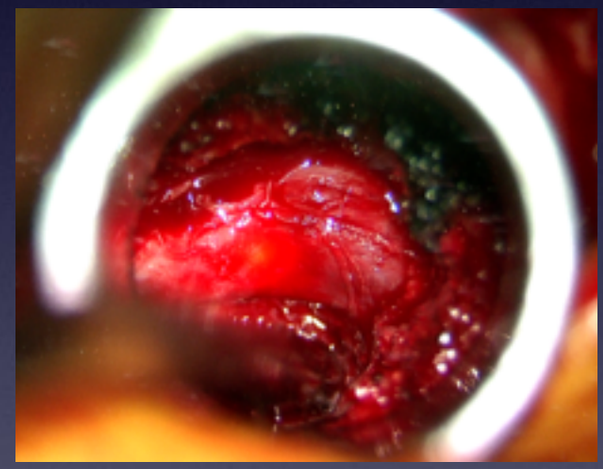
Alimi et al. Minimally invasive foraminotomy through tubular retractors via a contralateral approach in patients with unilateral radiculopathy. Neurosurgery. 2014 Sep;10 Suppl 3:436-47; discussion 446-7.

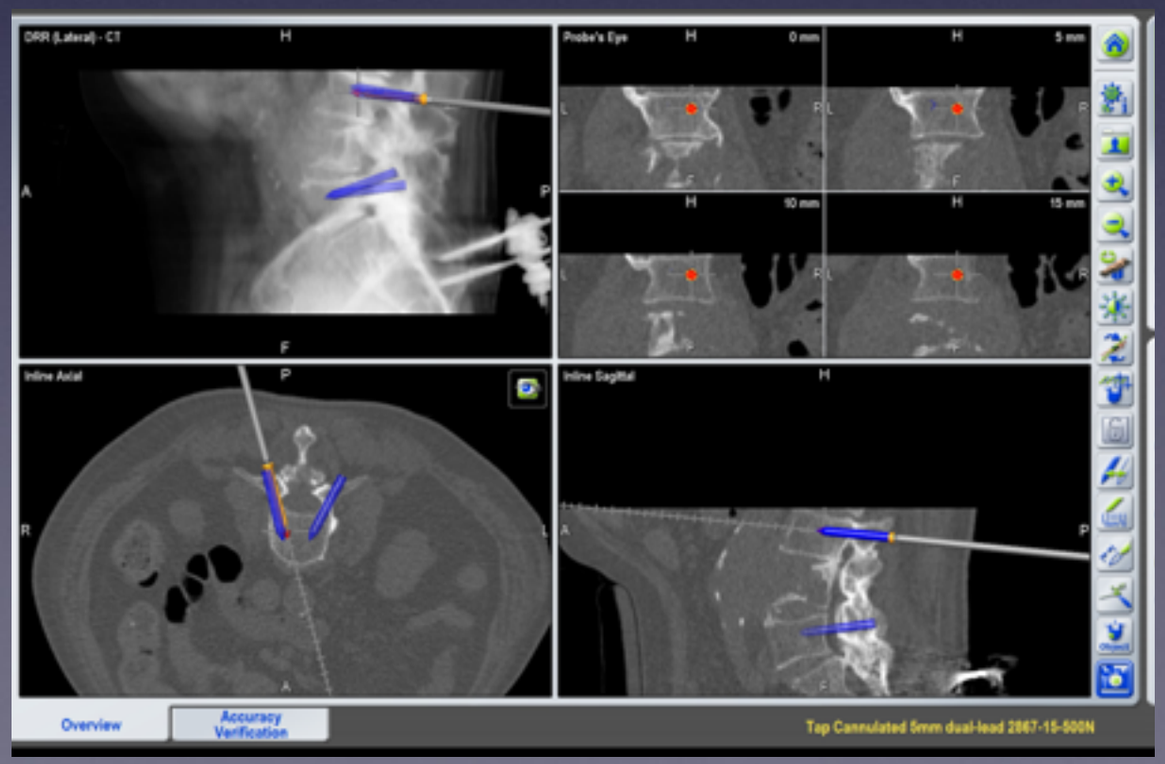
Minimally Invasive Spine Surgery for Malignant Spine Tumors

- 87 yo male who developed new LBP x 4 mos. L4 lesion concerning for malignancy. IR biopsy returned as Leiomyosarcoma. Represented with progressive low back pain, weakness, and left radicular leg pain.
- MIS decompression of left L4 nerve root and Percutaneous pedicle stabilization from L3-L5
    - Discharged to rehab POD3
    - Discharged to home POD14
- Stereotactic radiation therapy 2 weeks postop









Evolving Technologies and Therapeutics

- Surgery
  - Minimally invasive cranial surgical techniques (Endoscopic, Laser Interstitial Thermal Therapy)
  - Minimally invasive spine surgery (Minimally invasive decompression, Percutaneous stabilization, Vertebral augmentation)
- Radiation therapy
  - Stereotactic radiosurgery
- Tumor Treating Fields
- Targeted systemic therapy
- **Maximizing Benefit, Minimizing Harm**

Thank You