

Redefining Brain Metastases The Role of Cyberknife Radiosurgery

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Intracranial Oncology

- Brain Metastases
 - Most Common intracranial tumors in adults
 - 10x more frequent than primary brain tumors
 - 8-10% of cancer patients
- Advances in Systemic therapy
 - Patients living longer
 - Management of Brain mets important for long term outcomes
- Asymptomatic vs Symptomatic
 - High quality MRI
 - 2-3mm
 - Site specific symptoms

Management of Brain Metastases

- Systemic therapy
 - Blood brain barrier precludes efficacy
 - Certain immunotherapies may penetrate
- Surgery
 - Diagnosis
 - Mass effect
 - Symptomatic
- Radiation therapy
 - Stereotactic vs Whole Brain

Radiation Therapy for Brain Mets

- Whole Brain Radiation
 - Entire brain treated 30-35Gy
- Advantages
 - Treats subclinical disease as well as evident disease
- Disadvantages
 - Duration of treatment
 - 2-3 weeks
 - Can't give systemic therapy concurrently
 - No clinically meaningful outcome advantage vs SRS
 - Toxicity, toxicity, toxicity
 - Acute
 - Neurocognitive effects
- Sometimes a necessary evil
 - #of metastases
 - 10,20,30????
 - Breast vs other histologies

Radiation Therapy for Brain Mets

- Stereotactic Radiosurgery
 - Always preferred for treatment of limited brain disease
 - Higher doses to smaller volumes
 - Advantages
 - Duration
 - Typically can be done in single session (up to 5)
 - Allows initiation of systemic therapy
 - Better local control rates than WBRT alone
 - 80-90% at one year
 - Less toxic
- Avoid morbidity of surgery

Evolution of SRS for Brain Metastases

- Initial studies included whole brain +/- SRS, surgery +/- wbrt
- Movement towards SRS alone
 - SRS vs SRS+ WBRT
 - 4 Randomized trials ¹⁻⁴
 - No change in OS with WBRT
 - SRS alone
 - Improved cognitive preservation
 - Improved quality of life
- How many mets are too many?
 - Japanese trial⁵ shows treatment of up to 10 results in similar OS to <5
 - Volume of mets vs number of mets
 - Velocity of development
 - Histology (even small cell lung cancer)

Postoperative SRS

- SRS after surgery
 - Local recurrence after surgery alone up to 50% at 1-2 years
- Mahajan et al
 - Postop SRS vs observation for 1-3 completely resected mets
 - 12 month Freedom from Local Recurrence
 - 72% with SRS
 - 43% with surgery alone
- NCCTG Phase 3 trial
 - Postop SRS vs Postop WBRT
 - WBRT results in worse cognitive effects but no improvement in clinically significant outcomes

