IMRT of the Central Nervous System

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MTM has received previous support from Varian Medical Systems

WAKE FOREST UNIVERSITY SCHOOL of MEDICINE THE BOWMAN GRAY CAMPUS

Disclaimer

All material presented is intended to be illustrative. Information such as specific objectives, prescribed dose(s), structure definition, etc. need to be assessed and approved by the treating physician on a case-by-case basis.

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Objectives

At the conclusion of this presentation, one should have familiarity with:

1. The general practice of CNS IMRT
2. Details related to specific case studies
3. Current and future research related to CNS IMRT

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Course Outline

- Definitions / Justification
- General Guidelines
  - Imaging
  - Immobilization
  - Tx planning
  - QA
  - Delivery
- Case Reviews
- Recent/Future Advances
- Summary

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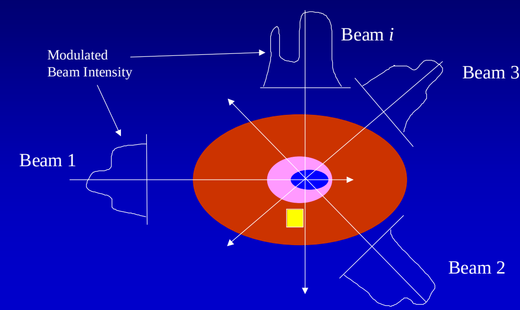
What Is IMRT?

- Automated computer-based technique that attempts to design and deliver very conformal radiation distributions using multiple gantry positions at which multileaf collimators (MLCs) modulate the dose

Intensity Modulated Treatment
"How to Paint Dose"



JD Bourland, Wake Forest University

IMRT Objectives

- **More accurately define/administer dose distributions**
  - **conform to complex 3D shape of target and deliver uniform dose to that complex shape**
  - **deliver non-uniform dose to meet an objective (i.e. bioanatomic modulation and/or concomitant boost)**
- **Maximize the dose to the target**
- **Minimize the dose to normal tissues**
- **Optimize planning, treating, QA strategies for efficiency**

Biologic Model of IMRT

Simultaneously desire to:

↑ Tumor Control Probability

- **increase target dose (homogeneous or heterogeneous dose escalation)**

↓ Normal Tissue Complication Probability

- **reduce normal tissue dose (optics, brainstem, cord, temporal lobes, etc.)**

If above accomplished, should therefore:

↑ Therapeutic Ratio

IMRT Process

- Immobilization
- Imaging
- Treatment planning
- Plan review and approval
- QA: Treatment plan and fluence maps verification
- Accurate and reproducible patient setup
- Treatment delivery

Why IMRT for the CNS?

- Improved conformality and avoidance of normal structures - multiple structures confined to cranial vault
- Improved homogeneous dose delivery (irregularly-shaped lesion and/or external contour)

Example: meningioma
homogeneous cell population
irregularly shaped (concave)

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Why IMRT for the CNS?

- Allow for dose escalation - improved local control

Example: GBM
heterogeneous cell population
increase dose/fx to gross tumor volume

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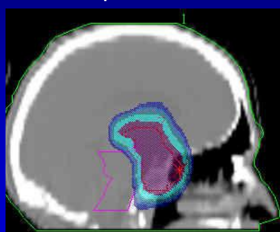
IMRT vs. 3DCRT?

Need to assess normal tissue sparing:
- high dose/fx
- total dose

Expected life span (> 6 mos)
- RTOG class V and VI high-grade glioma, class III metastasis?

Brain Tumors

Tortuous shape
Many critical structures:
Brainstem, Optic Nerves/Chiasm, Globes



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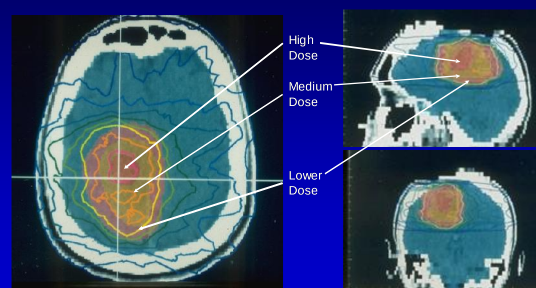
GBM Concomitant Boost



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Immobilization - general

Immobilization choice is based on what degree of precision is needed for patient setup. This depends on the margins prescribed for the target volume with respect to normal critical structures. Margin reduction does not depend on whether the treatment modality is IMRT, but is a function of immobilization.

