IMRT of the Central Nervous System

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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

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.

Course Outline

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

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:

1. Tumor Control Probability
   - increase target dose (homogeneous or heterogeneous dose escalation)

2. 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 conformity 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)

**Why IMRT for the CNS?**
- Allow for dose escalation - improved local control

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

**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

GBM Concomitant Boost

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

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

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

Organs at Risk

temporal lobes, chiasm, brainstem

Organs at Risk

olfactory center, contralateral brain

Organs at Risk

pituitary
Organs at Risk

nausea center (area postrema): intersection pons & medulla

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%)

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)

Plan Assessment
- max & min dose: PTV and OARs
- DVHs: absolute dose and volume
- review 3D distribution
Plan Assessment

- Target:
  - PTV considered adequately treated if covered by 95% IDL
  - ≤ 20% of PTV receives 110% prescribed dose

- Normal structures:
  - Are tolerances met?

Plan Assessment

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

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

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

\[ \text{CI (conformity index)} = \text{CF} \times \text{SF} \text{ (perfect=1.0)} \]

IMRT QA

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

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 tx

CT-on-rails+SBFS:
Paraspinal IMRT


OBI
Varian Medical Systems, Palo Alto, CA

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).

Case Studies

Irregular Frontal Lobe Lesion
- Spare: chiasm, brainstem, temporal lobes
- R optics, L globe, cord

Meningioma
- Conformal, uniform 54 Gy dose to PTV
- Minimize dose: brainstem, chiasm
Brainstem Astrocytoma

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

Beams:
- PG5L
- RG30A
- RG15P
- AG40S
- SG20P

Common sense: stay off left brain optic structures

Frontal lobe Oligodendrogloma

Compare: 3DCRT vs. IMRT
- 3D: 6 beams
- IMRT: same beams - 1
- IMRT more conformal
- IMRT better uniformity
- ~same normal tissue dose
Frontal Lobe Oligodendroglioma: Similar Normal Tissue Dose

Comparison of DVHs: 3D vs. IMRT

Meningioma: irregularly-shaped lesion located between optics, brain stem, temporal lobes

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 conformity

Meningioma

Both techniques 4 beams (same)

Same beams, ~same normal tissue DVHs
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

Spare: optics, temporal lobes

Conformal Tumor Bed Post Fossa Boost (COG ACNS0331)
Standard headholder
2340 cGy initial
3060 cGy boost (IMRT)
5400 cGy total
$PTV_{boost} = GTV + 1.5 \text{ cm} + 0.5 \text{ cm}$
$PTV_{boost}$ 50 Gy min

minimize dose:
hypothalamus, temporal lobes, cochlea, optics, other normal brain
Conformal Tumor Bed Post Fossa Boost (COG ACNS0331)

Beams:
- SG15F
- PG30L-T20S
- PG60L-T20S
- LT LAT
- RT LAT
- PG60R-T20S
- PG30R-T20S

Chiasm, temporal lobe sparing

Cochlea sparing

Fluence map

Cochlea avoidance

Esthesioneuroblastoma

Supine
- S-frame
- Head cast
- Lg angle knees
- Arms down
- 5940 cGy initial
- 1620 cGy boost
- 6660 cGy total
- Non-uniform margins
- Mean globe dose 48 Gy

Transverse view
**Esthesioneuroblastoma**

- Non-coplanar beam geometry: 7 gantry positions: laterals (2) + "mohawk" (5)
- Spare globes
- Normal brain

**Ependymoma Boost: small lesion, abutting normals**

- 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

**Ependymoma Boost**

- 9 non-coplanar beams

**Spinal Cord Meningioma**

- S-frame
- PTV= canal + 1 cm radially
- Greatly varying external contour
- Want uniform dose
- Top C1 - Bottom T2
Spinal Cord Meningioma: Beam Geometry

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

Spinal Cord Meningioma

Paraspinal IMRT

Inc local tumor control while lower cord toxicity
≥ 2mm from cord
MSKCC body frames
Mets: 20 Gy/4-5fxs, cord 6 Gy max (already received tolerance)
Primary: 70 Gy/35fxs, 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


TomoTherapy: Spinal Mets Retreatment

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

Mahan, et al UROBP 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

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

WFU IMRT Dose-Escalation Study
WFU IMRT Dose-Escalation Study

Non-homogeneous dose distribution: IMRT

MLC pattern at start of IMRT
MLC pattern at end of IMRT
Dose intensity map for the IMRT field shown

Treatment plan for 80Gy in 32 fractions of 180/250cGy each
(Phase I dose-escalation study: 70Gy & 75Gy & 80Gy)
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.

The Bioanatomic Target Volume?

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

MRS: 2D Chemical Shift Imaging

What if Choline:NAA Ratios Could Be Correlated to Radiation Dose Necessary to Achieve Local Control?
**MRS: 2D Chemical Shift Imaging**

The dose distribution would look like this...

**Pilot Study**

- **Brain Tumor Pilot:** 5 Patients
  - CT, MRS, PET Perfusion, PET Hypoxia
  - Registration methods, biological volumes, and quantitative analysis
  - IMRT for multi-compartment
  - Show feasibility

**Brain Pilot Study**

- **F-18 Misonidazole PET and MR Spectroscopy**

**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
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

Overall clinical utility still TBD in many cases:
- Decrease late side effects
- Cost justified (equipment, time, billing, inc. low dose volume)?
- Local control?
- More investigation needed

THANK YOU