SRS vs WBRT

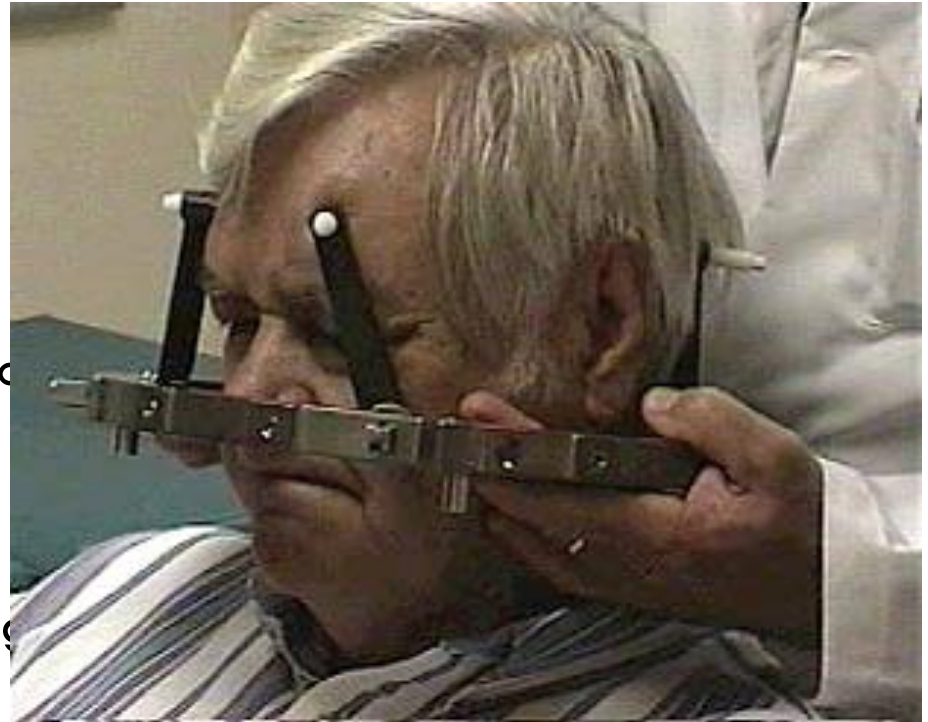
- We always favor SRS over WBRT
- Who should get WBRT?
 - Poor PS with significant volume of multiple brain mets
 - Leptomeningeal disease
- Decreasing neurotoxicity of WBRT
 - Hippocampal Sparing WBRT RTOG 0933
 - Less decline in memory shown
 - Memantine RTOG 0614
 - Trend towards less memory impairment
 - Improved time to cognitive decline