Immobilization - general

- IMRT is not a margin reduction tool
- Good immobilization may be a margin reduction tool

Immobilization-Verification

- Supine, arms down, lg angle support knees
- Head mask with head cup (post cut-out)
- Head mask with custom support
- S-frame
- optical/infrared system + mask
  - radiocamera
- IGRT
  - on-board and/or real-time multiplanar imaging
  - CT-on-rails
  - TomoTherapy

Cantilever off end of couch (collisions)

Radiocamera

reference to isocenter, not bony anatomy

- well-defined lesion
- patient compliance
- longevity

CT/MR Acquisition/Simulation

- CT scan of the head acquired
- MR registered to planning CT (visual, surface matching, MI)
  - T1 w/ contrast: excellent visualization meningioma, GBM
  - T2: edema (often involved by infiltrating gliomas)
  - T1 FLAIR: differentiate infiltrated brain vs. edema; delineation of non-enhancing lesions (grade 2 glioma)
- ~3 mm slice thickness maximum for accurate structure representation
- ~1 mm: stereotactic; small lesions

Structures of Interest Delineation

- Target and critical structure volumes may be defined by the physician, physicist and/or dosimetrist ⟶ multi-group effort
  - IMRT communication
- Contouring accuracy is very important (inverse planning)

CNS Tumors with a role for Radiotherapy

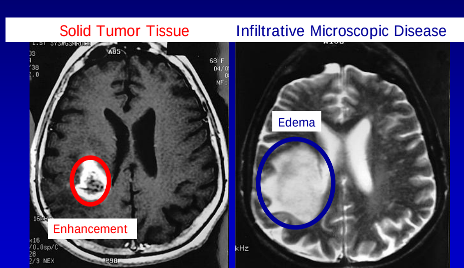
Low grade astrocytoma	Schwannoma
Anaplastic astrocytoma	Craniopharyngioma
GBM	Pituitary tumors
Low grade oligo	CNS germ cell tumors
Anaplastic oligo	Pilocytic astrocytoma
Mixed gliomas	Ganglioglioma
Ependymoma	Hemangioblastoma
PNET	Hemangiopericytoma
CNS lymphoma	Sarcoma
Meningioma	Choroid plexus carcinoma

Courtesy M. Mehta, M.D. - U. Wisconsin

Target definition

- GTV: T1-enhancing abnormality, non-enhancing FLAIR, or post-op cavity
- CTV: T2 or FLAIR abnormality (including edema)
- PTV: add margin for internal variations (edema during treatment) and setup uncertainty (immobilization)
  - –inverse planning (not to block edge)
  - –balance between control and toxicity
    - non-uniform margins

Anatomic MR Imaging of a GBM



EG Shaw, Wake Forest University

CNS Organs at Risk

- optic chiasm: 54 Gy (max threshold)
- optic nerves: 60 Gy
- optic globes: 50 Gy
- brainstem: 54 Gy
- temporal lobes: 25-30 Gy
- contralateral brain: 45 Gy or 25-30 Gy
- pituitary: 50 Gy
- spinal cord: 50 Gy
- inner ears: minimize
- area postrema (nausea): minimize
- other involved brain tissue: minimize

Organs at Risk

temporal lobes, brainstem, optic globes/nerves

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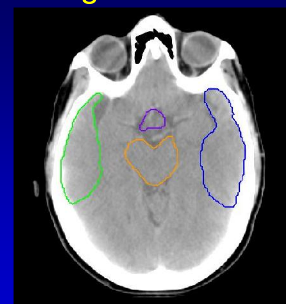
Organs at Risk



temporal lobes, chiasm, brainstem

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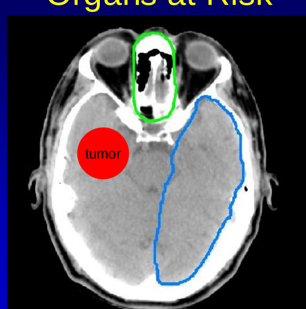
Organs at Risk



olfactory center, contralateral brain

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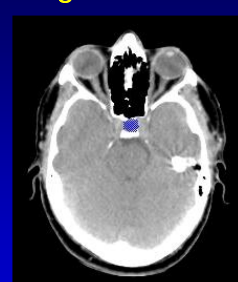
Organs at Risk



pituitary

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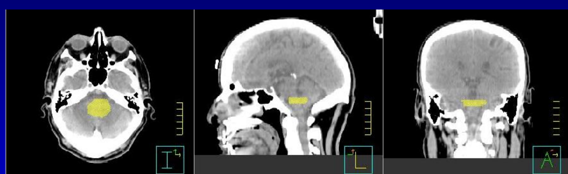
Organs at Risk



nausea center (area postrema): intersection pons & medulla

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General planning guidelines

1. Start with 3DCRT then look at IMRT to improve (resource cost)
2. 4-8 gantry locations (typically 5-7)
3. Unilateral tumor
   - Off contralateral brain (don't cross midline)
     45 Gy absolute max, cognitive standpoint: 24-30 Gy
4. Non-coplanar, non-opposed: less standardized
   - No optic intersection (if possible)
5. #3 & #4 above ⟶ beams oriented in sagittal plane
6. Global max objective: 105% Rx (allow up to 110%)

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Fractionation - toxicity

- Dose/fraction may be more important than total dose
  - Prescribe @ 180 cGy/fx, not over 2 Gy to large volume (significant complication increase)

want homogeneity (usually)

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Plan Assessment

- max & min dose: PTV and OARs
- DVHs: absolute dose and volume
- review <u>3D</u> distribution

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Plan Assessment

- Target:
  - PTV considered adequately treated if covered by 95% IDL
  - ≤ 20% of PTV receives 110% prescribed dose
- Normal structures:
  - Are tolerances met?

