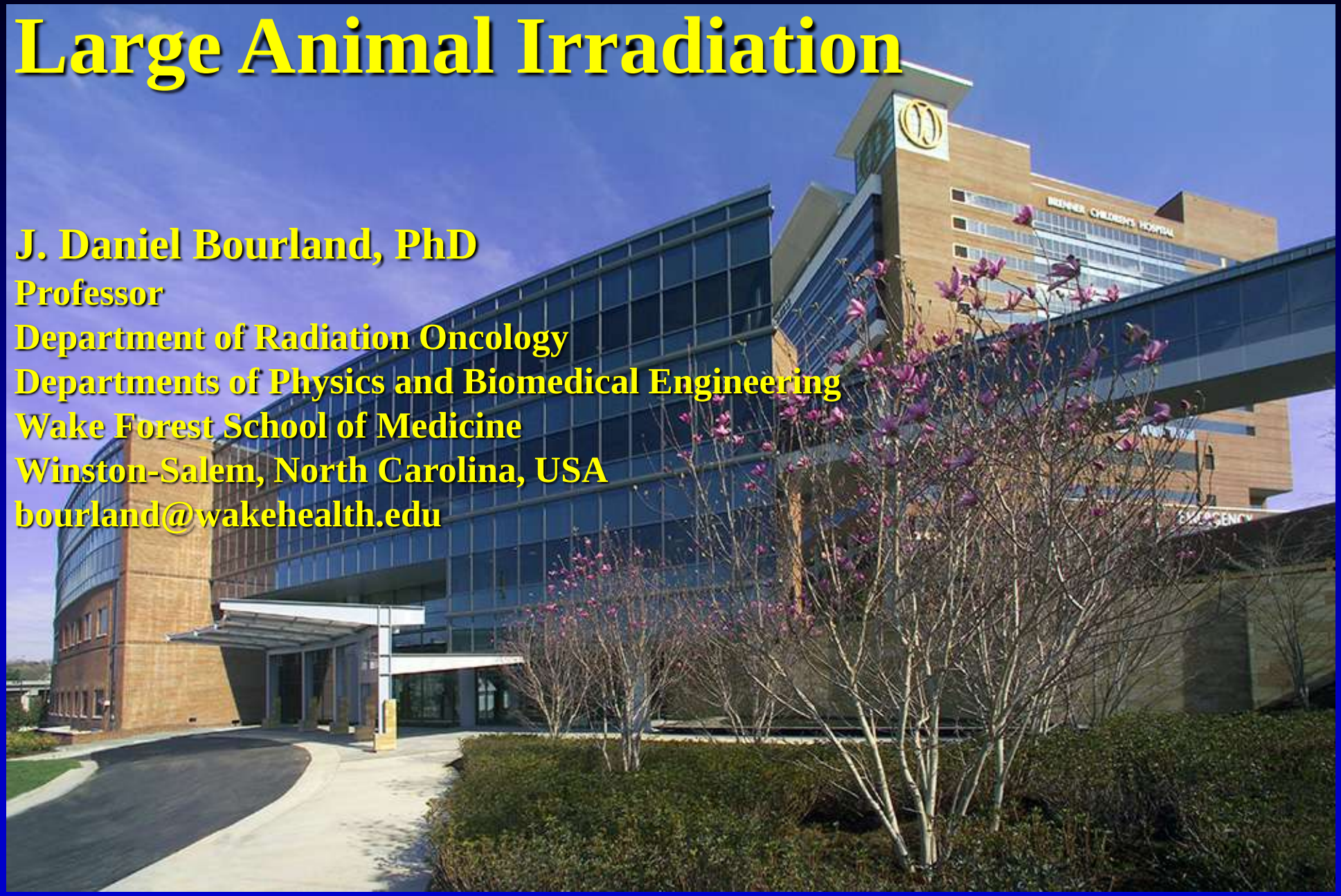
Large Animal Irradiation



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Outline

- NHP Whole Body
- NHP Whole Brain Fractionated
- NHP Lung
- Summary

Irradiation Issues

same as for humans

- Animal size (nominal L x W x H)
- Photon energy (to match size)
- Field size (coverage of the total body)
- Ease of use (set-up, irradiation efficiency)
- Beam characterization, dose constancy
- Homogeneity of dose
- Radiation protection of certain regions

Irradiation Device Selection

- Cesium Irradiator (0.662 MeV) (not TBI)
- Gamma Knife (1.25 MeV) (focused only)
- Orthovoltage X-Ray (0.3 MeV) (not available and not TBI)
- **Linear Accelerator, 6 MV** (or higher)
  - Same as used for human patients

Megavoltage Photon Beam
Percent Depth Dose Curve

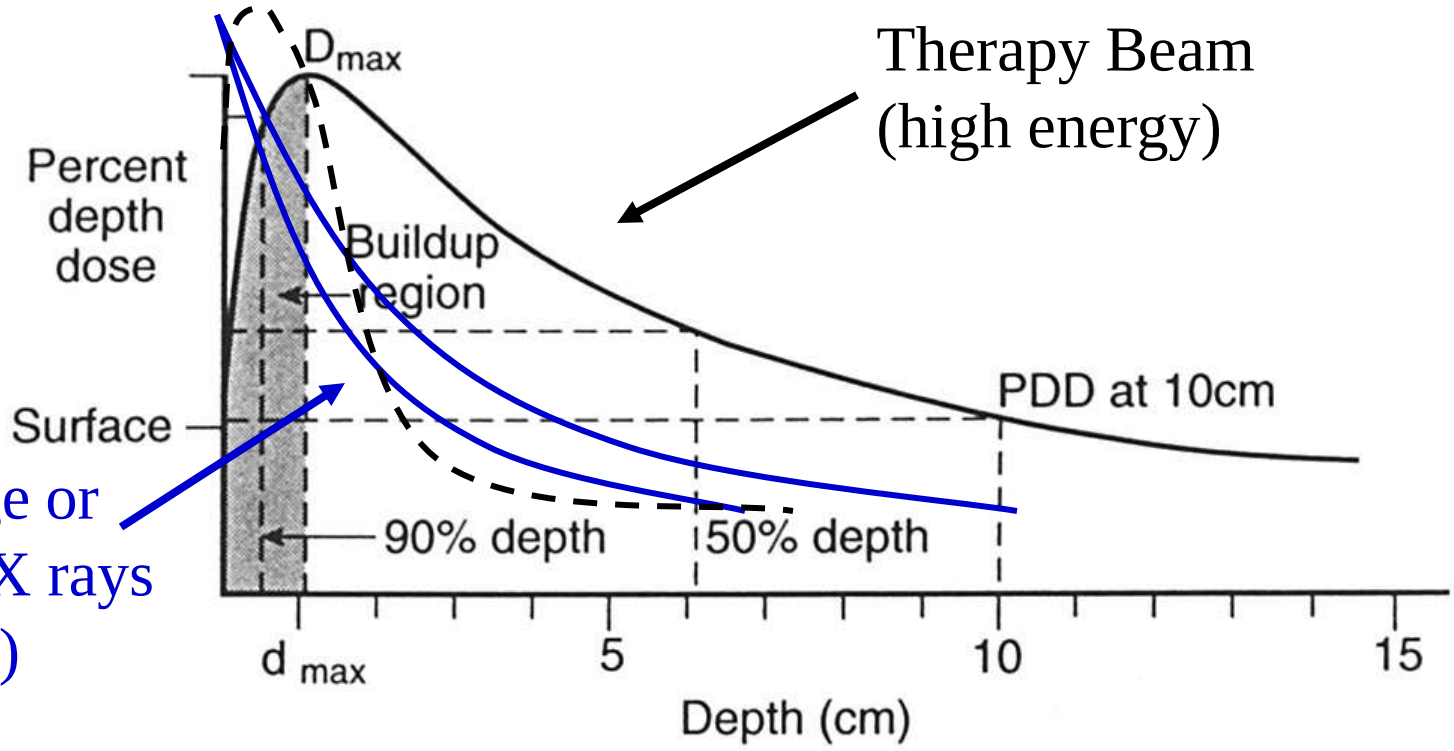
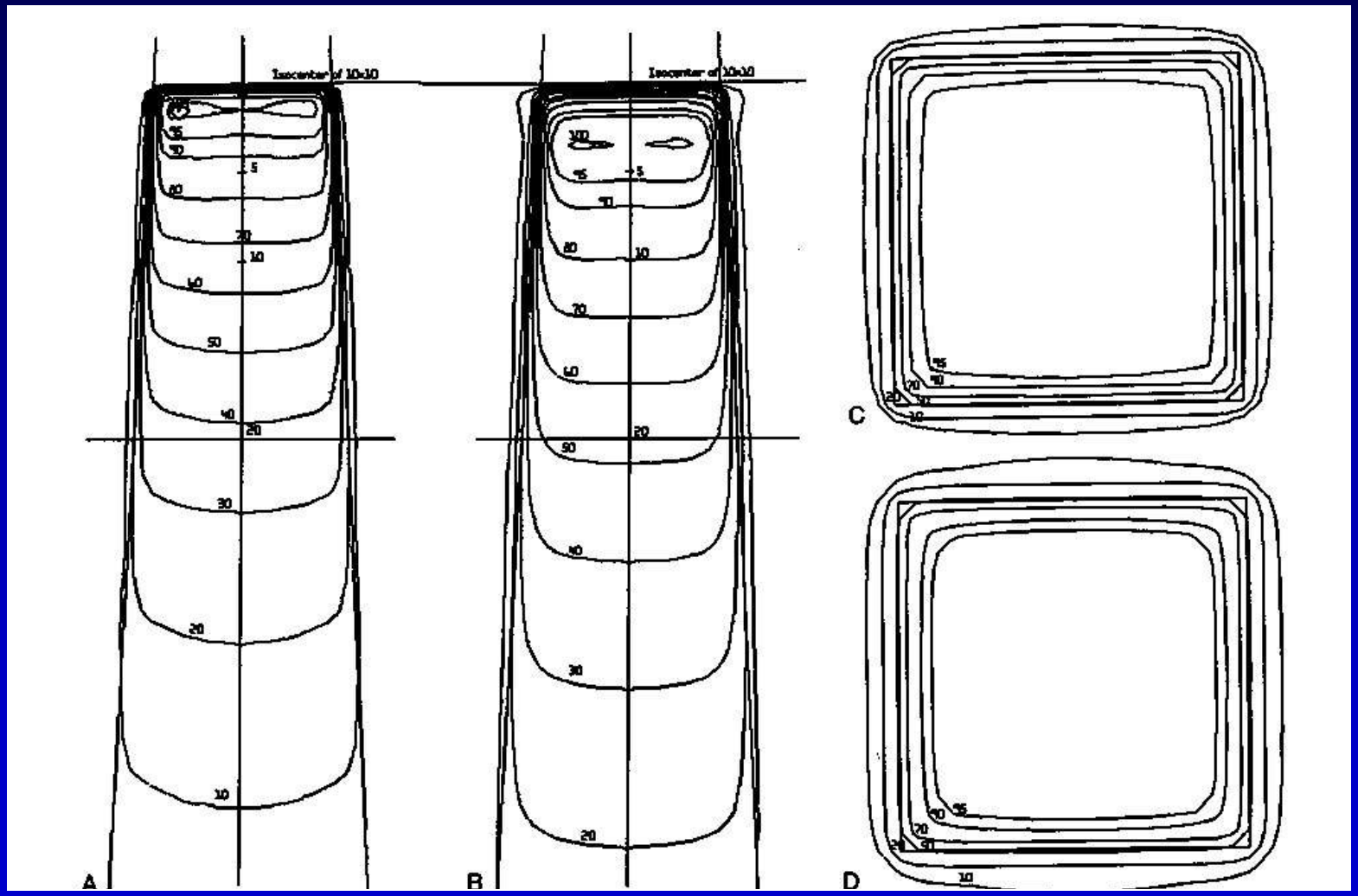