SRS delivery and side effects

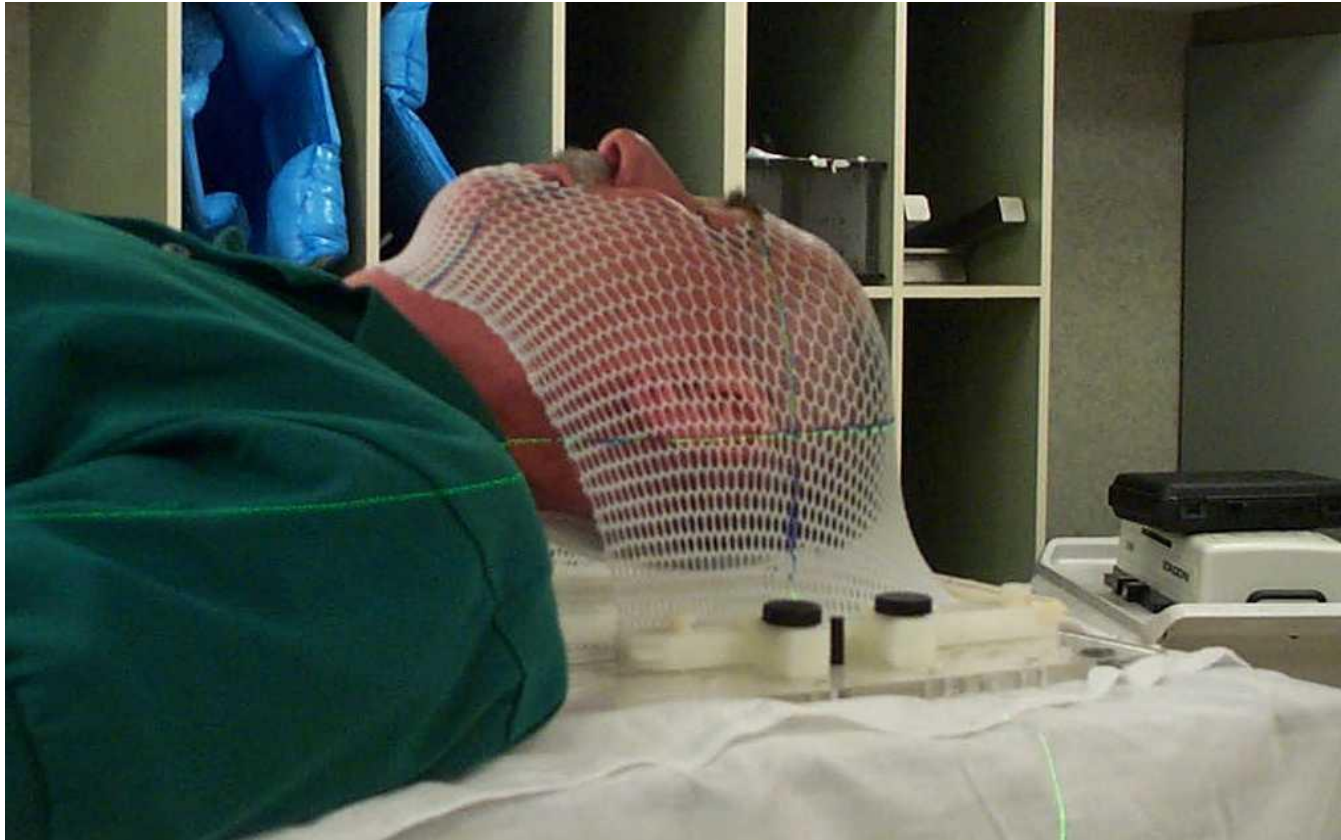
- Size determines dose and fractionation
 - <2cm 20-24Gy/1
 - 2-3cm 18Gy/1
 - 3-4 15-16Gy/1
 - >4cm fractionate 8Gyx3, 5-6Gyx5
- Side effects
 - Site specific, edema, Radiation necrosis
- Currently accruing study **NRG-BN013**
 - Evaluating 1 vs 3 fractions
 - 22-24Gy/1 (1-2cm) vs 30Gy/3
 - 18-20Gy/1 (2-3cm) vs 27/3