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Plan Assessment

Conformity index used to compare plans and/or treatment strategies (3DCRT, SRS, vs. IMRT):

$$\text{CF (cover factor)} = \frac{\text{\# pts.} \geq \text{Rx dose in PTV}}{\text{total \# pts. In PTV}}$$

$$\text{SF (spill factor)} = 1 - \frac{\text{\# pts.} \geq \text{Rx dose not in PTV}}{\text{total all pts.} \geq \text{Rx dose}}$$

CI (conformity index) = CF x SF (perfect=1.0)

RTOG 98-03

IMRT QA

- As needed for IMRT:
  - Films+chamber
  - Arrays

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Collision Avoidance

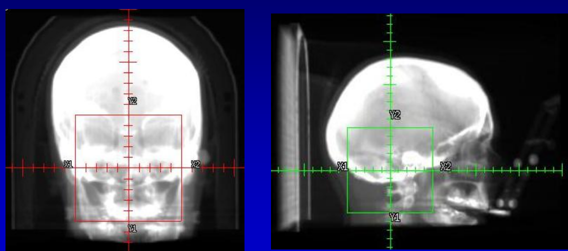
Non-coplanar beam geometry

↓

Verify gantry and couch positions to ensure no collisions

Setup Verification

Films/EPIs vs. DRRs compared and approved prior to 1st fx



EPIs, IGRT data, video, laser guidance stored for subsequent fractions to aid in patient positioning

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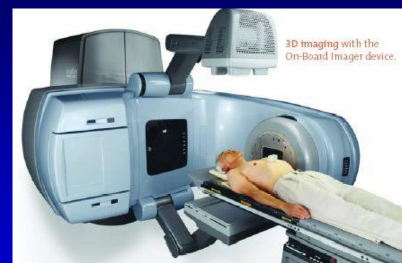
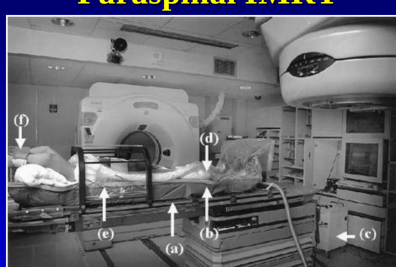
OBI



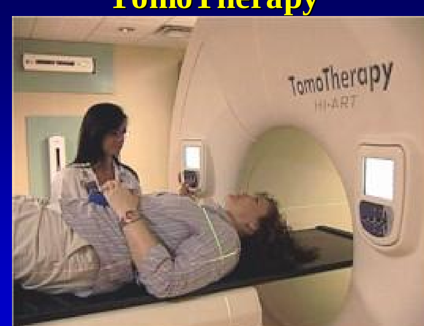
Varian Medical Systems, Palo Alto, CA

CT-on-rails+SBFS: Paraspinal IMRT



Shiu, et al IJROBP 57, 605-613, 2003

TomoTherapy



TomoTherapy, Inc., Madison, WI

IMRT Treatments

- Delivering intensity-modulated fields should be as easy as treatment of conventional fields with static MLC apertures after some experience is gained
- Less filming - no individual ports
- Radiocamera - longer setup time (5-7 mins. increase)

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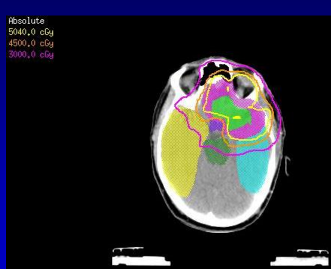
Case Studies

Irregular Frontal Lobe Lesion



Spare: chiasm, brainstem, temporal lobes
R optics, L globe, cord

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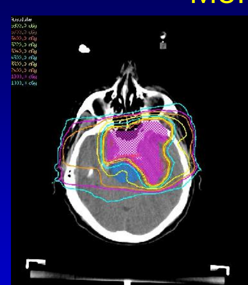
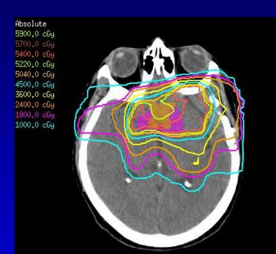
Meningioma





conformal, uniform 54 Gy dose to PTV
minimize dose: brainstem, chiasm

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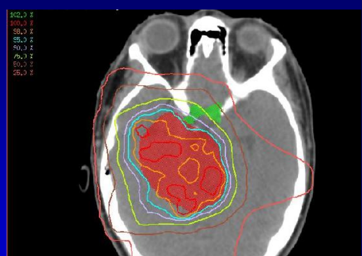
Brainstem Astrocytoma



standard headholder

GTV+1.5 cm=PTV

Objectives:
PTV min: Rx dose
PTV max: 105% Rx
chiasm: 50 Gy
L brain: 25 Gy max
Global max: 105% Rx