FIGURE 3–33.

A typical photon percent depth dose curve, characterized by surface dose, a buildup region, a point of maximum dose, and an exponen-

Isodose Curves

Representing a Radiation Dose Distribution



The Electron Linear Accelerator

Most Common Radiation Treatment Device

- Electrons are accelerated (must be charged particle)
- Creates photon beams or electron beams

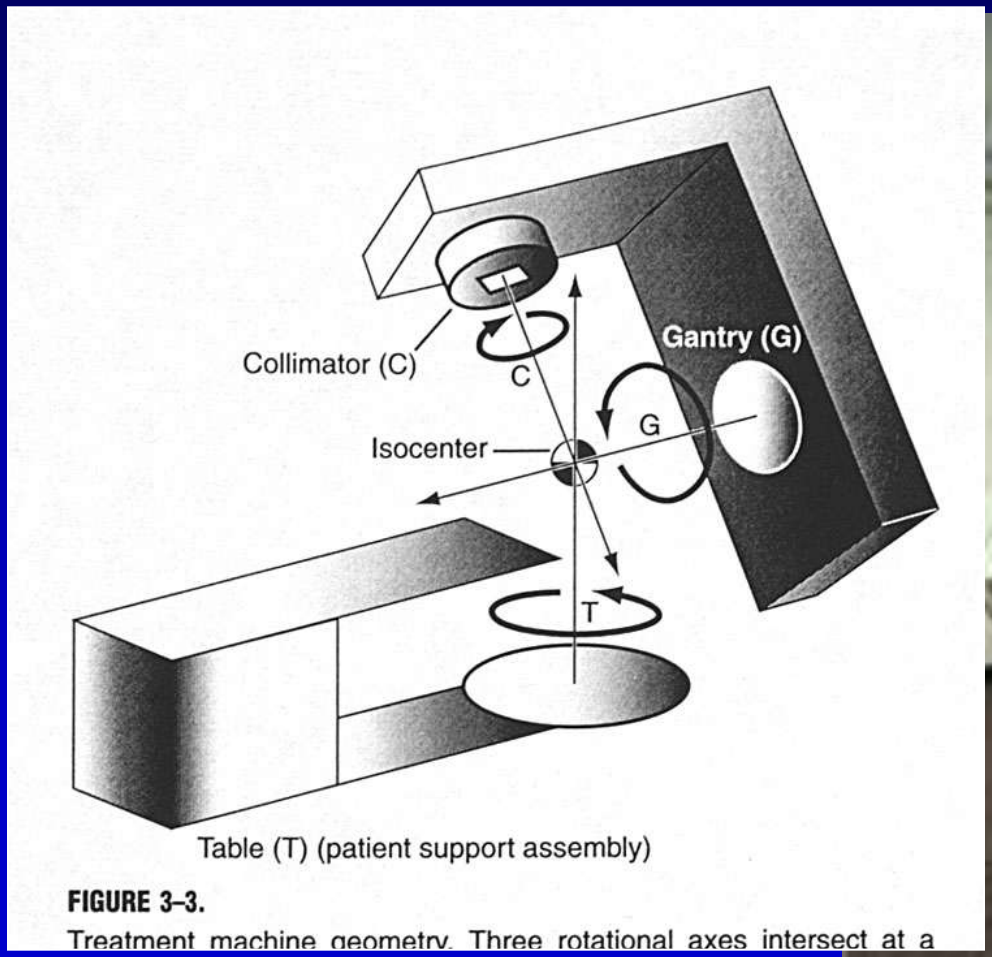


FIGURE 3–3.

Treatment machine geometry. Three rotational axes intersect at a

Project 1: Total Body Irradiation

dose escalation study

- 15 animals, matched by sex, weight
- Animal handling and irradiation logistics
  - After-hours irradiations
  - Blinded exposures and tissue doses
- Whole body irradiation (acute exposure)
  - 6 MV x rays; left side followed by right side
  - 0 Gy (sham) – 3 animals
  - 2 Gy – 6 animals
  - 5 Gy – 6 animals
- Tissues sampled for diverse research groups

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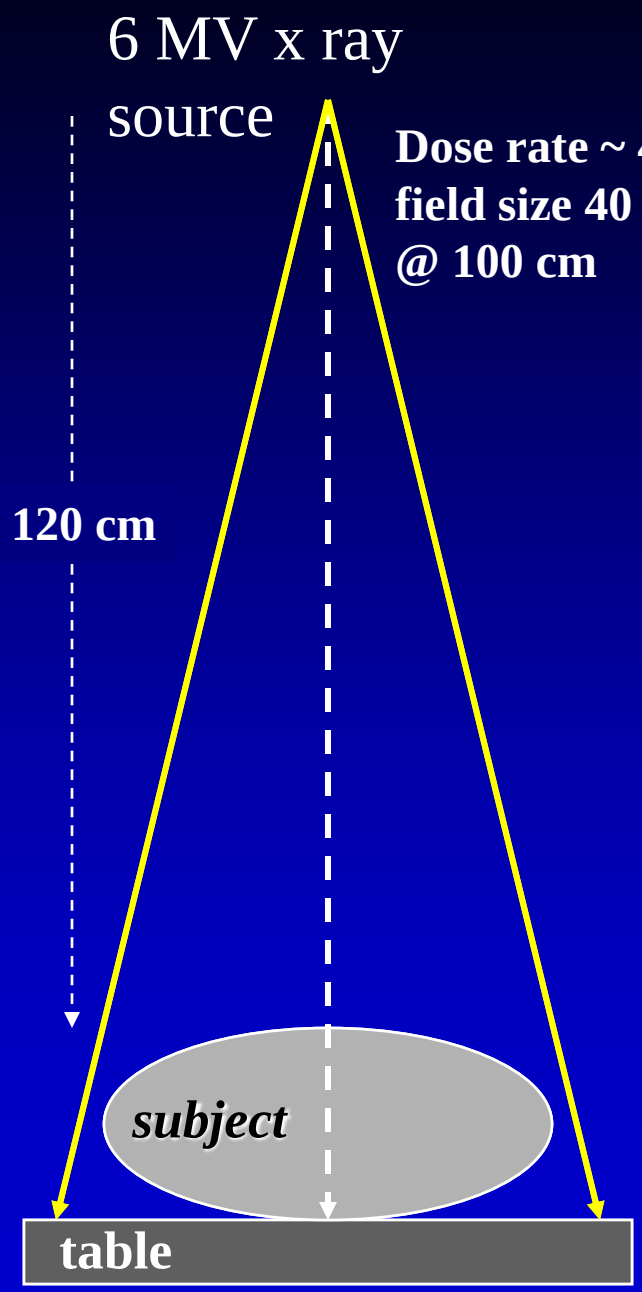
PRIMATE CENTER