Contemporary delivery of Brain SRS

- Lars Leksell 1951
 - Concept of SRS with RT
 - Gammaknife 1968
 - 192 individual Cobalt sources
- Gamma Knife and Linear Accelerator based SRS
 - Stereotactic Frame screwed directly to skull
 - 3D coordinate map for directing treatment
 - Planning and treatment all done in one day



Frameless Stereotactic Radiosurgery

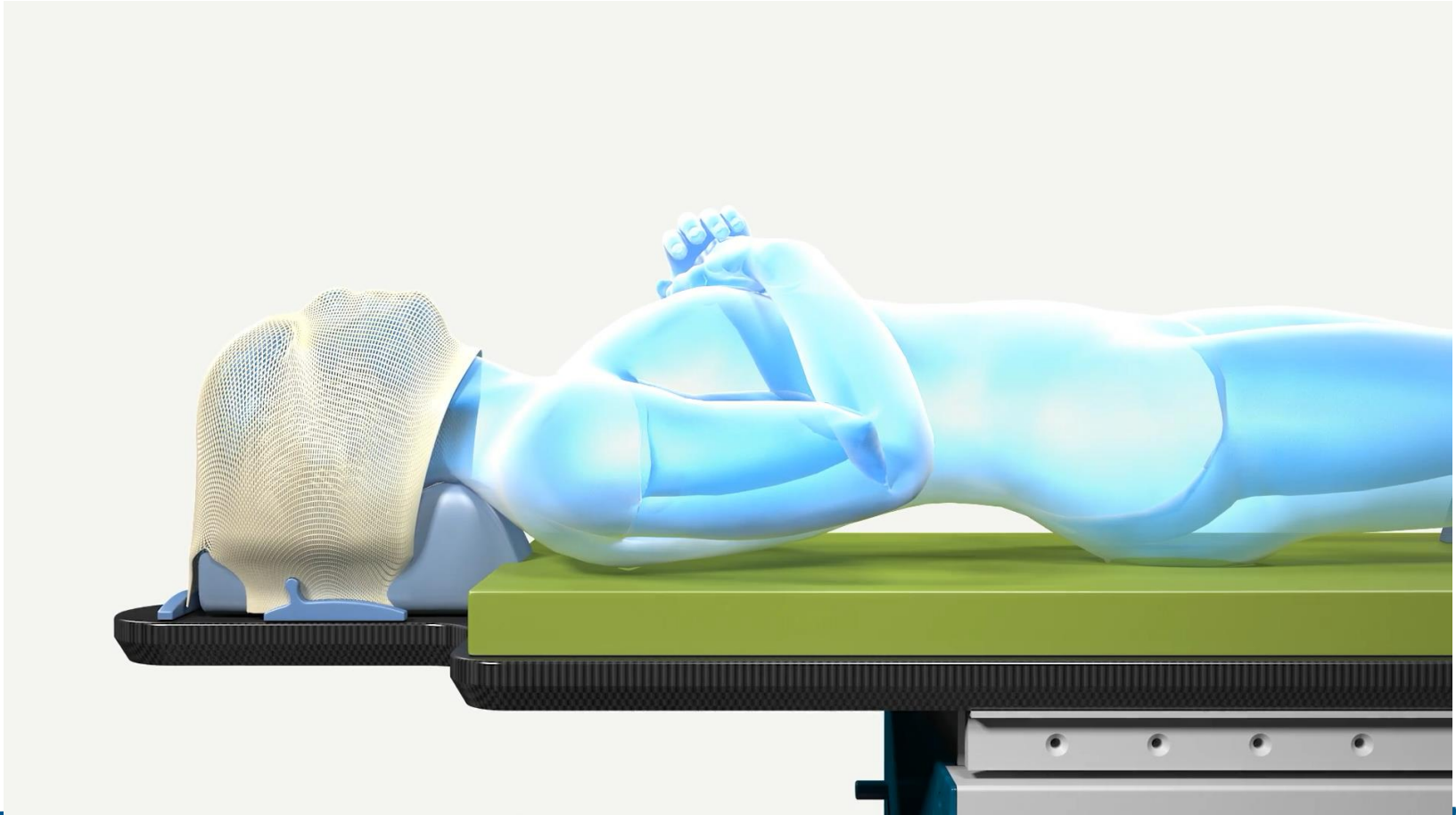


Aquaplast mask attached to table

Cyberknife Frameless SRS

- No Frame
 - Aquaplast mask
 - Customized mask for each patient
 - In tandem with real time adaptive tx allows submillimeter accuracy
- Real time Tracking
 - Allows for shifts to decrease setup error vs framed system
 - AI input
- Multiple tumors can be treated
 - Less whole brain
 - Simultaneously in less time

Ck Brain treatment



Advantages/Disadvantages for Frameless

- Frame allows precision without imaging
 - May be superior for treating functional syndromes
 - Thalmus
- Multiple trials show no clinical benefit to frame based systems
- Addition of real time adaptive treatment CK allows sub millimeter accuracy
- Well suited for treating multiple brain metastases
- Fractionated radiosurgery
 - Breakup treatment of multiple lesions
 - Larger lesions to decrease toxicity
 - NRG BN013 intact mets
 - NCT0411981 resected mets

Treating Metastatic Disease in 2026

- Exponential Advances in Medical Oncology
- Blood based testing
- Tumor directed therapies
- Patients living longer with Metastatic disease
 - Seeing more patients with brain mets
 - Atypical histologies
- Long term survivorship
- Somatic disease vs Brain Disease
- Oligometastatic disease paradigm

Then vs. Now

- Brain metastases typically the start of shift to palliative care
- Whole Brain toxicity
- Oligometastatic cancer
 - Cancer as a chronic disease
 - CK as an ongoing part of treatment

Cancer's progression

- Local Only Disease
- Evolution of the malignant cell
 - Acquired mutations, angiogenesis
 - Spread beyond primary site
- Establishment of metastatic site
 - Limited burden of disease
- Widespread dissemination