Minimize dose to chiasm

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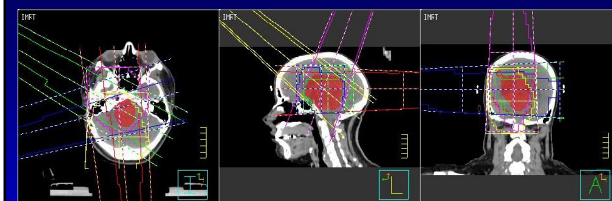
Brainstem Astrocytoma



Common sense:
stay off left brain
optic structures

Beams:
PG5L
RG30A
RG15P
AG40S
SG20P

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Frontal lobe Oligodendroglioma

Compare: 3DCRT vs. IMRT

- 3D: 6 beams
- IMRT: same beams - 1
- IMRT more conformal
- IMRT better uniformity
- ~same normal tissue dose

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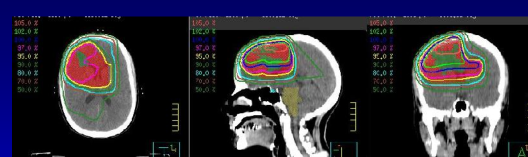
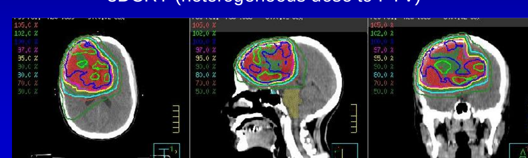
Frontal Lobe Oligodendroglioma



3DCRT (heterogeneous dose to PTV)



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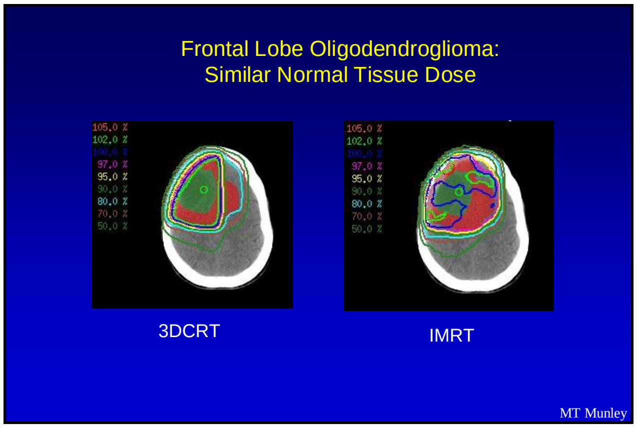
Frontal Lobe Oligodendroglioma:
Similar Normal Tissue Dose
3DCRT
IMRT
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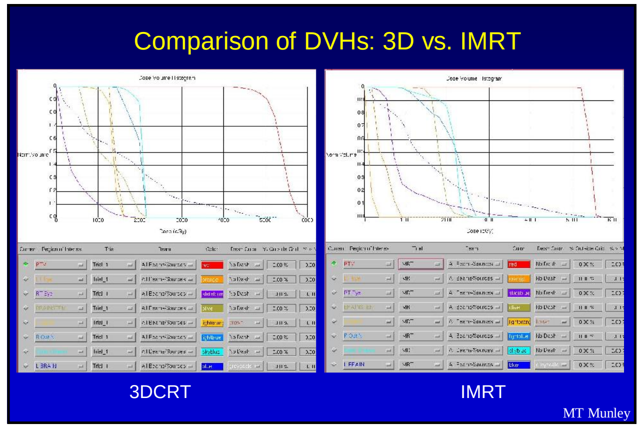
Comparison of DVHs: 3D vs. IMRT
3DCRT
IMRT
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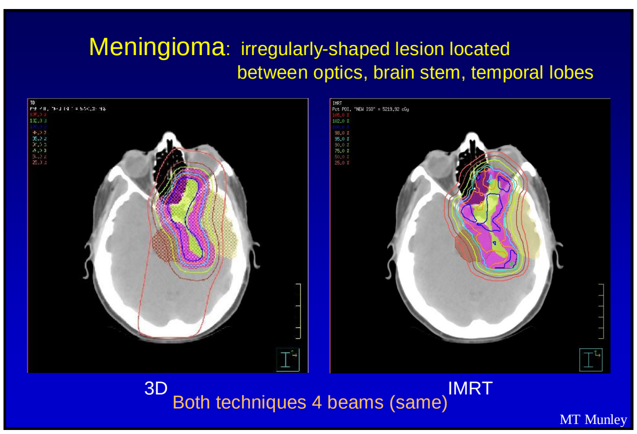
Meningioma: irregularly-shaped lesion located
between optics, brain stem, temporal lobes
3D
IMRT
Both techniques 4 beams (same)
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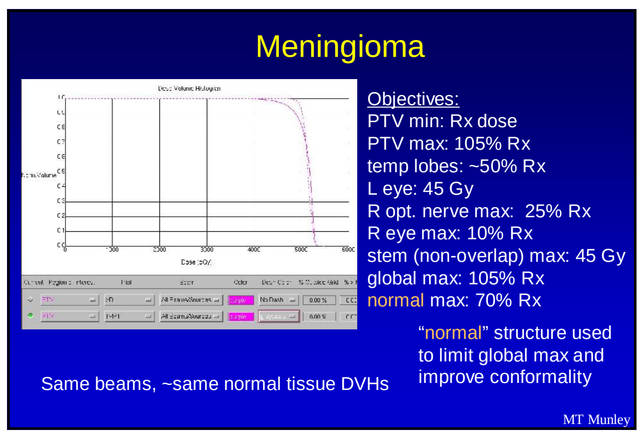
Meningioma
Objectives:
PTV min: Rx dose
PTV max: 105% Rx
temp lobes: ~50% Rx
L eye: 45 Gy
R opt. nerve max: 25% Rx
R eye max: 10% Rx
stem (non-overlap) max: 45 Gy
global max: 105% Rx
normal max: 70% Rx
"normal" structure used
to limit global max and
improve conformality
Same beams, ~same normal tissue DVHs
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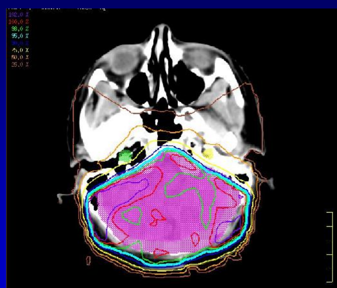
Post Fossa (whole) boost