Irradiation and Protocol Parameters

- Nominal animal thickness = 8 to 10 cm
- Dose calculated to mid-plane
  - Field size, SSD, mid-plane depth, 6 MV x rays
- Parameters verified before irradiation: linear accelerator geometry, nominal SSD, MU, dose rate
- Animals are under anesthesia during irradiation
- Universal Precautions must be followed: potential for disease transfer
- Imaging and sham irradiations included for all animals, based on randomization (depending on study design)

Total Body Irradiation Geometry



Summary

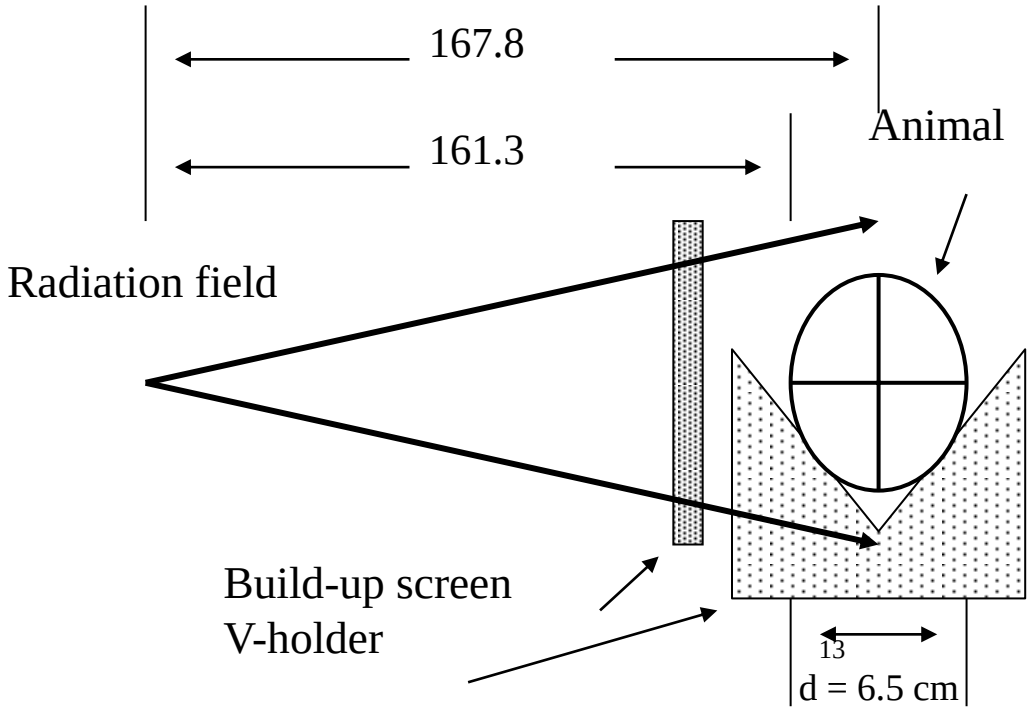
- Whole-body irradiations performed as scheduled
  - Irradiation geometry determined; quality assurance
  - Procedures, devices, people – all worked smoothly
- Investigation of dose to particular organs, points
  - Based on CT scan of a matched animal in both treatment positions
  - Report to the Core PI with any recommendations
- Turning animals works, but not best approach

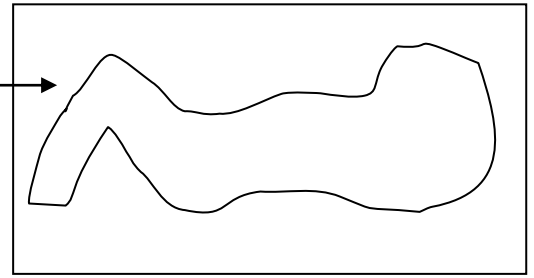
Project 2: Total Body Irradiation
2 Gy to mid-line

- 10 animals, matched by sex, weight
- Animal handling and irradiation logistics
  - After-hours irradiations
- Whole body irradiation: 2 Gy, 6 MV x rays
  - 1 Gy right lateral; 1 Gy left lateral
  - DR = 200 MU/min @ 100 cm = 68.7 cGy/min @ 167 cm
  - Extended SSD, with “turntable” for positioning
  - No change to animal position!
  - Build-up plate in place
- Anesthesia and Universal Precautions