Oligometastatic



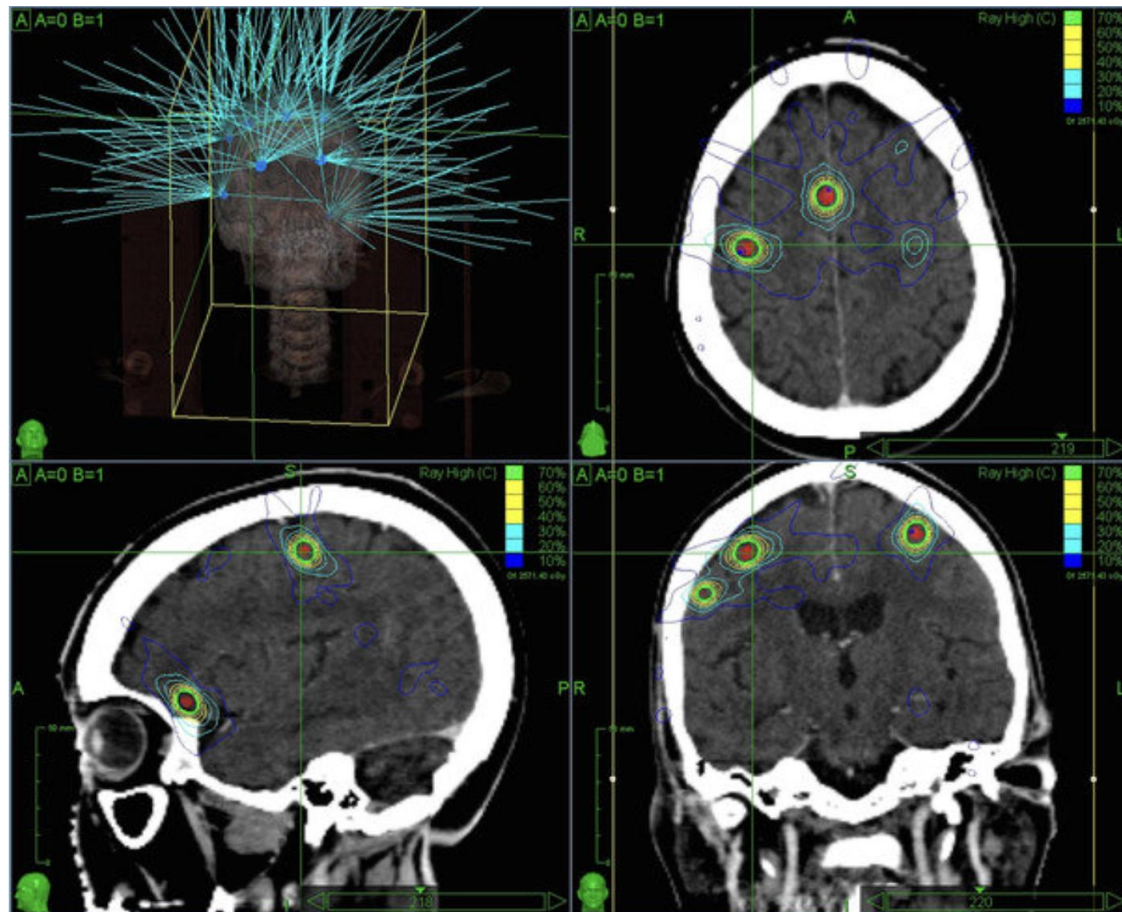
Oligometastatic Disease

- Earlier diagnosis and better staging exams
- More effective systemic treatments may control most microscopic metastatic deposits, leaving only a limited amount of visible residual mets
- The Brain as a sanctuary site from systemic therapy
 - Secondary Site for somatic disease resistant to current therapy