"standard" Head cast

bi-lateral cochlea sparing
off optics

PTV: 1800 cGy
Cochlea: 60% max
Optics chiasm: 75% max
Remaining optics: 20% max
Cord: 80% max

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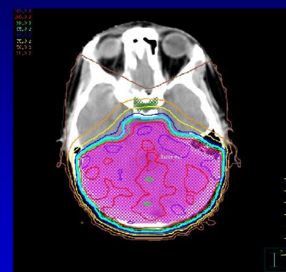
Post Fossa (whole) boost



Spare: optics, temporal lobes

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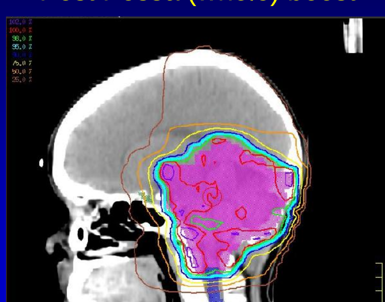
Post Fossa (whole) boost



sagittal plane

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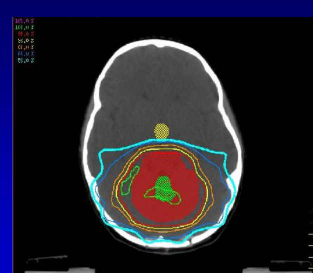
Conformal Tumor Bed Post Fossa Boost (COG ACNS0331)



Standard headholder

2340 cGy initial
3060 cGy boost (IMRT)
5400 cGy total
PTV_{boost}=GTV+1.5 cm+0.5 cm
PTV_{boost} 50 Gy min

minimize dose:
hypothalamus, temporal lobes, cochlea, optics, other normal brain

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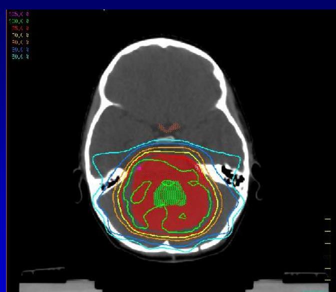
Conformal Tumor Bed Post Fossa Boost (COG ACNS0331)



chiasm, temporal lobe sparing

Beams:
- SG15P
- PG30L-T20S
- PG60L-T20S
- LT LAT
- RT LAT
- PG60R-T20S
- PG30R-T20S

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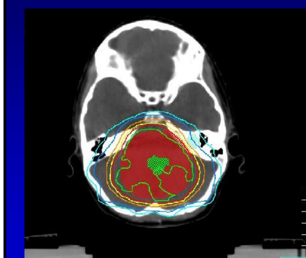
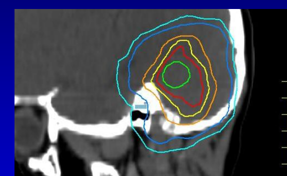
Conformal Tumor Bed Post Fossa Boost (COG ACNS0331)





cochlea sparing

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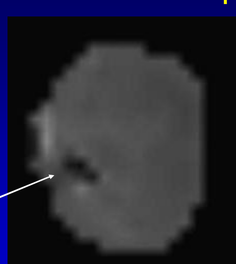
Fluence map



cochlea avoidance

left lateral

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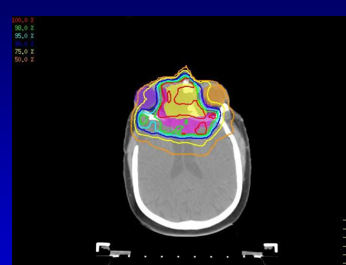
Esthesioneuroblastoma



transverse view

Supine
S-frame
Head cast
Lg angle knees
Arms down

5040 cGy initial
1620 cGy boost
6660 cGy total

Non-uniform margins

Mean globe dose 48 Gy

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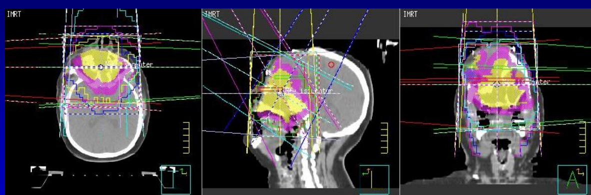
Esthesioneuroblastoma



non-coplanar beam geometry:
7 gantry positions: laterals (2) + “mohawk” (5)
spare globes
normal brain