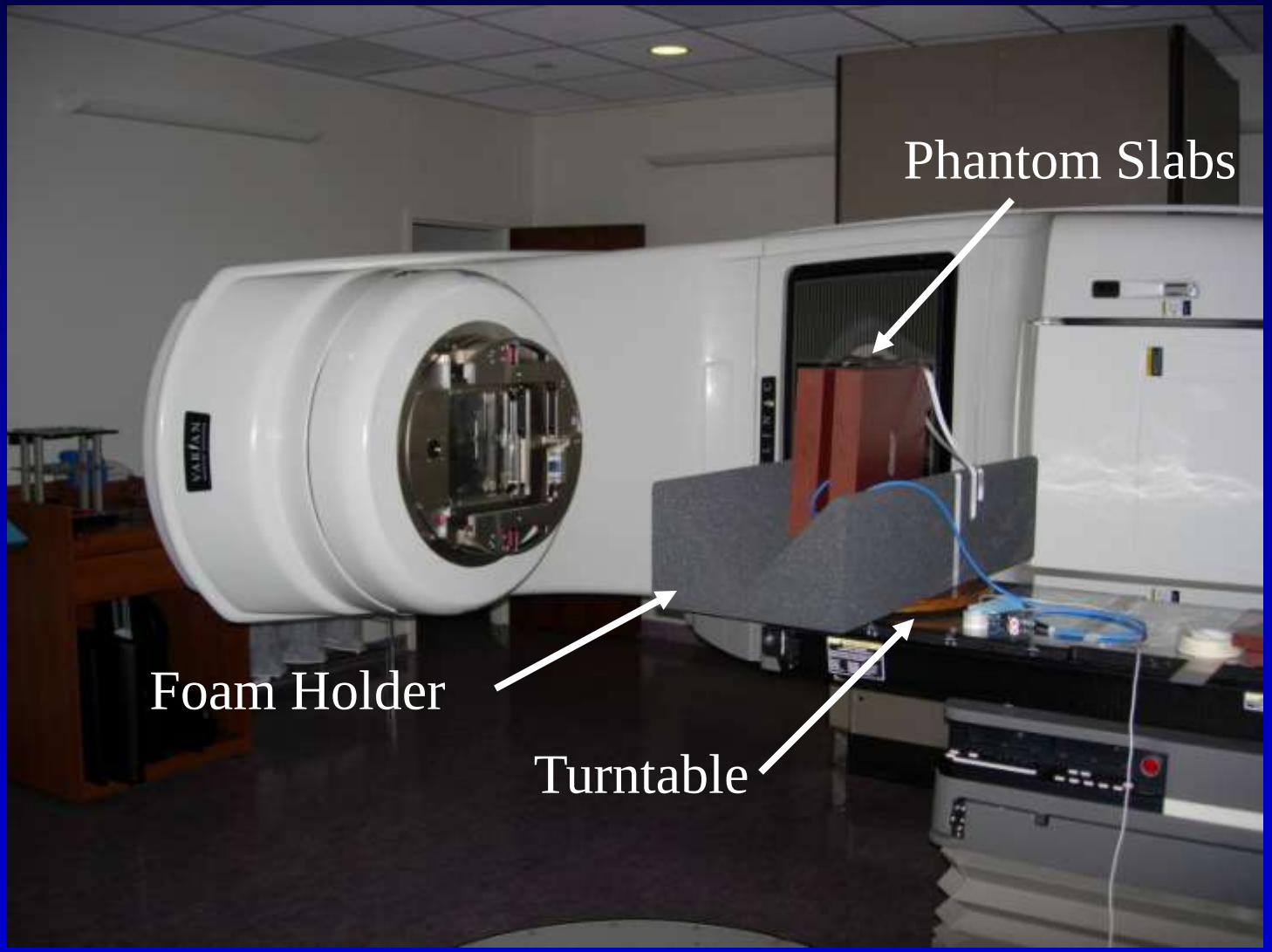
Irradiation Geometry

extended SSD/SAD; turntable for rotation

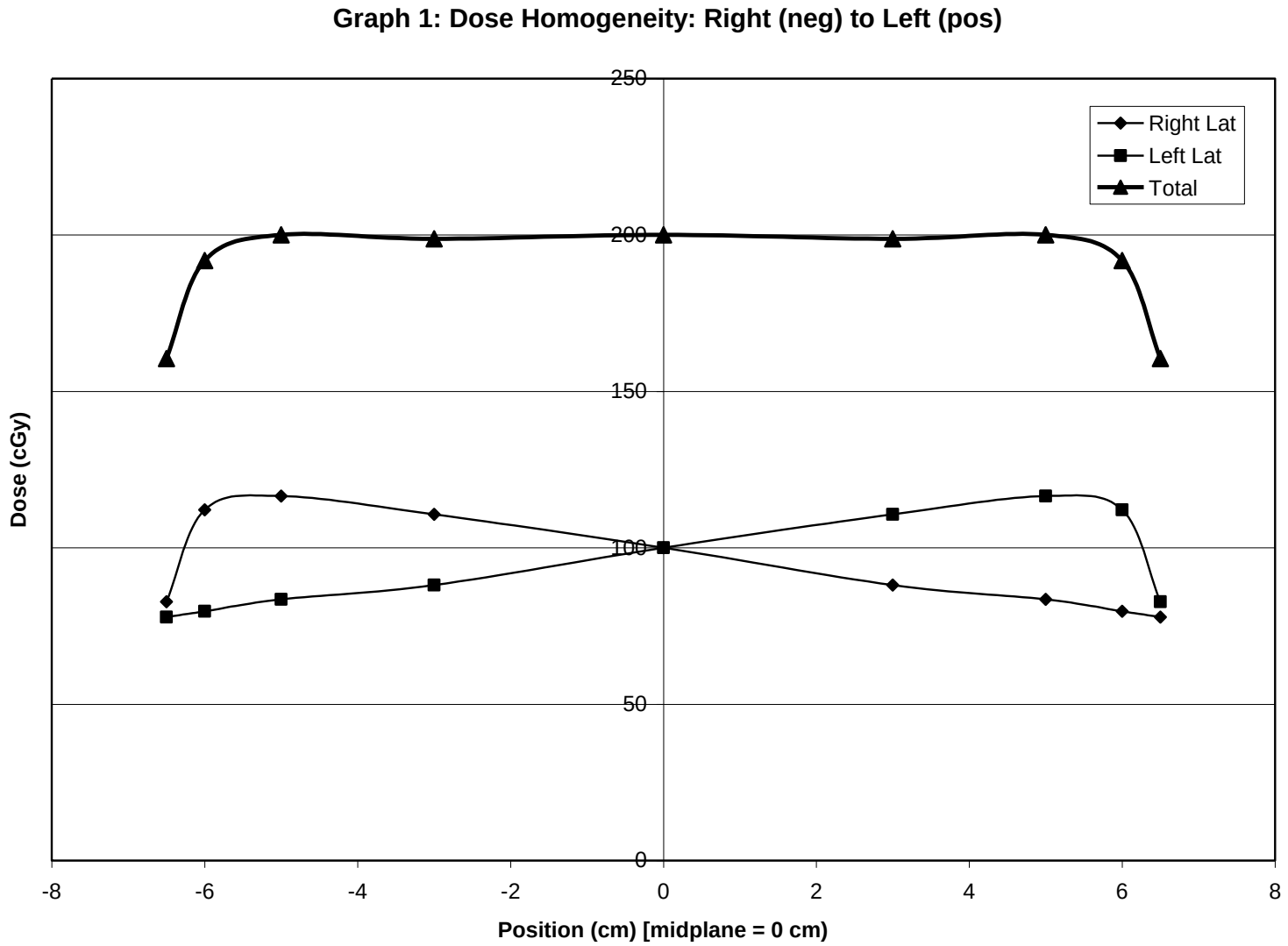




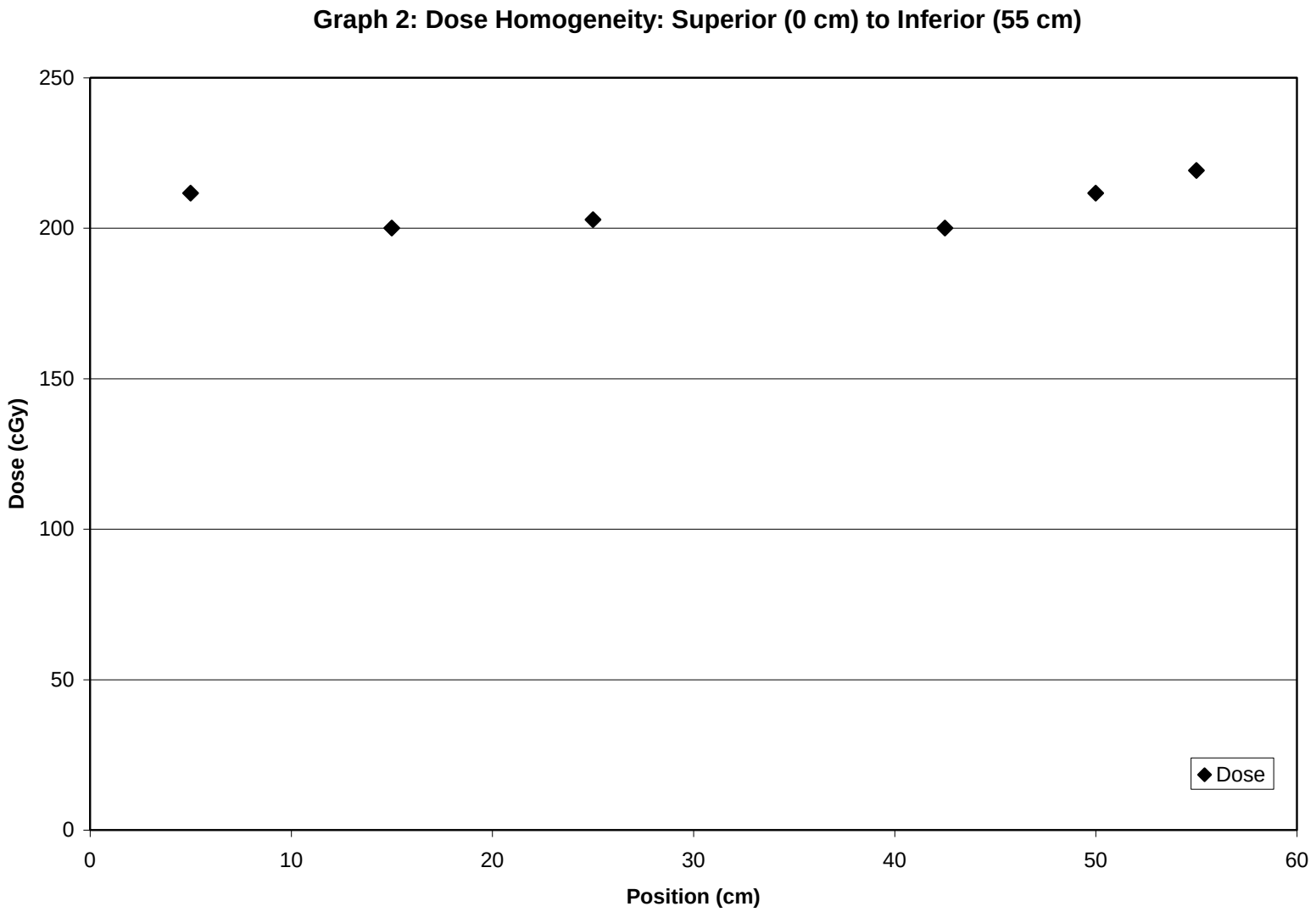
Irradiation Geometry and DoseVerification



Dose Homogeneity: Ideal



Dose Homogeneity: S-I Level



Irradiation Record

Animal #	Time In / Out (AM)	MU Rt	MU Lt	SSD	Field Size 40x20 @ 100 cm	Nominal Diameter (cm)	Mid-Plane Depth (cm)	Bolus Screen	Weight (kg)	Comment
	8:10 / 8:55	291	291	161.3	Y	13	6.5	N / Y		
	9:15 / 9:21	291	291	(163.1)	Y	(13)	(6.5)	Y		
	9:24 / 9:32	291	291	(163.1)	Y	(13)	(6.5)	Y		
	9:49 / 9:55	291	291	(163.1)	Y	(13)	(6.5)	Y		
	10:00 / 10:07	291	291	(163.1)	Y	(13)	(6.5)	Y		
	10:23 / 10:29	291	291	(163.1)	Y	(13)	(6.5)	Y		
	10:32 / 10:40	281	281	162.8	Y	10	5.0	Y		
	11:00 / 11:07	291	291	(163.1)	Y	(13)	(6.5)	Y		
	11:09 / 11:16	291	291	(163.1)	Y	(13)	(6.5)	Y		
	11:19 / 11:25	286	286	162	Y	11.5	5.8	Y		