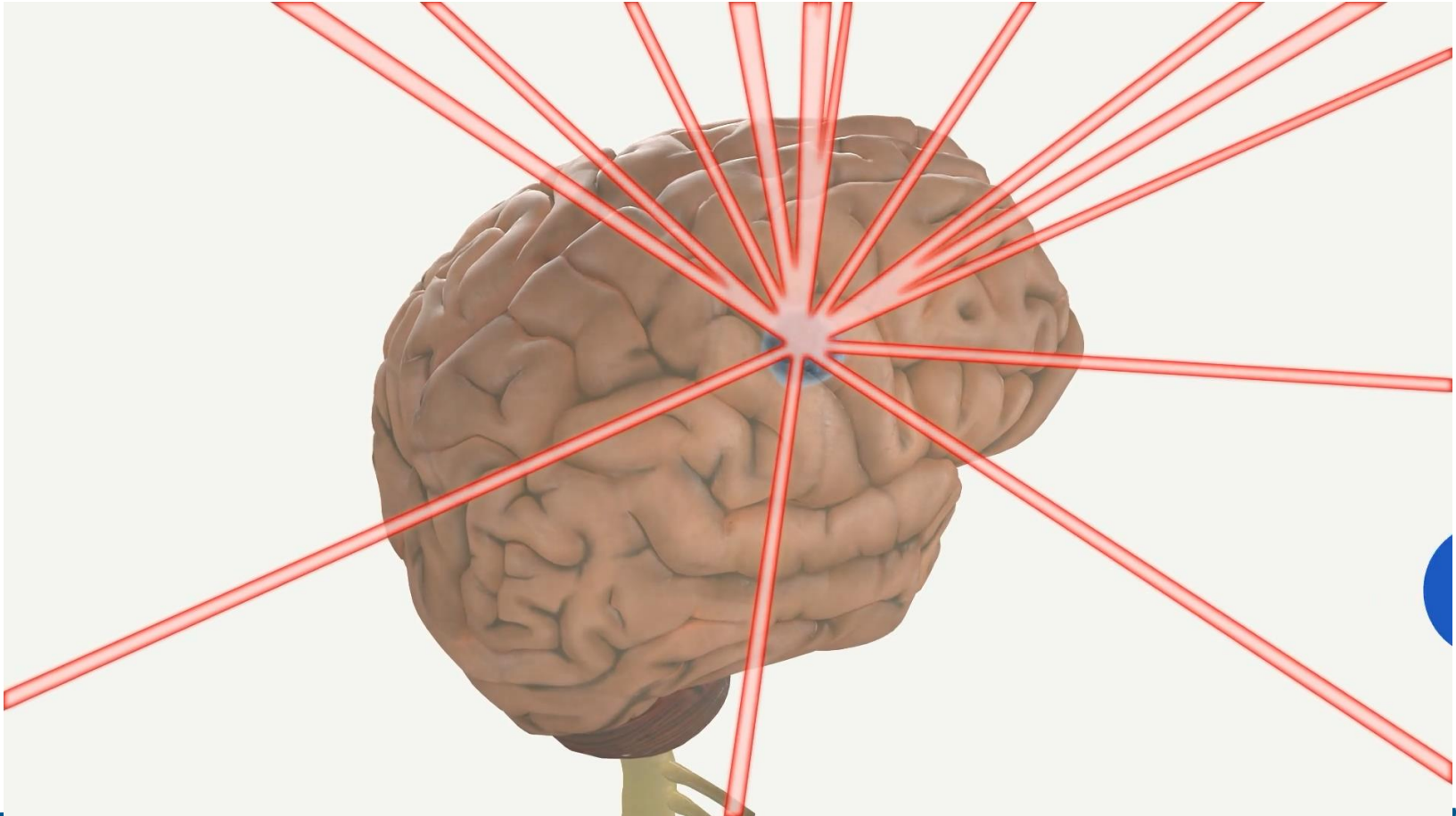
Brain Cyberknife for the patient

- MRI
 - Fine cut necessary vs standard
- CT simulation
 - Aquaplast mask
- Contouring and Planning
- Delivery

CK Planning



CK Delivery



Beyond Brain Mets

- Cyberknife in the Brain
 - Recurrent primary disease after prior RT
 - Benign disease
 - Acoustic Neuroma
 - Meningioma
 - AVMs
 - Pituitary Adenomas
 - Trigeminal neuralgia

Cyberknife for Brain Metastases

- Multidisciplinary oncology care
 - Surgical Oncology
 - Medical Oncology
 - Radiation Oncology
- More versatile machine for delivery of SRS for brain mets
 - More brain mets
 - Fractionated radiosurgery
- Is this a palliative treatment or and adjuvant treatment
 - Riding the wave of improved systemic agents
 - Targeted agents

QUESTIONS?



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