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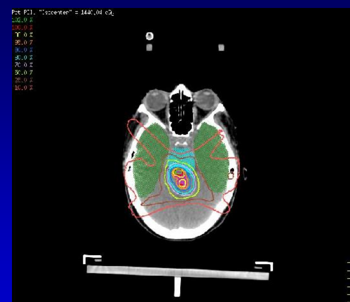
Ependymoma Boost: small lesion, abutting normals



95% IDL covers PTV
Spare: temporal lobes, optics, brain stem

Radiocamera (biteblock)
Headcast
“stereotactic” approach

PTV min: Rx dose
PTV max: 105% Rx
Cord max: 50% Rx
Stem max: 50% Rx
Temp lobes: 20% Rx
Otic max: 50% Rx
Orbits max: <10% Rx
Global max: 105% Rx
Above depends on dose from initial fields.

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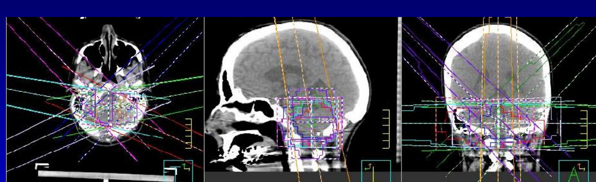
Ependymoma Boost



9 non-coplanar beams

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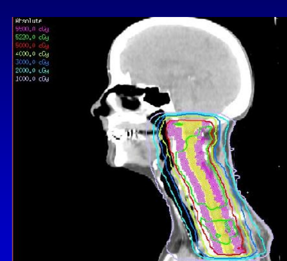
Spinal Cord Meningioma



top C1 - bottom T2

S-frame

PTV= canal + 1 cm radially

greatly varying external contour
→ want uniform dose

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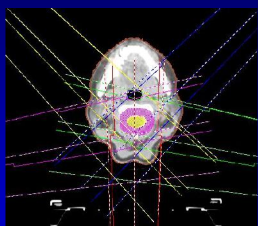
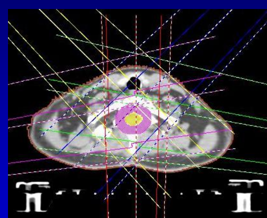
Spinal Cord Meningioma: Beam Geometry





5 beams: POST, PG80L, AG45L, AG45R, PG80R (coplanar)
avoid oral cavity, couch, S-frame rails

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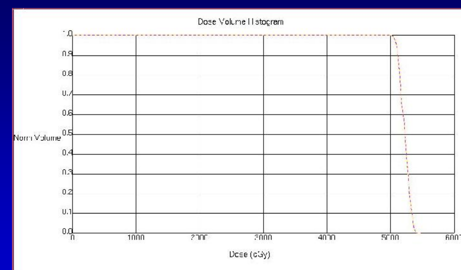
Spinal Cord Meningioma



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Paraspinal IMRT

Inc local tumor control while lower cord toxicity

≥ 2mm from cord

MSKCC body frames
Mets: 20 Gy/4-5 fxs, cord 6 Gy max (already received tolerance)
Primary: 70 Gy/35 fxs, cord 16 Gy

Results:
15 F/U: 13 reduction or no increase, 2 progressed
Pain improved 11/11
Long term control not established
No myelopathy at median 12 mos F/U

Bilsky, et al Neurosurgery 54: 823-831, 2004

TomoTherapy: Spinal Mets Retreatment

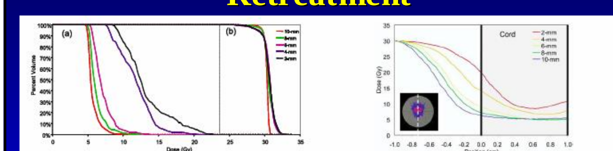


Fig. 5. (a) Spinal cord and (b) planning target volume dose–volume histograms for the 10-mm, 8-mm, 6-mm, 4-mm, and 2-mm spinal cord retreatment geometric test cases.

Fig. 6. Measured anterior-posterior film profile through the planning target volume, gap, and 2-mm, 4-mm, 6-mm, 8-mm, and 10-mm spinal cord retreatment geometric test cases.