Summary

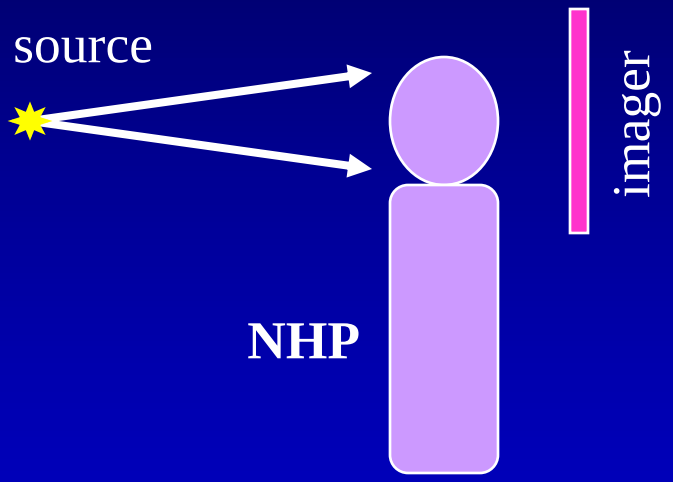
- Ten NHPs received mid-plane dose of 200 cGy
- Dose homogeneity = +/- 5% of mid-plane dose
  - surface dose is low (-20%, or 160 cGy) – build-up screen used
  - ankle mid-plane dose is high +10% (~220 cGy).
- Irradiations proceeded as planned
  - Any exceptions noted
  - Use of record/verify system very helpful

Project TSI: NHP Whole Brain Irradiation and Cognition

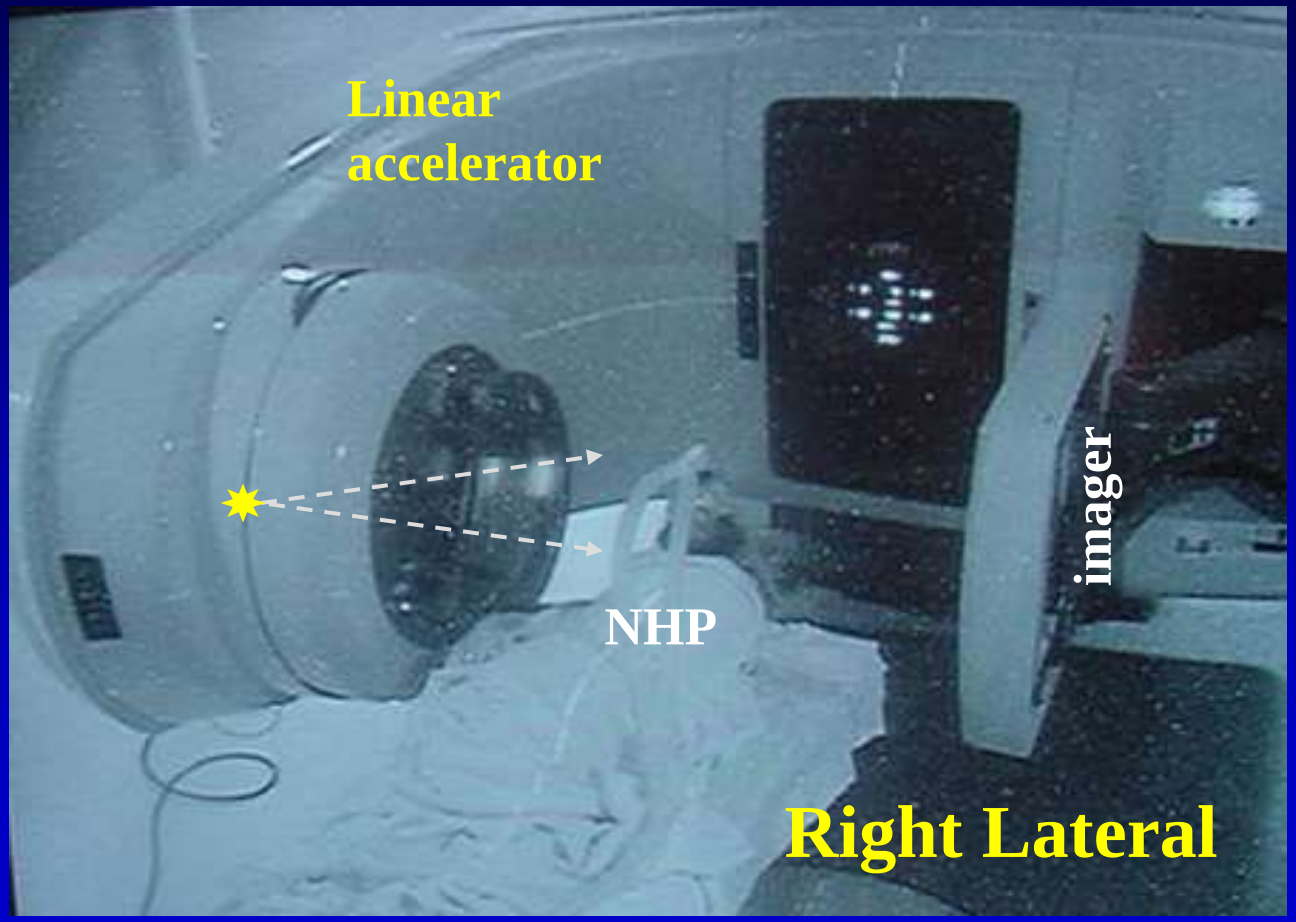
- 4 animals, male, ages 6 – 10 years
- Animal handling and irradiation logistics
  - After-hours irradiations, every Monday and Thursday
- Whole brain irradiation: 40 Gy; 5 Gy / fx x 8 fxs over 4 weeks, 6 MV x rays
  - 2.5 Gy right lateral; 2.5 Gy left lateral
  - CAX at canthus, eye block in for shielding
  - No change to animal position
  - IMPAC R/V used for setup and EPID capture
- Gas anesthesia and Universal Precautions

Irradiation Geometry

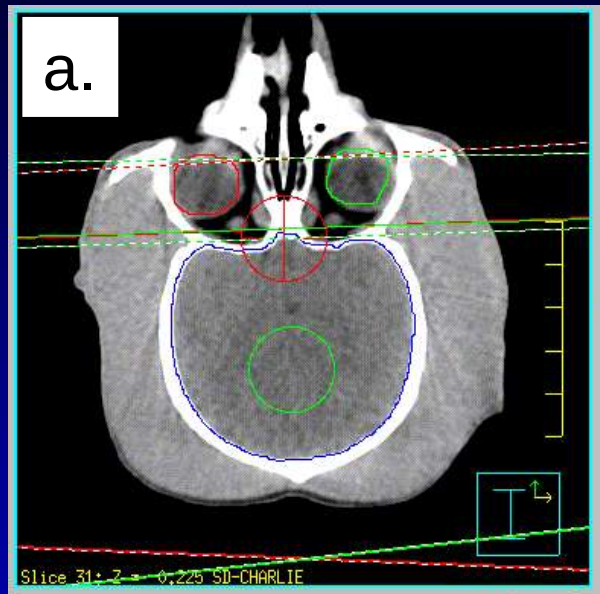
6 MV x rays, 8 x 12 cm^2 field size, 96 cm SSD

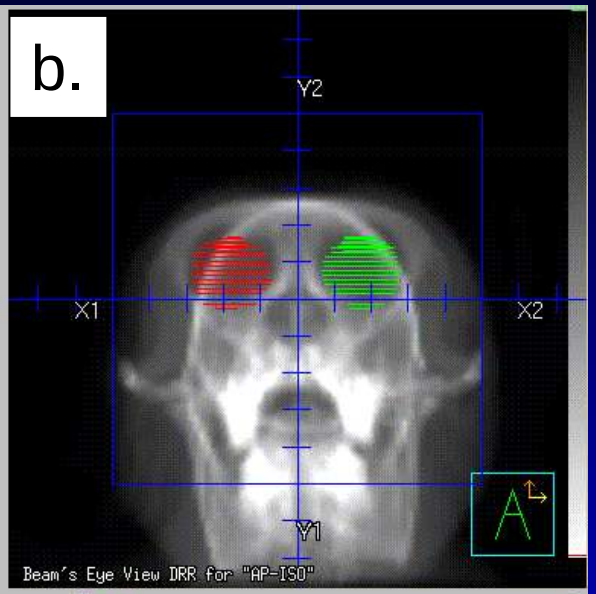


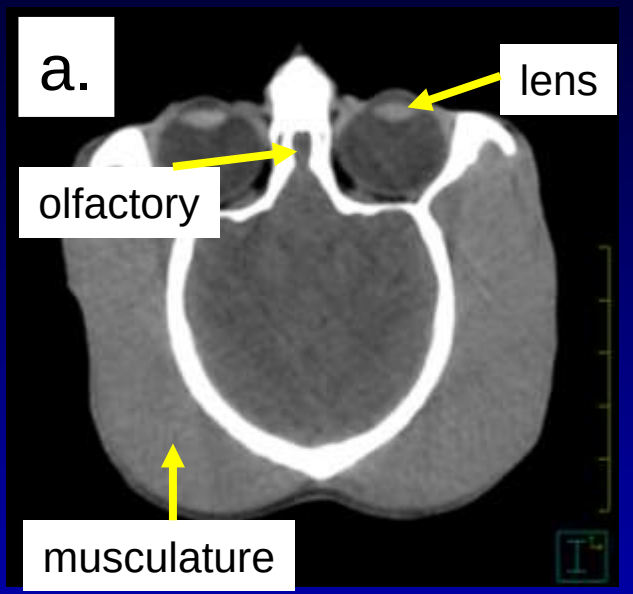
Right Lateral
(view from above)