10%/mm dose gradients possible
accuracy within 1.2 mm w/o special stereotactic immob (phantom)
N=8 patients, no myelopathy

Mahan, et al IJROBP 63:1576-1583, 2005

Disadvantages of IMRT

- Sharp dose fall off
  - Tumor edges are poorly defined: miss target
- Small fields
  - Higher susceptibility to motion
  - Slightest motion results in huge misses
- More expensive

Courtesy M. Mehta, M.D. - U. Wisconsin

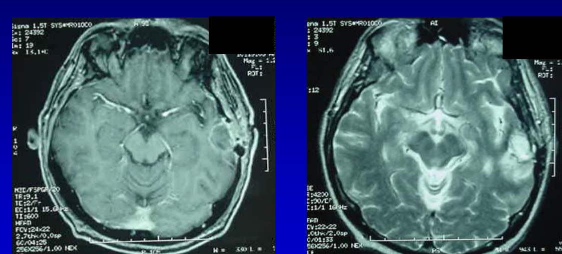
Recent/Future Studies

GBM - The Outcome

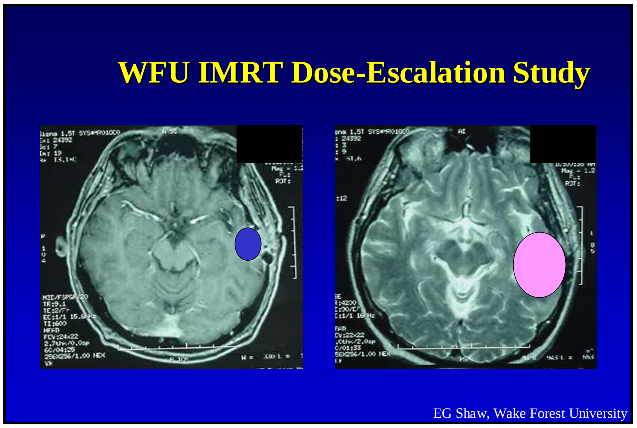
- **Median survival time**
  - **9-12 months in adults**
  - **18-36 months in children**
- **5-year survival rate**
  - **1-5% in adults**
  - **25-33% in children**
- **Local recurrence at the primary tumor site is universal except in the rare patient who achieves long-term local control and survival**

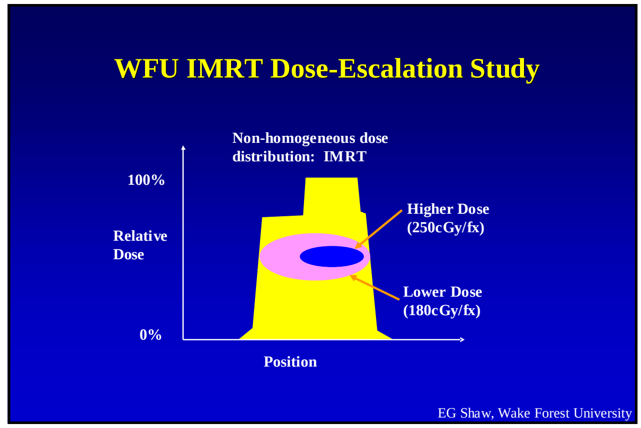
EG Shaw, Wake Forest University

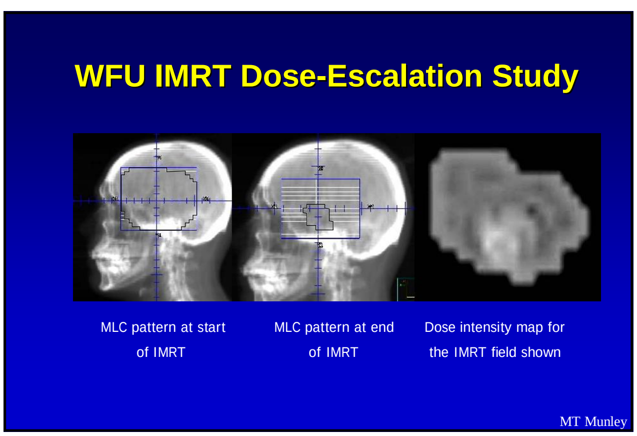
WFU IMRT Dose-Escalation Study

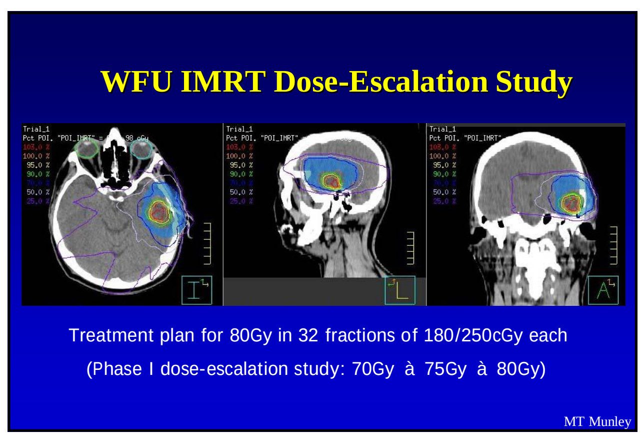


EG Shaw, Wake Forest University


WFU IMRT Dose-Escalation Study
EG Shaw, Wake Forest University


WFU IMRT Dose-Escalation Study
Non-homogeneous dose distribution: IMRT
100%
Relative Dose
0%
Higher Dose (250cGy/fx)
Lower Dose (180cGy/fx)
Position
EG Shaw, Wake Forest University