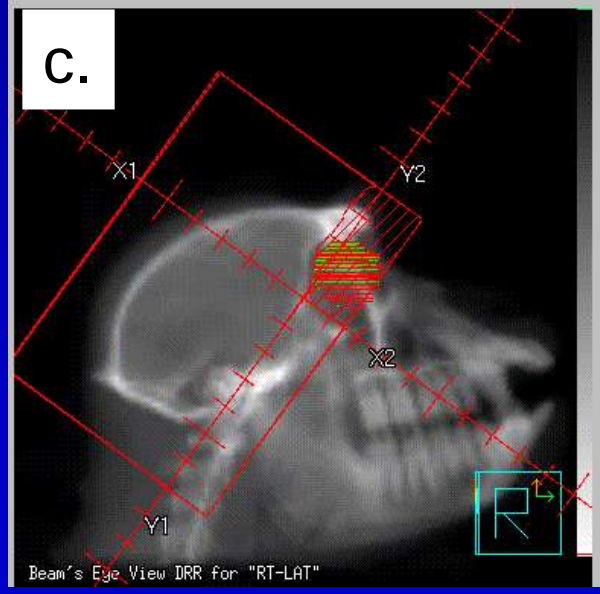


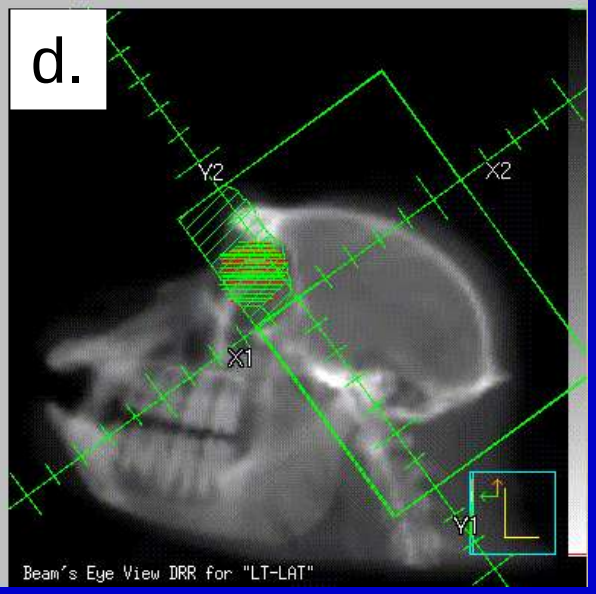
Irradiation Planning - Geometry

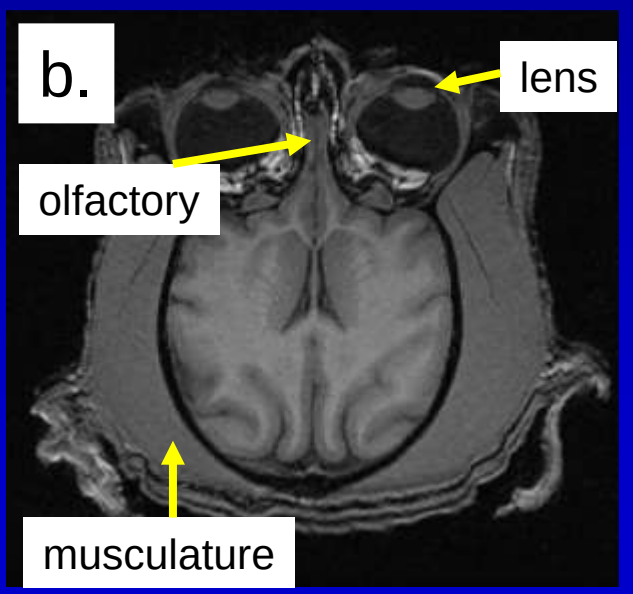




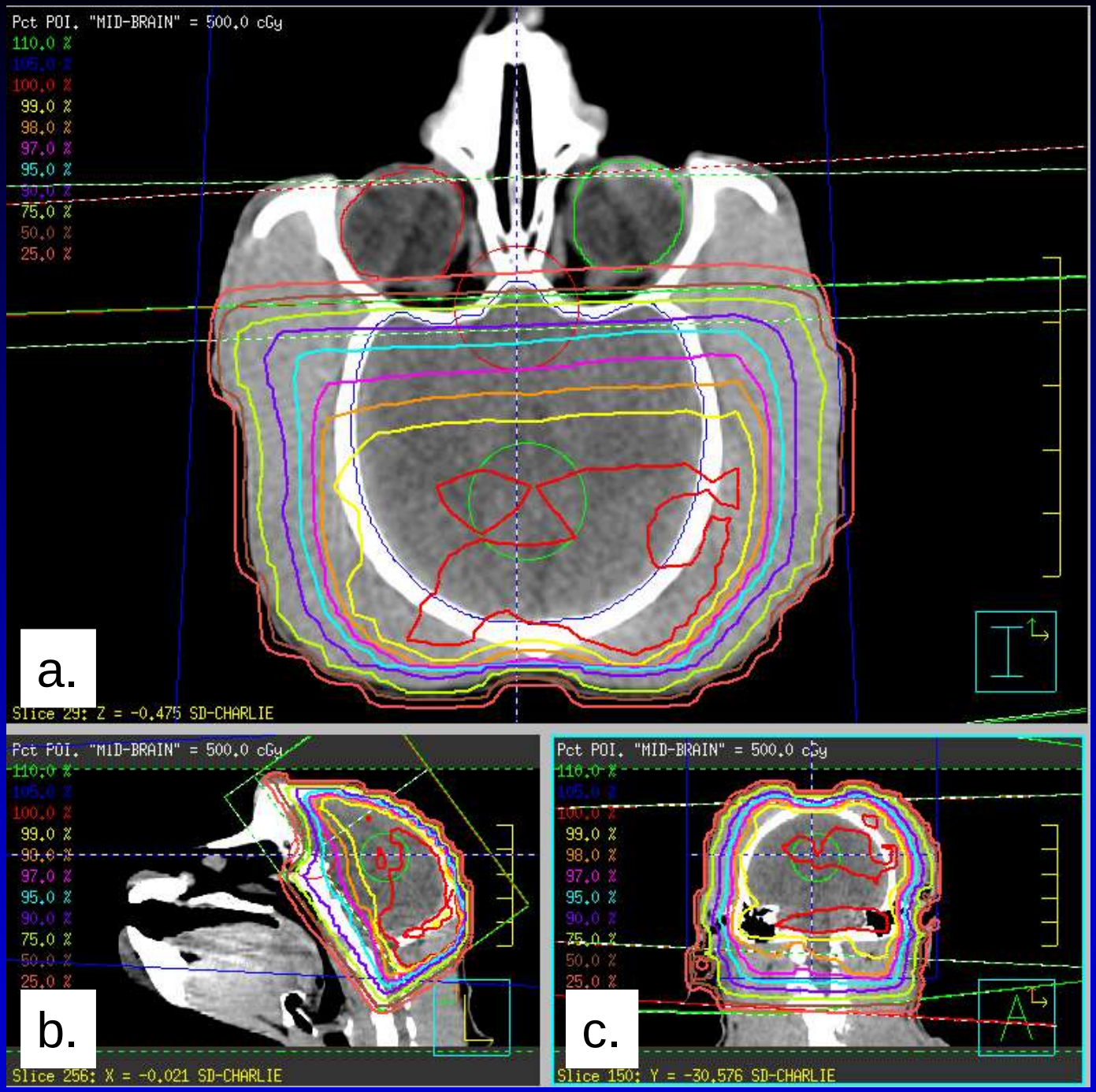








Irradiation Planning - Dose



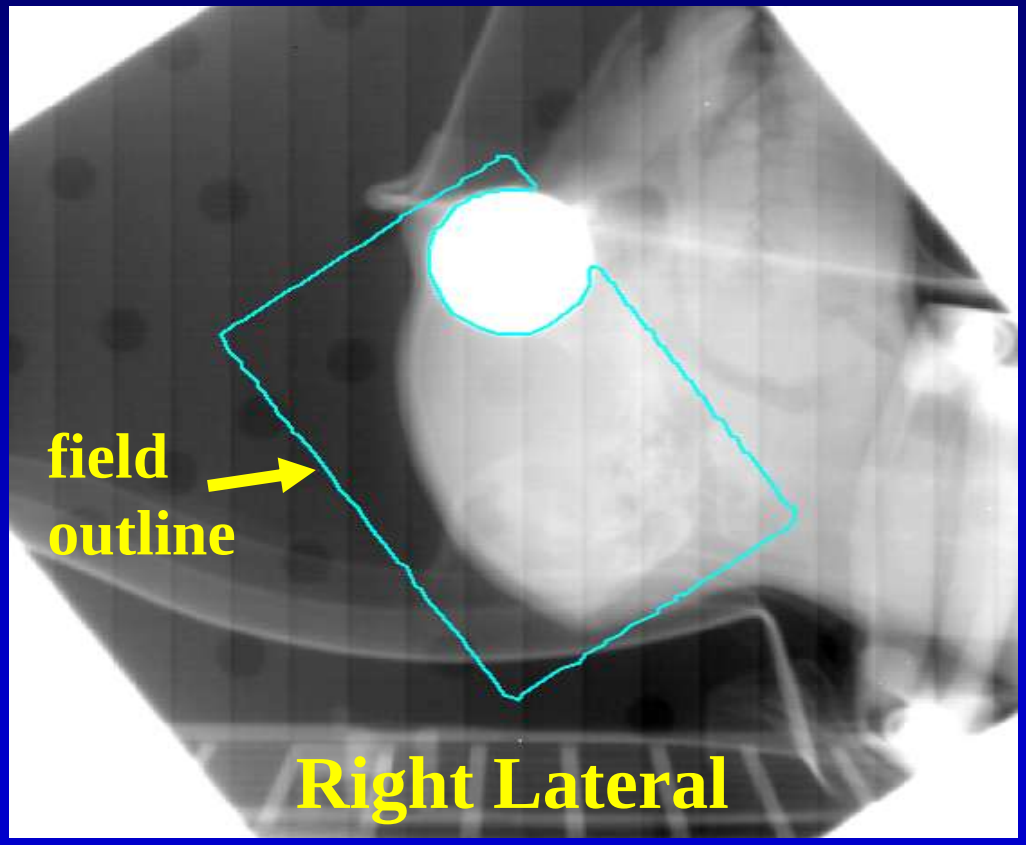
Whole Brain Irradiation Fields

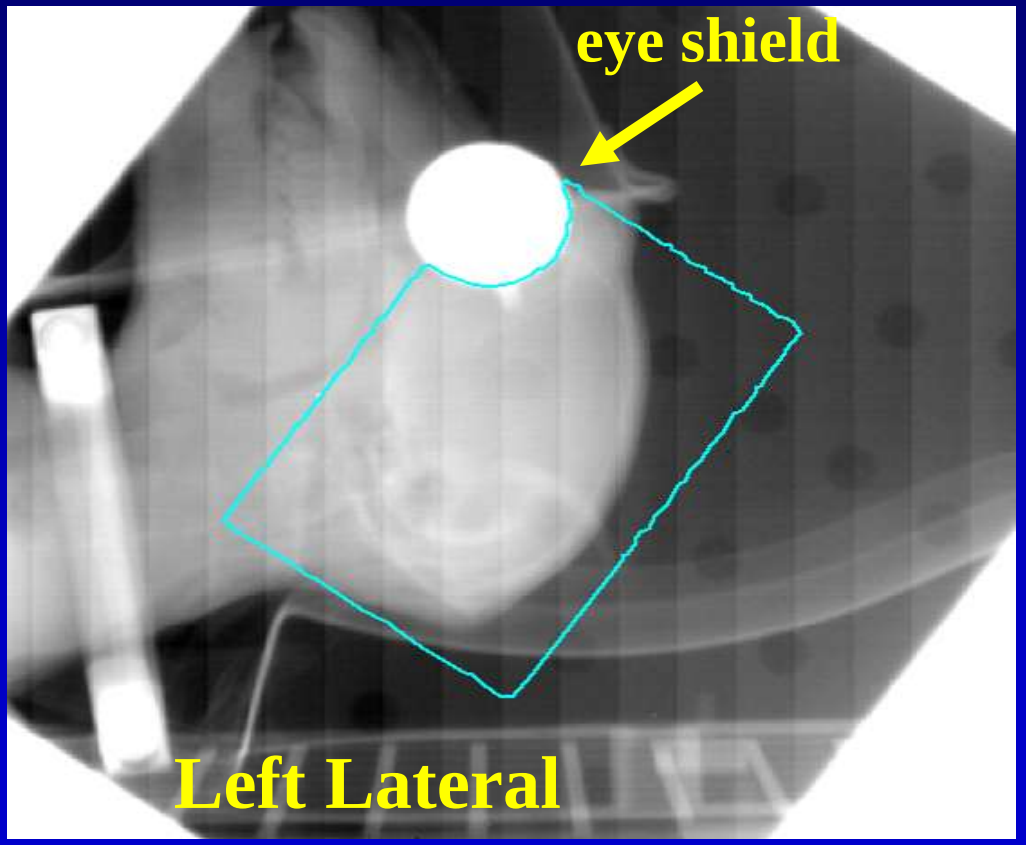
Pre-irradiation image guidance used

BR, 8/25/08 : radiation field outline in blue

6 MV x rays; 40 Gy total

5 Gy/fx x 8 fxs; 2.5 Gy/field, eye shield in place





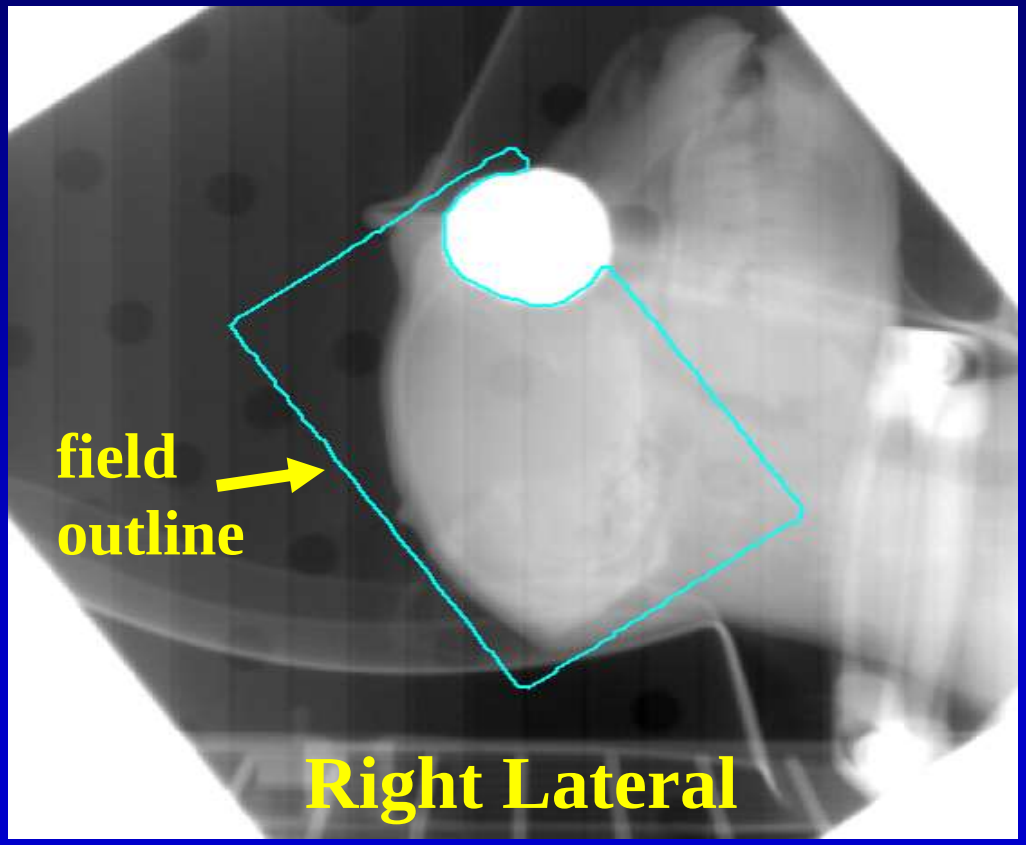
Whole Brain Irradiation Fields

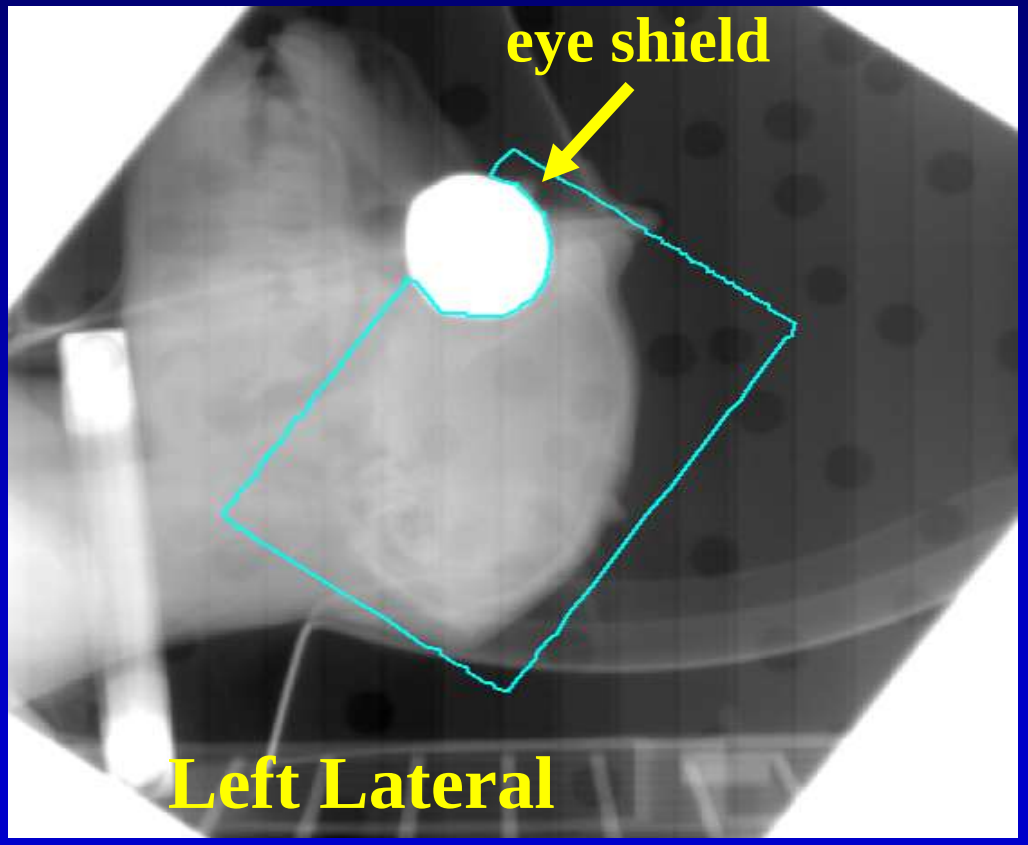
Pre-irradiation image guidance used

BR, 9/11/08: radiation field outline in blue

6 MV x rays; 40 Gy total

5 Gy/fx x 8 fxs; 2.5 Gy/field; eye shield in place





Summary: NHP Whole Brain

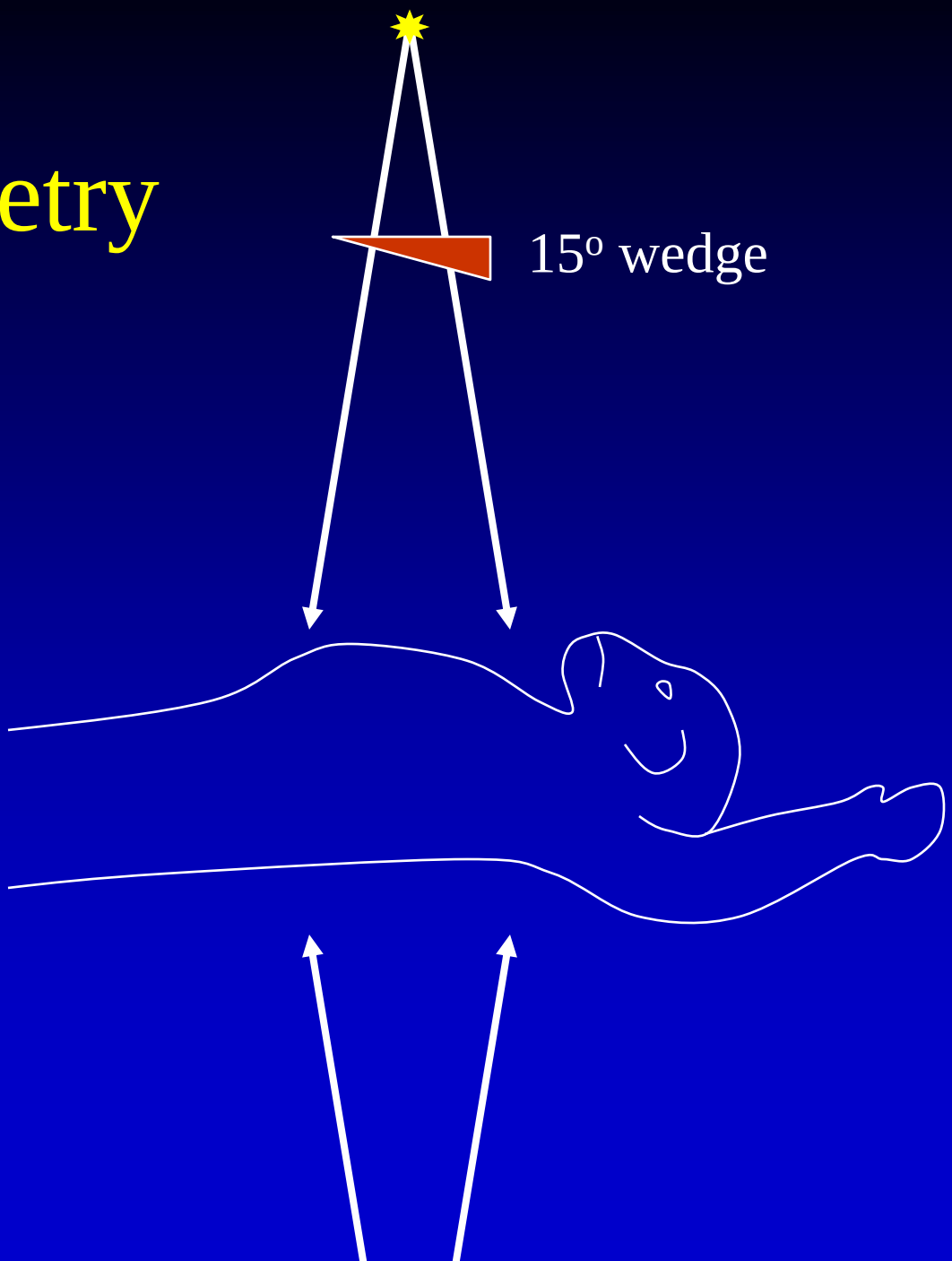
- 40 Gy whole brain delivered in 8 fxs
- NHP cognition model: rat → NHP → human
- Cognition being assessed monthly
- Pre-irradiation MR imaging