WFU IMRT Dose-Escalation Study
MLC pattern at start of IMRT
MLC pattern at end of IMRT
Dose intensity map for the IMRT field shown
MT Munley


WFU IMRT Dose-Escalation Study
Treatment plan for 80Gy in 32 fractions of 180/250cGy each
(Phase I dose-escalation study: 70Gy à 75Gy à 80Gy)
MT Munley

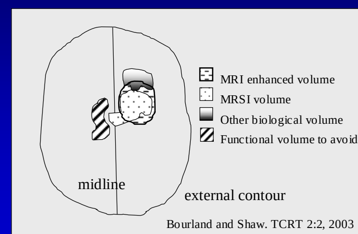
A phase I dose escalating study of intensity modulated radiation therapy (IMRT) for the treatment of glioblastoma multiforme (GBM)

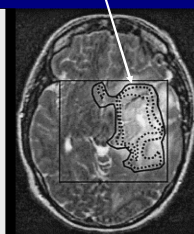
- **An IMRT-based concomitant boost approach for the treatment of GBM is feasible and safe at total doses of up to 80 Gy using 2.5 Gy per fraction to enhancing gross tumor with minimal margin.**

VW Stieber et al, Wake Forest University

The Bioanatomic Target Volume?

Choline:N-Acetyl-Aspertate index (CNI) > 2:1 +





Pirzkall et al., UCSF

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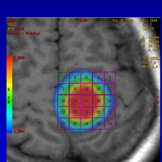
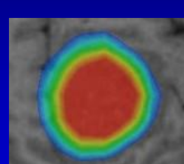
MRS: 2D Chemical Shift Imaging

What if Choline:NAA Ratios Could Be Correlated to Radiation Dose Necessary to Achieve Local Control?



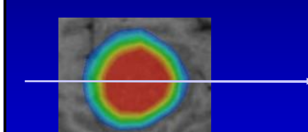


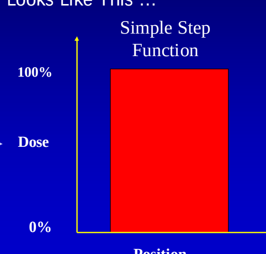
Pirzkall et al., UCSF

EG Shaw, Wake Forest University

MRS: 2D Chemical Shift Imaging

Instead of a Conventional Dose Distribution That Looks Like This …





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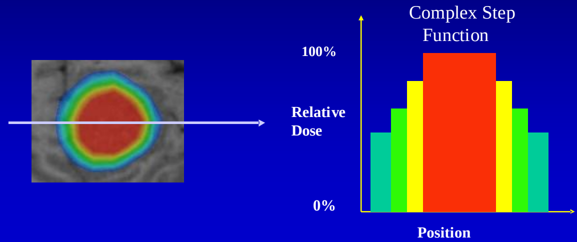
MRS: 2D Chemical Shift Imaging

The Dose Distribution Would Look Like This …



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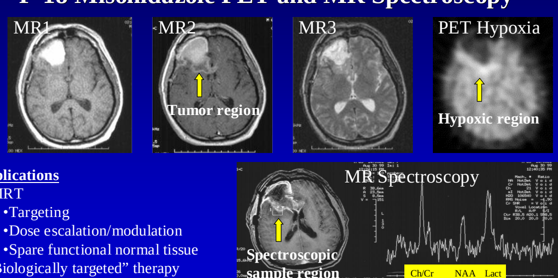
Pilot Study

- Brain Tumor Pilot: 5 Patients
  - CT, MRI/S, PET Perfusion, PET Hypoxia
  - Registration methods, Biological volumes, and Quantitative analysis
  - IMRT for multi-compartments
  - Show feasibility

JD Bourland, Wake Forest University

Brain Pilot Study

F-18 Misonidazole PET and MR Spectroscopy



Applications
- IMRT
  - Targeting
  - Dose escalation/modulation
  - Spare functional normal tissue
- "Biologically targeted" therapy
- If serial F/U, then response assessment

JD Bourland, Wake Forest University

Challenges

- Image quantitation/interpretation (structure delineation)
- Image registration accuracy (MR to CT)
- Need precise patient setup for every fraction
- Heterogeneous target dose (new strategy)
- Increased physics and dosimetry effort
- Integral dose effects?
- Demonstrate clinical benefit

MT Munley

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Summary

- IMRT use for CNS is increasing
- IMRT allows the treatment of irregularly-shaped volume in close proximity to normal structures (common CNS)
- IMRT appears to give improved conformity and uniformity when desired vs. 3DCRT (esp. large, irregular lesions)
- IMRT can be used to give a concomitant boost (GBM) or to modulate dose to a specific biologic property

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Summary

Overall clinical utility still TBD in many cases:

- Decrease late side effects → probably
- Cost justified (equipment, time, billing, inc. low dose volume)?
- Local control?
- More investigation needed

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THANK YOU

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