- Post-irradiation MR + PET imaging planned
- Teamwork greatly required and appreciated

Project 3: Total Lung Irradiation
10 Gy to mid-line

- 16 animals, matched by sex, weight
- Lung radioprotectant study
- Animal handling and irradiation logistics
  - After-hours irradiations
- Whole lung irradiation: 10 Gy, 6 MV x rays
  - 5 Gy AP; 5 Gy PA x 1 fx
  - No change to animal position
  - “Lung” estimated from CT scans
- Anesthesia and Universal Precautions

Irradiation Geometry

- AP-PA, 6 MV x rays
- 96 cm SSD
- FS: 10.0 x [5.0, 7.5] cm^2
- 1 cm bolus, AP field
- Table + post tissue, PA
- New non-ketamine anesthesia – great flexibility for positioning without rigidity



Status: Total Lung Irradiation

- Baseline, pre-irradiation, full-inflation CT scans
- 2-month post-irradiation, full-inflation CT scans
- Animals randomized to:
  - Total lung irradiation
  - Receipt of radioprotectant
- 1-year post-irradiation, full-inflation CT scans
- CT image-based assessment of lung injury

Challenges and Opportunities

- NHP data acquisition
  - Manual measurements of dimensions
  - Imaging: eg, “CT simulation”
- Immobilization needs to be addressed
- Dosimetric validation of experimental geometry
- Defined roles for animal handlers and operators
- Availability of resources
  - Imaging and irradiation devices
  - Planning tools
  - Irradiation delivery verification
- Physics and biology expertise - communication

Summary

- NHP irradiation techniques vary by study goal/design
- Irradiation personnel and animal handlers are key
- Irradiation techniques use “clinical” measurements
- Manual/computer monitor unit calculations – 2 methods
- RTP system with CT +/- MR imaging for anatomy and geometry assessment
- Advantages of clinical-grade equipment: reliability, standardized quality assurance, robust planning tools, positioning tools, geometrical and dosimetrical accuracy and precision, image-guided irradiation

Acknowledgements

- Wake Forest School of Medicine
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- Conference Organizers: NIAID, NIST, NCI